



Dose Recommendations for Anti-Cancer Drugs in Patients with Renal or Hepatic Impairment

The following reference is acknowledged as the primary source of information for dosing advice in patients receiving Systemic Anti-Cancer Therapy originally published in The Lancet Oncology.

Policy Owner: Directorate of Cancer Services (Cancer and Tertiary Services)
Approved by: SACT Service Improvement Group
Version: 1
Issue date: May 2024
Review date: May 2025

Document No: CID4892

THE LANCET Oncology

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed.
We post it as supplied by the authors.

Supplement to: Giraud EL, de Lijster B, Krens SD, Desar IME, Boerrigter E, van Erp NP.
Dose recommendations for anticancer drugs in patients with renal or hepatic
impairment: an update. *Lancet Oncol* 2023; **24**: e229.

Supplementary Figure 1: Search strategy used for PubMed

("Renal Insufficiency, Chronic"[MeSH] OR "Renal Insufficiency"[MeSH:noexp] OR "Renal Insufficiency"[ti] OR "Renal Impairment"[ti] OR "Renal Dysfunction"[ti] OR "impaired renal function"[ti] OR "renal function"[ti] OR "haemodialysis"[ti] OR "Hepatic insufficiency"[MeSH] OR "Liver failure"[MeSH] OR "hepatic insufficiency"[ti] OR "liver failure"[ti] OR "liver impairment"[ti] OR "hepatic dysfunction"[ti] OR "impaired liver function"[ti] OR "liver dysfunction"[ti] OR "impaired hepatic function"[ti] OR "hepatic impairment" [ti]) AND ("XX" [Supplementary Concept or MeSH] OR "XX"[Tiab])

XX indicates the anticancer drug to be evaluated with its corresponding MeSH term or Supplementary Concept

Supplementary Table 1: Dose recommendations for anticancer drugs in patients with renal or hepatic impairment

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
1	Abemaciclib	Abemaciclib is primarily metabolised in the liver to active metabolites (M2, M18 and M20) which contribute to the clinical effect. Abemaciclib and its metabolites are excreted in feces (81%), predominantly as metabolites. Approximately 3% is excreted in urine.	EMA/FDA: CLcr ≥ 30 ml/min: no dose adjustment CLcr < 30 ml/min: not studied HD: not studied	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	FDA: Child-Pugh A: 1.2 fold increase in AUC Child-Pugh B: 1.1-fold increase in AUC Child-Pugh C: 2.4-fold increase in AUC, reduce dose frequency to QD EMA: Child-Pugh A/B: no dose adjustment Child-Pugh C: decrease in dosing frequency to QD is advised	Child-Pugh A/B: no dose adjustment is needed Child-Pugh C: reduce dose frequency to QD	Verzenio label ¹ SPC Verzenio ²
2	Abiraterone	Abiraterone acetate is hydrolysed to abiraterone, which is then metabolised in the liver to metabolites which contribute to the clinical effect. Abiraterone and its metabolites are predominantly excreted in feces (81%) and to a lesser extent in urine (5%).	EMA/FDA: Renal impairment: no dose adjustment HD: dose after dialysis, no dose adjustment Marbury <i>et al.</i> ESRD requiring haemodialysis: AUC _{0-inf} : 65.0% (90% CI 34.3-123.2%)	Renal impairment: no dose adjustment is needed HD: no dose adjustment is needed	EMA/FDA: Child-Pugh A: no dose adjustment Child-Pugh B: 25% of the dose, 250 mg QD (FDA) / caution (EMA) Child-Pugh C: not recommended Marbury <i>et al.</i> Child-Pugh A: AUC _{0-inf} : 111% (90% CI 59.6-208.4%) Child-Pugh B: AUC _{0-inf} : 357% (90% CI 190.9-667.5%) Child-Pugh C with 16 fold dose reduction: AUC _{0-inf} : 43.6% (90% CI 18.4-103.5%)	Child-Pugh A: no dose adjustment is needed Child-Pugh B: 25% of the original dose Child-Pugh C: avoid	Zytiga label ¹ SPC Zytiga ² Marbury <i>et al.</i> ³
3	Acalabrutinib	Acalabrutinib is primarily metabolised by CYP3A enzymes. Its major metabolite, ACP-5862, is 50% less potent than acalabrutinib. Acalabrutinib is mainly excreted in feces (84%) and minorly in urine (14%, < 2% unchanged).	EMA/FDA: eGFR ≥ 30 ml/min/1.73m ² : no dose adjustment eGFR < 30 ml/min/1.73m ² : no data available HD: no data available	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no dose adjustment is expected HD: no need for dose adjustment is expected	EMA: Child-Pugh A/B or mild/moderate no dose adjustment Child-Pugh C or severe: not recommended FDA: Child-Pugh A and B: no dose adjustment Child-Pugh C: no data available	Child-Pugh A/B or mild/moderate: no dose adjustment is needed Child-Pugh C or severe: not recommended	Calquence label ¹ SPC Calquence ² Xu <i>et al.</i> ⁴

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
					<i>Xu et al.</i> Child-Pugh A: AUC_{0-inf}: 146·2% (90% CI 84·0-254·5%) Child-Pugh B: AUC_{0-inf}: 130·5% (90% CI 74·9-227·1%) Child-Pugh C: AUC_{0-inf}: 467·3% (90% CI 282·1-774·1%)		
4	Adagrasib	Adagrasib is metabolised primarily by CYP3A4 and inhibits its own CYP3A4 metabolism following multiple dosing to steady-state which permits CYP2C8, CYP1A2, CYP2B6, CYP2C9, and CYP2D6 to contribute to its metabolism at steady-state. 75% of the dose was recovered in feces (14% as unchanged) and 4·5% recovered in urine (2% as unchanged).	FDA: CLcr 15-90 mL/min: no clinically significant differences in the pharmacokinetics are expected. CLcr < 15 mL/min: not studied HD: not studied	GFR ≥ 15 mL/min: no need for dose adjustment is expected GFR < 15 mL/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	FDA: Child-Pugh classes A to C or mild to severe: no clinically significant differences in the pharmacokinetics are expected.	Child-Pugh A to C or mild to severe: no need for dose adjustment is expected. Monitor closely for liver toxicity	Adagrasib label ¹
5	Afatinib	Afatinib metabolism is minimal. Afatinib is predominantly excreted unchanged in feces (85%). Renal excretion is minimal (4%).	FDA: eGFR ≥ 30 mL/min/1·73m²: 40 mg QD eGFR 15-29 mL/min/1·73m²: 30 mg QD eGFR < 15 mL/min/1·73m²: not studied EMA: eGFR ≥ 15 mL/min/1·73m²: 40 mg QD eGFR < 15 mL/min/1·73m²: not recommended HD: not recommended Wiebe et al. eGFR 30-59 mL/min/1·73m²: AUC_{0-inf}: 122·4% (90% CI 96·1-155·9) eGFR 15-29 mL/min/1·73m²: AUC_{0-inf}: 150·1 (105·6-213·3) Imai et al. HD: 30 mg QD was tolerated and effective.	eGFR ≥ 15 mL/min: no dose adjustment is needed eGFR < 15 mL/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	EMA/FDA: Child-Pugh A/B: no dose adjustment Child-Pugh C: not studied Schnell et al. Child-Pugh A: AUC_{0-inf}: 92·6% (90% CI 68·0-126·3%) Child-Pugh B: AUC_{0-inf}: 94·9% (90% CI 72·3-124·5%) Child-Pugh C: not studied	Child-Pugh A/B: no dose adjustment is needed Child-Pugh C: no need for dose adjustment is expected	Gilotrif label¹ SPC Giotrif² Wiebe et al.⁵ Schnell et al.⁶ Imai et al.⁷

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
6	Aflibercept	Aflibercept is catabolised by proteolytic degradation to smaller peptides. No renal or hepatic clearance.	EMA/FDA: Renal impairment: no dose adjustment HD: not studied	Renal impairment: no dose adjustment is needed HD: no need for dose adjustment is expected	EMA/FDA: Mild and moderate: no dose adjustment Severe: not studied	Mild and moderate: no dose adjustment is needed Severe: no need for dose adjustment is expected	Zaltrap label ¹ SPC Zaltrap ²
7	Alectinib	Alectinib is metabolised in the liver. The major metabolite M4 contributes to the clinical effect. Alectinib and its metabolites are predominantly excreted in feces (98%). Excretion in urine is minimal (<1%).	EMA/FDA: CLCr ≥ 30 ml/min: no dose adjustment CLCr < 30 ml/min: not studied HD: not studied	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	EMA/FDA: Child-Pugh A/B: no dose adjustment Child-Pugh C: 75% of the original dose (450 mg BID) Morcos et al. Alectinib and M4 combined exposure: Child-Pugh A: not studied Child-Pugh B: AUC _{0-inf} : 136% (90% CI 94-196) Child-Pugh C: AUC _{0-inf} : 176% (90% CI 98-315)	Child-Pugh A/B: no dose adjustment is needed Child-Pugh C: 75% of the original dose (450 mg BID)	Alecensa label ¹ SPC Alecensa ² Morcos et al. ⁸
8	Alpelisib	Alpelisib is primarily metabolised by systemic (non-hepatic) amid hydrolysis in the pharmacological inactive metabolite BZG791, followed by a minor contribution of CYP3A4. Alpelisib and its metabolites are mainly excreted in feces (81%). Approximately 13-5% is excreted in urine (2% unchanged alpelisib).	EMA/FDA: CLCr ≥ 30 ml/min: no dose adjustment CLCr < 30 ml/min: not studied HD: not studied	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	EMA/FDA: Mild, moderate or severe or Child-Pugh A, B or C: no dose adjustment	Hepatic impairment: no dose adjustment is needed.	Piqray label ¹ SPC Piqray ²
9	Amivantamab	Amivantanab is catabolised by proteolytic degradation to smaller peptides. No renal or hepatic clearance.	EMA: CLCr ≥ 30 ml/min: no clinically meaningful effect on PK CLCr < 30 ml/min: not studied FDA: CLCr ≥ 30 ml/min: no clinically meaningful differences in PK CLCr < 30 ml/min: not studied	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	EMA/FDA: Mild: no clinically meaningful effect in PK Moderate and severe: no data available	Mild: no dose adjustment is needed. Moderate and severe: no need for dose adjustment is expected.	Rybrevant label ¹ SPC Rybrevant ²
10	Amsacrine	Amsacrine is extensively metabolised in the liver to inactive metabolites. Amsacrine and its metabolites are predominantly excreted in	MHRA: Renal impairment: 70-80% of the original dose (60-75mg/m ²) HD: not studied	GFR < 60 ml/min: 70-80% of the original dose HD: 70-80% of the original dose may be considered	MHRA: Hepatic impairment: 70-80% of the original dose (60-75mg/m ²)	Mild and moderate: 70-80% of the original dose Severe: not recommended.	SPC Amsidine ⁹

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
		feces (bile) and to a lesser extent in urine (42%).					
11	Anastrozole	Anastrozole is metabolised in the liver. Anastrozole and its metabolites are mainly excreted in urine (10% unchanged) and to a lesser extent in feces.	FDA/MHRA: CLcr 30-60 ml/min: no dose adjustment CLcr < 30 ml/min: total clearance was reduced by 10%, no dose adjustment needed Langenegger et al. HD: normal dose resulted in therapeutic exposure	Renal impairment: no dose adjustment is needed HD: no dose adjustment is needed	FDA: Mild and moderate: no dose adjustment Severe: not studied MHRA: Mild: no dose adjustment Moderate and severe: not studied	Mild and moderate: no dose adjustment is needed. Severe: not recommended.	Arimidex label ¹ SPC Arimidex ⁹ Langenegger et al. ¹⁰
12	Apalutamide	Apalutamide is metabolised in the liver. The major metabolite N-desmethyl apalutamide contributes to the clinical effect. Apalutamide and its metabolites are predominantly excreted in urine (65%) and to a lesser extent in feces (24%)	EMA/FDA: eGFR ≥ 30 ml/min/1.73m ² : no dose adjustment eGFR < 30 ml/min/1.73m ² : not studied HD: not studied	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	EMA/FDA: Child-Pugh A/B: no dose adjustment Child-Pugh C: not studied	Child-Pugh A/B: No dose adjustment is needed. Child-Pugh C: no need for dose adjustment is expected.	Erleada label ¹ SPC Erleada ²
13	Arsenic trioxide	Arsenic trioxide hydrolyses to the active arsenious acid (AS ^{III}). Arsenious acid is metabolised to arsenic acid and pentavalent metabolites, primarily in the liver. Arsenic trioxide and its metabolites are excreted in urine (15% unchanged).	EMA/FDA: CLcr ≥ 30 ml/min: no dose adjustment is needed CLcr < 30 ml/min: dose reduction may be warranted HD: not studied Firkin et al. A 50% dose decrease in two patients with eGFRs of 18-19 ml/min/1.73m ² and a dose adjustment to 10 mg three times weekly in one patient receiving HD, resulted in whole-blood arsenic levels comparable to normal renal function. Sweeney et al. CLcr ≤ 30 ml/min: mean AUC _{0-t} of AS ^{III} 40% higher compared to patients with normal renal function after multiple doses.	GFR ≥ 30 ml/min: no need for dose adjustment is expected GFR < 30 ml/min: consider 50% of the original dose HD: consider 10 mg three times weekly post-dialysis	FDA: Child-Pugh A/B: no dose adjustment is needed Child-Pugh C: AUC _{0-24h} increased by 40% compared to normal hepatic function. EMA: Mild and moderate: no accumulation of arsenious acid and arsenic acid was observed following twice weekly infusion. Severe: limited information	Child-Pugh A/B: no need for dose adjustment is needed. Use with caution due to risk of hepatotoxicity Child-Pugh C: consider 50% of the original dose.	Trisenox label ¹ SPC Trisenox ² Firkin et al. ¹¹ Sweeney et al. ¹² Perrault et al. ¹³

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
			Perrault <i>et al.</i> HD: dialysed (approximately 38% removed). Arsenic trioxide 10 mg three times weekly post-dialysis was safe and effective.				
14	Asciminib	Asciminib is metabolised by CYP3A4, UGT2B7 and UGT2B17. Asciminib is mainly excreted in feces (80%, 56% unchanged) and to a lesser extent in urine (11%).	EMA: CLcr ≥ 15 ml/min: no dose adjustment HD: not studied FDA: eGFR ≥ 15 ml/min/1.73m ² : no dose adjustment HD: not studied Hoch <i>et al.</i> Higher exposure in patients with severe renal impairment compared with healthy controls (49-56% higher AUC). The increase in AUC was below the threshold for clinical relevance	GFR ≥ 15 ml/min: no dose adjustment is needed GFR < 15 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	EMA: Hepatic impairment: no dose adjustment FDA: Mild to severe hepatic impairment: no dose adjustment Hoch <i>et al.</i> Higher exposure of unbound asciminib in patients with mild (14-15%) and severe (44-51%) hepatic impairment compared with healthy subjects. The increase in AUC was below the threshold for clinical relevance.	Hepatic impairment: no dose adjustment is needed	Scemblix label ¹ SPC Scemblix ² Hoch <i>et al.</i> ¹⁴
15	Asparaginase	Asparaginase is thought to be degraded within the reticulo- histiocytic system and by serum proteases. No renal clearance.	EMA: Renal impairment: no dose adjustment HD: not studied	Renal impairment: no dose adjustment is needed HD: no need for dose adjustment is expected	EMA: Mild and moderate: no dose adjustment Severe: contraindicated	Mild and moderate: no dose adjustment is needed Severe: not recommended due to hepatotoxicity	SPC Spectrila ²
16	Atezolizumab	Atezolizumab is catabolised by proteolytic degradation to smaller peptides. No renal or hepatic clearance.	EMA/FDA: eGFR ≥ 30 ml/min/1.73m ² : no dose adjustment eGFR < 30 ml/min/1.73m ² : not studied HD: not studied	eGFR ≥ 30 ml/min: no dose adjustment is needed eGFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	EMA/FDA: Mild: no dose adjustment Moderate and severe: not studied	Mild: no dose adjustment is needed Moderate and severe: no need for dose adjustment is expected	Tecentriq label ¹ SPC Tecentriq ²
17	Avapritinib	Avapritinib is primarily metabolised by CYP3A4 and to a lesser extent by CYP2C9. Avapritinib is mainly excreted in feces (70%; 11% unchanged) and minorly in urine (18%; 0.23% unchanged)	EMA/FDA: CLcr ≥ 30 ml/min: no dose adjustment CLcr < 30 ml/min: no data available HD: no data available	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	EMA: Mild and moderate: no dose adjustment Severe and Child-Pugh C: not studied FDA: Mild and moderate: no dose adjustment	Mild and moderate: no dose adjustment is needed Severe: not recommended	Ayvakit label ¹ SPC Ayvakyt ²

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
					Severe: not studied		
18	Avelumab	Avelumab is catabolised by proteolytic degradation to smaller peptides. No renal or hepatic clearance.	EMA: CLcr $\geq$ 30 ml/min: no dose adjustment CLcr < 30 ml/min: not studied FDA: CLcr $\geq$ 15 ml/min: no dose adjustment	GFR $\geq$ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	EMA/FDA: Mild: no dose adjustment Moderate and severe: not studied	Mild: no dose adjustment is needed Moderate and severe: no need for dose adjustment is expected	Bavencio label ¹ SPC Bavencio ²
19	Axitinib	Axitinib is metabolised in the liver Axitinib and its metabolites are excreted in feces (60%) and to a lesser extent in urine (23%).	EMA/FDA: CLcr $\geq$ 15 ml/min: no dose adjustment CLcr < 15 ml/min: caution when used Thiery-Vuillemin <i>et al.</i> HD: axitinib is not dialysed	Renal impairment: no dose adjustment is needed HD: no need for dose adjustment is expected	EMA/FDA: Child-Pugh A: no dose adjustment Child-Pugh B: approximately 50% of the original dose Child-Pugh C: not studied Tortorici <i>et al.</i> Child-Pugh A: AUC _{0-inf} 78-34%(90% CI 39-92-153 ·75) Child-Pugh B: AUC _{0-inf} 195 ·25% (90% CI 99-49-383 ·18)	Child-Pugh A: no dose adjustment is needed Child-Pugh B: 50% of the original dose Child-Pugh C: not recommended	Inlyta label ¹ SPC Inlyta ² Thiery-Vuillemin <i>et al.</i> ¹⁵ Tortorici <i>et al.</i> ¹⁶
20	Azacitidine	Azacitidine is hydrolysed and deaminated by cytidine deaminase. Azacitidine and its metabolites are predominantly excreted in urine (50-85%) with less than 1% excreted in feces.	EMA/FDA: Renal impairment: no initial dose adjustment is needed Laille <i>et al.</i> CLcr < 30 ml/min/1.73m ² : AUC _{0-inf} : 141·2% (90% CI 92·2-216 ·2%) Ham <i>et al.</i> HD: no initial dose adjustment is needed	Renal impairment: no dose adjustment is needed HD: no dose adjustment is needed	EMA/FDA: Hepatic impairment: not studied Contraindicated: albumin <30 g/L, advanced malignant hepatic tumours	Mild or moderate: no need for dose adjustment is expected If albumin <30 g/L/or advanced malignant hepatic tumours: not recommended	Vidaza label ¹ SPC Vidaza ² Laille <i>et al.</i> ¹⁷ Ham <i>et al.</i> ¹⁸
21	Belantamab mafodotin	Belantamab mafodotin is expected to undergo catabolism to small peptides, amino acids and unconjugated cys-mcMMAF. Cys-mcMMAF has limited metabolic clearance. In animal studies, belantamab mafodotin was excreted in feces (87%) and minorly in urine (13%, no metabolites were found).	EMA/FDA: eGFR $\geq$ 30 ml/min/1.73m ² : no dose adjustment is needed eGFR < 30 ml/min/1.73m ² : not studied HD: not studied	eGFR $\geq$ 30 ml/min: no dose adjustment is needed. eGFR < 30 ml/min: No need for dose adjustment is expected HD: No need for dose adjustment is expected	EMA/FDA: Mild: no dose adjustment needed Moderate and severe: no data available	Mild: no dose adjustment is needed. Moderate and severe: No data available and therefore not recommended yet.	Blenrep label ¹ SPC Blenrep ²

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
22	Belinostat	Belinostat is metabolised in the liver. Belinostat and its metabolites are predominantly excreted in urine (84·8%, 1·7% unchanged) and to a lesser extent in feces (9·7%).	FDA: CLcr > 39 ml/min: No dose adjustment is needed CLcr ≤ 39 ml/min: not studied HD: not studied	GFR > 39 ml/min: no dose adjustment is needed GFR ≤ 39 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	FDA: Mild: no dose adjustment is needed Moderate and severe: not studied	Mild: no dose adjustment is needed Moderate and severe: not recommended	Beleodaq label ¹
23	Belzutifan	Belzutifan is primarily metabolised by UGT2B17 and CYP2C19 and to a lesser extent by CYP3A to less active metabolites. Routes of elimination have not been identified. Mass-balance study is ongoing.	FDA: eGFR ≥ 30 ml/min/1·73m ² : no dose adjustment is needed eGFR < 30 ml/min/1·73m ² : not studied HD: not studied	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: not recommended HD: not recommended	FDA: Mild: no dose adjustment is needed Moderate and severe: not studied	Mild: no dose adjustment is needed Moderate and severe: not recommended	Welireg label ¹
24	Bendamustine	Bendamustine is cleared by hydrolysis and is metabolised in the liver. Bendamustine and its metabolites are predominantly excreted in urine and to a lesser extent in feces.	FDA: CLcr 30-80 ml/min: no dose adjustment is needed CLcr < 30 ml/min: not studied, contraindicated MHRA: CLcr > 10 ml/min: no dose adjustment is needed CLcr ≤ 10 ml/min: limited data available HD: no dose adjustment is needed	Renal impairment: no dose adjustment is needed HD: no dose adjustment is needed	FDA: Mild: no dose adjustment is needed Moderate and severe: not studied, contraindicated MHRA: Mild (bilirubin <20 µmol/L): no dose adjustment is needed Moderate (bilirubin 20 -51 µmol/L): 70% of the original dose Severe (bilirubin > 51 µmol/L): not studied, contraindicated	Mild (bilirubin <20 µmol/L): no dose adjustment is needed Moderate (bilirubin 20 -51 µmol/L): 70% of the original dose Severe (bilirubin > 51 µmol/L): not recommended	Treanda label ¹ SPC Levact ⁹
25	Bevacizumab	Bevacizumab is catabolised by proteolytic degradation to smaller peptides. No renal or hepatic clearance.	EMA/FDA: Not studied in patients with renal impairment. Ganier-Viougeat <i>et al.</i> HD: 50% of the dose resulted in dose proportional AUC reduction, bevacizumab is not dialysed	Renal impairment: no need for dose adjustment is expected HD: no need for dose adjustment is expected	EMA/FDA: Not studied in patients with hepatic impairment	Hepatic impairment: no need for dose adjustment is expected	Avastin label ¹ SPC Avastin ² Garnier-Viougeat <i>et al.</i> ¹⁹
26	Bicalutamide	The R-enantiomer of bicalutamide has antiandrogenic activity. Bicalutamide is extensively metabolised in the liver. Excretion is both hepatic and renal.	EMA/FDA: No dose adjustment is needed for patients with renal impairment Ito <i>et al.</i> HD: plasma concentration is	Renal impairment: no dose adjustment is needed HD: no dose adjustment is needed	EMA/FDA: No dose adjustment is necessary for patients with hepatic impairment. Half-life may be prolonged in patients with severe hepatic	Hepatic impairment: no dose adjustment is needed	Casodex label ¹ SPC Casodex ⁸ Ito <i>et al.</i> ²⁰

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
			unaffected by haemodialysis.		impairment.		
27	Binimetinib	Binimetinib is metabolised in the liver. The active metabolite M3 contributes to the clinical effect. Binimetinib and its metabolites are predominantly excreted in feces (62%, 32% unchanged) and to a lesser extent in urine (31%, 6-5% unchanged)	FDA: eGFR $\leq$ 29 ml/min/1.73m ² : no important changes in binimetinib exposure HD: not studied, unlikely to be dialysed EMA: eGFR $\leq$ 29 ml/min/1.73m ² : no dose adjustment	Renal impairment: no dose adjustment is needed HD: no need for dose adjustment is expected	FDA: Mild: no dose adjustment Moderate and severe: 67% of original dose EMA: Child-Pugh A: no dose adjustment Child-Pugh B/C: not recommended, as encorafenib is also not recommended	Mild: no dose adjustment is needed Moderate and severe: 67% of the original dose (30mg BID)	Mektovi label ¹ SPC Mektovi ²
28	Bleomycin	Bleomycin is widely distributed to normal tissues and inactivated by bleomycin hydrolases. Bleomycin is excreted in urine (approximately 67% unchanged).	MHRA: GFR > 50 ml/min: no dose adjustment GFR 10-50 ml/min: 75% of the original dose GFR < 10 ml/min: 50% of the original dose Crooke et al. HD: bleomycin is not dialysed	GFR > 50 ml/min: no dose adjustment is needed GFR 10-50 ml/min: 75% of the original dose GFR < 10 ml/min: 50% of the original dose HD: 50% of the original dose may be considered	MHRA: Not studied in patients with hepatic impairment	Hepatic impairment: no need for dose adjustment is expected	SPC Bleomycin ⁹ Crooke et al. ²¹
29	Blinatumomab	Blinatumomab is catabolised by proteolytic degradation to smaller peptides. No renal or hepatic clearance.	EMA/FDA: CLcr $\geq$ 30 ml/min: values within the range observed in normal renal function. CLcr < 30 ml/min: not studied HD: not studied	GFR $\geq$ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	EMA/FDA: Not studied in patients with hepatic impairment Zhu et al. No association between blinatumomab clearance and baseline ALT or AST levels	Hepatic impairment: no need for dose adjustment is expected	Blinicyto label ¹ SPC Blincyto ² Zhu et al. 2016 ²²
30	Bortezomib	Bortezomib is metabolised in the liver. The elimination of bortezomib and its metabolites is unknown, but is believed to be hepatically.	EMA: CLcr $\geq$ 20 ml/min/1.73 m ² : no dose adjustment CLcr < 20 ml/min/1.73 m ² : not studied HD: no dose adjustment, administer after dialysis FDA: Renal impairment: no dose adjustment HD: no dose adjustment, administer after dialysis	Renal impairment: no dose adjustment is needed HD: no dose adjustment is needed, administer after haemodialysis	EMA/FDA: Mild: no dose adjustment Moderate and severe: 54% of the original dose (0.7 mg/m ²) LoRusso et al. Mild: AUC _{0-last} 90-2% (90% CI 66.2-122.8) Moderate: AUC _{0-last} 146.8% (90% CI 104.7-205.7) Severe: AUC _{0-last} 158.1% (90% CI 116.8-214.0)	Mild: no dose adjustment Moderate and severe: 54% of the original dose (0.7 mg/m ²)	Velcade label ¹ SPC Velcade ² LoRusso et al. ²³ Leal et al. ²⁴

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
			Leal <i>et al.</i> Bortezomib pharmacokinetics are not influenced by CLcr				
31	Bosutinib	Bosutinib is metabolised in the liver (CYP3A4). Bosutinib and its metabolites are predominantly excreted in feces (91.3%) with minimal amounts in urine (3.3%)	EMA/FDA: CLcr 51-80 ml/min: no dose adjustment is needed CLcr 30-50 ml/min: 300 mg QD (newly diagnosed) 400 mg QD (pretreated) CLcr < 30 ml/min: 200mg QD (newly diagnosed) 300 mg QD (pretreated) HD: not studied Abbas <i>et al.</i> CLcr 30-50 ml/min: AUC 135.02% (90 % CI 98.53–185.01) CLcr < 30 ml/min: AUC 159.76 % (90 % CI 115.52–220.92)	GFR > 50 ml/min: no dose adjustment is needed GFR < 50 ml/min: 75% of the original dose HD: 75% of the original dose may be considered	EMA/FDA: Child-Pugh A, B and C: 200 mg QD Abbas <i>et al.</i> Child-Pugh A: AUC 225% (90% CI 160-315) Child-Pugh B: AUC 200% (90% CI 143-281) Child-Pugh C: AUC 191% (90% CI 137-268)	Child-Pugh A, B and C: 50% of the original dose (200mg QD)	Bosulif label ¹ SPC Bosulif ² Abbas <i>et al.</i> ²⁵ Abbas <i>et al.</i> ²⁶
32	Brentuximab vedotin	The anti-CD30 antibody is catabolised by proteolytic degradation to smaller peptides. No renal or hepatic clearance. Only a small fraction of Monomethyl auristatin E (MMAE) is metabolised by CYP3A4/5. Brentuximab vedotin is predominantly excreted unchanged in feces, and to a lesser extent in urine.	FDA: CLcr 50-80 ml/min: no dose adjustment CLcr 30-50 ml/min: no dose adjustment CLcr < 30 ml/min: not recommended HD: not studied EMA: CLcr < 30 ml/min: approximately 67% (1.2 mg/kg) Zhao <i>et al.</i> CLcr 51-80 ml/min: MMAE AUC _{0-inf} 0.85 (90% CI 0.39-1.84) CLcr 30-50ml/min: MMAE AUC _{0-inf} 1.09 (90% CI 0.49-2.42) CLcr < 30 ml/min: MMAE AUC _{0-inf} 1.90 (90% CI 0.85-4.21)	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: 67% of the original dose HD: 67% of the original dose	FDA: Child-Pugh A: 67 or 75% of the original dose (0.9 or 1.2 mg/kg) Child-Pugh B and C: not recommended EMA: Child-Pugh A/B/C: 67% of the original dose (1.2mg/kg) Zhao <i>et al.</i> Child-Pugh B: MMAE AUC _{0-inf} : 2.21 (90% CI 1.11-4.44)	Child-Pugh A: 67% of the original dose Child-Pugh B and C: not recommended	Adcetris label ¹ SPC Adcentris ² Zhao <i>et al.</i> ²⁷

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
33	Brigatinib	Brigatinib is metabolised in the liver. Brigatinib and its metabolites are excreted in feces (65%, 41% unchanged) and to a lesser extent in urine (25%, 86% unchanged).	FDA: CLcr $\geq$ 30 ml/min: no dose adjustment CLcr 15-29 ml/min or HD: reduce the dose by approximately 50% EMA: eGFR $\geq$ 30 ml/min: no dose adjustment eGFR < 30 ml/min: reduced starting dose of 60 mg QD for the first 7 days, then 90 mg QD Gupta et al. Renal clearance of patients with severe renal impairment was ~20% of that observed in volunteers with normal renal function. Reduce dose with 50% in these patients.	GFR 30-90 ml/min: no dose adjustment is needed GFR < 30 ml/min: 50% of the original dose may be considered HD: 50% of the original dose may be considered	FDA: Child-Pugh A/B: no dose adjustment Child-Pugh C: reduce the QD dose by approx. 40% EMA: Mild and moderate: no dose adjustment Severe: reduced starting dose of 60 mg QD for the first 7 days, then 120 mg QD	Child-Pugh A/B: no dose adjustment is needed Child-Pugh C: approximately 60% of the original dose may be considered	Alunbrig label¹ SPC Alunbrig² Gupta et al.²⁸
34	Busulfan	Busulfan is mainly metabolised in the liver. Approximately 30% (1-2% unchanged) of busulfan is excreted in urine with negligible amounts in feces.	EMA/FDA: Not studied in patients with renal impairment Masauzi et al. Busulfan clearance comparable to normal patients on non-HD day, accelerated clearance on HD day.	Renal impairment: no dose adjustment is needed, dosing is based on busulfan plasma levels HD: no initial dose adjustment is needed, dose according to busulfan plasma levels	EMA/FDA: Not studied in patients with hepatic impairment	Mild and moderate: no need for dose adjustment is expected. Severe: not recommended	Busulfex label¹ SPC Busulfan Fresenius Kabi² Masauzi et al.²⁹
35	Cabazitaxel	Cabazitaxel is extensively metabolised in the liver. Metabolites are predominantly hepatically excreted (76%) and to a lesser extent renally (3.7%)	EMA/FDA: CLcr 15-80 ml/min: no dose adjustment CLcr < 15 ml/min: not studied HD: not studied Azaro et al. eGFR 30-49 ml/min/1.73m² and eGFR < 30 ml/min/1.73m²: no change in AUC compared to normal renal function.	GFR $\geq$ 15 ml/min: no dose adjustment is needed GFR < 15 ml/min or HD: no need for dose adjustment is expected	EMA/FDA: Mild: 20 mg/m² Moderate: 15 mg/m² Severe: not recommended Sarantopoulos et al. Minimal impact of hepatic impairment on cabazitaxel PK parameters. Recommended dosages based on safety data are 20 and 15mg/m² for patients with mild and moderate hepatic	Mild: 20 mg/m² Moderate: 15 mg/m² Severe: not recommended	Jevtana label¹ SPC Jevtana² Azaro et al.³⁰ Sarantopoulos et al.³¹

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
					impairment respectively		
36	Cabozantinib	Cabozantinib is metabolised in the liver by CYP3A4 and is predominantly excreted in feces (54%, 43% unchanged) and to a lesser extent in urine 27% (only metabolites).	EMA/FDA: CLcr 30-80 ml/min: no dose adjustment CLcr < 30 ml/min: not studied. HD: not studied Nguyen <i>et al.</i> eGFR ≥ 60 ml/min/1.73m ² : AUC _{0-inf} 130·1% (90% CI 98·9-171·3) eGFR 30-59 ml/min/1.73m ² : AUC _{0-inf} 105·6% (90% CI 79·6-140·1)	GFR 30-80 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	FDA: Mild: no dose adjustment Moderate or Child-Pugh B: 66% of the original dose (40 mg QD) Severe: not studied EMA: Mild: no dose adjustment Moderate or Child-Pugh B: insufficient data, not recommended Severe: not studied and therefore not recommended Nguyen <i>et al.</i> Child-Pugh A: AUC _{0-inf} 181·2% (90% CI 121·4-270·3) Child-Pugh B: AUC _{0-inf} 162·7% (90% CI 107·4-246·7)	Child-Pugh A/B or mild and moderate: consider a starting dose 66% of the original dose, increase if tolerated Child-Pugh C or severe: not recommended	SPC/label Cabometyx ^{1,2} SPC/label Cometriq ^{1,2} Nguyen <i>et al.</i> ³²
37	Capecitabine	Capecitabine (prodrug) is enzymatically converted to 5- fluorouracil (5-FU). 5-FU is converted intracellularly to inactive metabolites by dihydropyrimidine dehydrogenase (DPD). Capecitabine and its metabolites are predominantly excreted renally (95·5%) and to a lesser extent hepatically (2·6%).	EMA/FDA: CLcr: 51-80 ml/min: no dose adjustment CLcr 30-50 ml/min: 75% of the original dose CLcr < 30 ml/min: not recommended HD: not studied Poole <i>et al.</i> No effect of renal impairment on the systemic exposure of capecitabine or 5-FU. Based on safety data: CLcr 30-50 ml/min 75% of original dose CLcr < 30 ml/min: not recommended.	GFR 51-80 ml/min: no dose adjustment is needed GFR 30-50 ml/min: 75% of the original dose GFR < 30 ml/min: not recommended HD: not recommended	EMA/FDA: Mild and moderate due to liver metastases: AUC and C _{max} of capecitabine increased by 60%, AUC of 5-FU was unaffected. severe: not studied Joerger <i>et al.</i> Normal – severe: no dose adjustment is needed, although hepatic impairment was associated with low clearance of capecitabine. Twelves <i>et al.</i> No statistically significant increase in capecitabine or 5-FU AUC _{0-inf} in patients with mild – moderate hepatic impairment due to liver metastases (WHO based grading system).	Hepatic impairment: no dose adjustment is needed	Xeloda label ¹ SPC Xeloda ² Poole <i>et al.</i> ³³ Joerger <i>et al.</i> ³⁴ Twelves <i>et al.</i> ³⁵
38	Capmatinib	Capmatinib is primarily metabolised by CYP3A4 and aldehyde oxidase.	EMA: CLcr ≥ 30 ml/min: no dose adjustment	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need	EMA/FDA: Child-Pugh A to C and mild to severe: no dose adjustment	Hepatic impairment: no dose adjustment is needed	Tabrecta label ¹ SPC Tabrecta ² Chen <i>et al.</i> ³⁶

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
		Capmatinib is mainly excreted in feces (78%, 42% unchanged) and to a lesser extent in urine (22%, unchanged negligible).	CLcr < 30 ml/min: no data available FDA: CLcr ≥ 30 ml/min: no dose adjustment CLcr < 30 ml/min: no data available	for dose adjustment is expected HD: no need for dose adjustment is expected	Chen et al. Mild, moderate and Child-Pugh A-C: no dose adjustment Mild: AUC _{0-inf} 0.767 (90% CI 0.532-1.11) Moderate: AUC _{0-inf} 0.914 (90% CI 0.652-1.28) Severe: AUC _{0-inf} 1.24 (90% CI 0.858-1.78)		
39	Carboplatin	Carboplatin is not metabolised. It is highly protein-bound (87%) and is primarily excreted in urine	MHRA: Dose according to Calverts formula: dose [mg] = target AUC * (GFR +25) Watanabe et al. HD: carboplatin dose was calculated with GFR equals 0 according to Calverts formula for a target AUC of 5 µg*min/ml. HD was performed 16-hours after start and resulted in free platinum AUC of 4.43 µg* min/ml.	Renal impairment: dose calculation based on renal function according to Calverts formula HD: dose according to Calvert formula with GFR equals 0. Perform HD between 12 and 24 hours after administration.	MHRA: Not studied in patients with hepatic impairment	Hepatic impairment: No need for dose adjustment is expected	SPC Carboplatin ⁹ Calvert et al. ³⁷ Watanabe et al. ³⁸
40	Carfilzomib	Carfilzomib is rapidly metabolised into inactive metabolites by peptidase cleavage and epoxide hydrolysis. Carfilzomib is mainly cleared extrahepatically, approximately 25% is excreted in urine as metabolites.	EMA/FDA: Renal impairment: no dose adjustment is needed HD: no dose adjustment is needed, dose after dialysis Badros et al. No difference in carfilzomib AUC _{0-inf} and CL in patients with renal impairment (CLcr 15-80 ml/min) or HD. Quach et al. HD: AUC _{0-inf} 138.1% (90% CI 102.8-185.5)	Renal impairment: no dose adjustment is needed HD: no dose adjustment is needed	EMA/FDA: Mild and moderate: 75% of the original dose Severe: not studied Brown et al. 27 mg/m ² Mild: AUC _{0-inf} 151-84% (90% CI 113.59-202.96) Moderate: AUC _{0-inf} 143-53% (90% CI 103.28-199.45) 56 mg/m ² Mild: AUC _{0-inf} 181-90% (90% CI 96.4-343.24) Moderate: AUC _{0-inf} 152-59% (90% CI 74.87-310.96)	Mild and moderate: 75% of the original dose. Severe: not recommended	Kyprolis label ¹ SPC Kyprolis ² Badros et al. ³⁹ Quach et al. ⁴⁰ Brown et al. ⁴¹
41	Carmustine	Carmustine is metabolised in the liver. Carmustine and its metabolites are mainly excreted in urine (60-70%) and approximately 10% is excreted as respiratory CO ₂ .	FDA: Do not administer to patients with compromised renal function EMA:	GFR 46-60 ml/min: 80% of the original dose GFR 31-45 ml/min: 75% of the original dose GFR < 30 ml/min: not recommended HD: not	EMA/FDA: Hepatic impairment: no advise given	Mild and moderate: no need for dose adjustment is expected Severe: not recommended	Bicnu label ¹ SPC Carmustine Obvius ² Kintzel et al. ⁴²

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
			Reduce dose if GFR is reduced, CLcr < 10 ml/min: contra-indicated Kintzel <i>et al.</i> CLcr 60 ml/min: 80% CLcr 45 ml/min: 75% CLcr < 30 ml/min: not recommended HD: not studied	recommended			
42	Cemiplimab	Cemiplimab is catabolised by proteolytic degradation to smaller peptides. No renal or hepatic clearance	EMA/FDA: CLcr ≥ 30 ml/min: no dose adjustment CLcr < 30 ml/min: no dose adjustment	Renal impairment: no need for dose adjustment is expected HD: no need for dose adjustment is expected	EMA/FDA: Mild: no dose adjustment Moderate and severe: not studied	Mild: no dose adjustment is needed Moderate and severe: no need for dose adjustment is expected	Libtayo label ¹ SPC Libtayo ²
43	Ceritinib	Ceritinib is metabolised in the liver. Excretion of ceritinib and its metabolites is predominantly in feces (92%, 68% unchanged) with minimal excretion in urine (1-3%)	EMA/FDA: CLcr ≥ 30 ml/min: no dose adjustment CLcr < 30 ml/min: not studied HD: not studied	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	EMA/FDA: Child-Pugh A: no dose adjustment (18% increase in AUC _{0-inf}) Child-Pugh B: no dose adjustment (2% increase in AUC _{0-inf}) Child-Pugh C: 67% of the original dose (66% increase in AUC _{0-inf})	Child-Pugh A/B: no dose adjustment is needed Child-Pugh C: 67% of original dose	Zykadia label ¹ SPC Zykadia ²
44	Cetuximab	Cetuximab is catabolised by proteolytic degradation to smaller peptides. No renal or hepatic clearance.	EMA/FDA: Not studied in patients with renal impairment Inauen <i>et al.</i> HD: not dialysed, no dose adjustment needed	Renal impairment: no need for dose adjustment is expected HD: no need for dose adjustment is expected	EMA/FDA: Not studied in patients with hepatic impairment	Hepatic impairment: no need for dose adjustment is expected	Erbix label ¹ SPC Erbitux ² Inauen <i>et al.</i> ⁴³
45	Chlorambucil	Chlorambucil is extensively metabolised in the liver, forming the active metabolite phenylacetic acid mustard (PAAM). Excretion of chlorambucil and PAAM in urine is <1%.	EMA/FDA: Renal impairment: no dose adjustment is needed HD: not dialysable, no dose adjustment needed (FDA)	Renal impairment: no dose adjustment is needed HD: no need for dose adjustment is expected	EMA/FDA: Not studied in patients with hepatic impairment; consider dose reduction in severe hepatic impairment.	Mild and moderate: no need for dose adjustment is expected Severe: not recommended	Leukeran label ¹ SPC Leukeran ²
46	Chlormethine	Chlormethine is rapidly metabolised after administration. Its metabolites are mainly excreted in urine.	FDA: Renal impairment/HD: no advise given	Renal impairment: no need for dose adjustment is expected HD: no need for dose adjustment is expected	FDA: Hepatic impairment: no advise given	Mild: no need for dose adjustment is expected Moderate and severe: not recommended	Mustargen label ¹
47	Cisplatin	Cisplatin is not metabolised. It is highly	FDA: CLcr < 60 ml/min:	Curative GFR 50-59 ml/min: 75% of	FDA/MHRA: No advise given	Hepatic impairment: no need for dose	Cisplatin label ¹ SPC Cisplatin ⁹

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
		protein bound (90%) and is excreted predominantly in urine and to a minimal extent in feces.	contraindicated MHRA: Dose should be reduced adequately Watanabe <i>et al.</i> HD: Dialysed. Dose escalation from 50% to full dose (80 mg/m²) was tolerated in patients receiving HD started 10 minutes after completion of cisplatin administration. Platinum PK parameters were comparable to patients with normal renal function. After multiple administration a tendency for decreased total platinum clearance and prolonged hematological toxicity was observed. Kintzel <i>et al.</i> GFR 60 ml/min: 75% of the original dose GFR 45 ml/min: 50% of the original dose GFR 30 ml/min: not recommended	the original dose GFR 40-49 ml/min: 50% of the original dose GFR < 40 ml/min: not recommended HD: 50% of the original dose may be considered Palliative GFR 50-59 ml/min: 75% of the original dose GFR < 50 ml/min: not recommended HD: not recommended, consider carboplatin		adjustment is expected	Watanabe <i>et al.</i> ⁴⁴ Kintzel <i>et al.</i> ⁴²
48	Cladribine	The prodrug cladribine is metabolised intracellularly to its active metabolite. Cladribine is mainly excreted in urine (15-18% unchanged).	EMA: CLcr ≤ 50 ml/min: not studied, contraindicated Crews <i>et al.</i> Half-life increased approximately 2-fold in a child on CVVH/HD	GFR ≤ 50 ml/min: not recommended HD: not recommended	EMA: Mild: not studied, no dose adjustment Moderate and severe (Child-Pugh B or C): not recommended	Mild: no need for dose adjustment is expected Moderate and severe or Child-Pugh B/C: not recommended	SPC Litak ² Crews <i>et al.</i> ⁴⁵
49	Clofarabine	The prodrug clofarabine is metabolised intercellularly to its active metabolite. Clofarabine is mainly excreted in urine (60% unchanged).	EMA/FDA: CLcr 30-59 ml/min: 50% of the original dose CLcr <30 ml/min: not studied HD: not studied Benitez <i>et al.</i> HD: clofarabine was not effectively dialysed during	GFR 30-59 ml/min: 50% of the dose GFR <30 ml/min: not recommended HD: not recommended	FDA: Not studied in patients with hepatic impairment EMA: No experience in patients with hepatic impairment (serum bilirubin > 1.5 x ULN plus AST and ALT > 5 x ULN)	Mild and moderate: no need for dose adjustment is expected Severe: not recommended	Cloclar label ¹ SPC Evoltra ² Benitez <i>et al.</i> ⁴⁶

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
			intermittent HD, $T_{1/2}$ interdialytic and on haemodialysis was approximately 2.5-3 times higher than in patients without renal impairment.		Severe: contraindicated		
50	Cobimetinib	Cobimetinib is metabolised in the liver. Cobimetinib is mainly excreted in feces (76%, 6.6 unchanged) and to a lesser extent in urine (17.8%, 1.6% unchanged).	EMA/FDA: CLcr ≥ 30 ml/min: no dose adjustment CLcr < 30 ml/min: not studied HD: not studied Cheeti <i>et al.</i> No effect of mild and moderate hepatic impairment on the total cobimetinib exposure (C_{max} and AUC) compared to patients with a normal hepatic function.	Renal impairment: no dose adjustment is needed HD: no need for dose adjustment is expected	EMA/FDA: Child-Pugh A, B and C: no dose adjustment	Hepatic impairment: no dose adjustment is needed	Cotellic label ¹ Cotellic SPC ² Cheeti <i>et al.</i> ⁴⁷
51	Copanlisib	Copanlisib is metabolised by CYP3A (>90%) and CYP1A1 (<10%). Copanlisib is mainly excreted in feces (64%, 30% unchanged) and to a lesser extent in urine (22%, 15% unchanged).	FDA: CLcr ≥ 30 ml/min: no clinically significant effect on PK of copanlisib CLcr < 30 ml/min: no data available HD: no data available	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: not recommended HD: not recommended	FDA: Child-Pugh A: no dose adjustment Child-Pugh B: 45 mg Child-Pugh C: 30 mg	Child-Pugh A: no dose adjustment is needed. Child-Pugh B: 75% of the original dose. Child-Pugh C: 50% of the original dose	Aliqopa label ¹
52	Crizotinib	Crizotinib is metabolised in the liver. Crizotinib and its metabolites are mainly excreted in feces (63%, 53% unchanged), and to a lesser extent in urine (22%, 1.3% unchanged).	EMA/FDA: CLcr ≥ 30 ml/min: no dose adjustment CLcr < 30 ml/min: 250 mg QD Tan <i>et al.</i> CLcr ≥ 30 ml/min : no relevant change in steady-state PK CLcr < 30 ml/min: AUC _{0-inf} : 179.5 (90% CI 126.8-254.0) (single-dose)	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: 50% of the original dose (250 mg QD) HD: a need for dose adjustment to 50% of the original dose is expected (250 mg QD)	FDA: Moderate: 200 mg BID Severe: 250 mg QD EMA: Mild: no dose adjustment Moderate: 200 mg BID Severe: 250 mg QD El-Khoueiry <i>et al.</i> Geometric mean compared to normal liver function (250 mg BID): Mild (250 mg BID) : AUC _{0-24h} 91.12% (90% CI 56.56-146.79) Moderate (200 mg BID): AUC _{0-24h} 114.08 % (90% CI 73.57-176.89) Severe (250 mg QD): AUC _{0-24h} 64.67 (90%CI 39.50-105.89)	Mild: no dose adjustment is needed Moderate: 80% of starting dose BID (200 mg BID) Severe: 50% of starting dose QC (250 mg QD), increase if tolerated	Xalkori label ¹ SPC Xalkori ² Tan <i>et al.</i> ⁴⁸ El-Khoueiry <i>et al.</i> ⁴⁹

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
53	Cyclophosphamide	Cyclophosphamide (prodrug) is metabolised in the liver in its active metabolites. Liver metabolism also forms the cytotoxic and urotoxic metabolite acrolein. Cyclophosphamide and its metabolites are predominantly excreted in urine (10-20% unchanged) and minimally in feces.	FDA: CLcr 10-24 ml/min: monitor closely for toxicity HD: dialysed MHRA: GFR < 10 ml/min: 50% of the original dose HD: dialysed Wang et al. HD: dialysed, mean of 37% of administered cyclophosphamide was removed during 4-hour dialysis. Haubitz et al. CLcr 25-50 ml/min: 42% increase in AUC_{0-inf} CLcr 10-24 ml/min: 77% increase in AUC_{0-inf} CLcr < 10 ml/min and a 3-hour HD sessions seven hours after administration: 23% increase in AUC_{0-inf} Juma et al. Significantly higher AUC of plasma alkylating activity in group of patients with CLcr 0-51 ml/min compared to patients with normal renal function (47.77±19.93 nmol/mL*h vs. 25.15±8.67 nmol/mL*h)	GFR ≥ 30 ml/min: no dose adjustment is needed GFR 10-29 ml/min: consider 75% of the original dose GFR < 10 ml/min: not recommended, if unavoidable consider 50% of the original dose HD: not recommended, if unavoidable consider 50% of the original dose	FDA: Potentially reduced efficacy in patients with hepatic impairment MHRA: 3-1-5mg/dL: 75% of the original dose Juma et al. Significantly prolonged Cyclophosphamide half-life in patients with severe liver failure (all cirrhosis due to hepatitis) compared to normal controls. Fewer adverse events in the liver failure group.	Mild and moderate: no need for dose adjustment is expected. Severe: not recommended, due to risk of reduced efficacy	Cyclophosphamide injection Baxter – label¹ SPC Cyclophosphamide injection 1 g⁹ Wang et al.⁵⁰ Haubitz et al.⁵¹ Juma et al.⁵² Juma et al.⁵³
54	Cytarabine (high-dose ≥ 1 g/m²) for low-dose no dose adjustments are needed	Cytarabine is converted intracellularly to its active metabolite aracytidine-5'-triphosphate. Cytarabine is further metabolised, primarily in the liver, among others to uracil arabinoside (Ara-U), which can cause neurotoxicity. Cytarabine and its metabolites, are predominantly excreted in	MHRA: Renal impairment: use with caution and at reduced dose. HD: dialysed Kintzel et al. CLcr 60 ml/min: 60% of the original dose CLcr 45 ml/min: 50% of the original dose CLcr 30 ml/min:	GFR ≥ 60 ml/min: no dose adjustment is needed GFR 31-59 ml/min: 50% of the original dose GFR < 30 ml/min: not recommended HD: 50% of the original dose, start HD 4-5 h after administration	MHRA: Hepatic impairment: use with caution and at reduced dose Barker et al. 1 g/m² every other day for three days was tolerated in a patient with bilirubin > 15 mg/dL.	Mild and moderate: no need for dose adjustment is expected Severe: consider 25-50% of the original dose and increase if tolerated	Cytarabine 100 mg/ml, Pfizer Ltd.⁹ Kintzel et al.⁴² Smith et al.⁵⁴ Radeski et al.⁵⁵ Barker et al.⁵⁶

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
		urine (90% as metabolites, 5-8% unchanged).	not recommended Radeski <i>et al.</i> HD: no dose adjustment, HD initiated 6 h after administration of 1 g/m ² resulted in 63% Ara-U removal.				
55	Dabrafenib	Dabrafenib is primarily metabolised in the liver to hydroxy-dabrafenib and desmethyl-dabrafenib, which both contribute to the clinical effect. Dabrafenib and its metabolites are predominantly excreted in feces (71%) and to a lesser extent in urine (23%).	EMA/FDA: eGFR ≥ 30 ml/min/1.73m ² : no dose adjustment eGFR < 30 ml/min/1.73m ² : not studied Park <i>et al.</i> HD: not dialysed, plasma concentrations comparable to patients with normal renal function	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min or HD: no need for dose adjustment is expected	EMA/FDA: Mild: no dose adjustment Moderate and severe: not studied	Mild: no dose adjustment is needed Moderate and severe: 50% of the original dose may be considered	Tafinlar label ¹ SPC Tafinlar ² Park <i>et al.</i> ⁵⁷
56	Dacarbazine	Dacarbazine (prodrug) is metabolised in the liver to its reactive metabolites. These metabolites are also inactivated by the liver. Approximately 20- 50% of dacarbazine is excreted unchanged in urine by tubular secretion.	MHRA: Mild and moderate without hepatic impairment: no dose adjustment Severe: no advice In patients with combined renal and hepatic impairment elimination is prolonged HD: not studied	GFR ≥ 30 ml/min without hepatic impairment: no dose adjustment is needed GFR < 30 ml/min: 70% of the original dose may be considered HD: 70% of the original dose may be considered	MHRA: Mild and moderate without renal impairment: no dose adjustment Severe: no advice in patients with combined renal and hepatic impairment elimination is prolonged	Mild and moderate without renal impairment: no dose adjustment is needed Severe: not recommended	SPC Dacarbazine ⁹
57	Dacomitinib	Dacomitinib is primary metabolised by oxidation and glutathione conjugation. Dacomitinib is mainly excreted in feces (20% as dacomitinib) and minorly 3% in urine (<1% as dacomitinib)	EMA/FDA: CLcr ≥ 30 ml/min: no dose adjustment CLcr < 30 ml/min: no data available HD: no data available	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	FDA: Child-Pugh A-C: no dose adjustment needed EMA: Mild and moderate or Child-Pugh A/B: no dose adjustment needed Severe or Child-Pugh C: no PK changes, recommended starting dose 30 mg QD (33% dose reduction) based on safety and tolerability	Mild and moderate: no dose adjustment is needed Severe: 66% of the original dose, increase if tolerated	Vizimpro label ¹ SPC Vizimpro ²
58	Dactinomycin	Dactinomycin is minimally metabolised. Approximately 30% of the dose is excreted in urine and feces.	FDA/MHRA: Not studied in patients with renal impairment HD: not studied	Renal impairment: no need for dose adjustment is expected HD: no need for dose adjustment is expected	FDA/MHRA: Not studied in patients with hepatic impairment	Mild and moderate: no need for dose adjustment is expected Severe: not recommended	Cosmegen label ¹ SPC Cosmegen ⁹

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
59	Daratumumab	Daratumumab is catabolised by proteolytic degradation to smaller peptides. No renal or hepatic clearance.	FDA: CLcr: ≥ 15 ml/min: no dose adjustment is needed EMA: Renal impairment: no dose adjustment needed	Renal impairment: no dose adjustment is needed HD: no need for dose adjustment is expected	FDA: Mild and moderate: no dose adjustment Severe: not studied EMA: Hepatic impairment: no dose adjustment needed	Hepatic impairment: no dose adjustment is needed	Darzalex label ¹ SPC Darzalex ²
60	Darolutamide	Darolutamide is metabolised primarily by oxidative metabolism BY CYP3A4 and glucuronidation by UGT1A9 and UGT1A1. Darolutamide is mainly excreted in urine (63·4%; 7% unchanged) and in feces (32·4%; 30·7% unchanged).	EMA/FDA: eGFR ≥ 30 ml/min/1·73m ² : no dose adjustment eGFR 15-29 ml/min/1·73m ² : 50% dose reduction eGFR < 15 ml/min/1·73m ² : no data available HD: no data available Zurth et al. Severe: compared to healthy subjects, C _{max} increased 1·6-fold and AUC ₀₋₄₈ increased 2·5-fold.	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: 50% of the original dose HD: 50% of the original dose	FDA: Mild: no dose adjustment Moderate or Child-Pugh B: 50% dose reduction Severe or Child-Pugh C: no data available EMA: Mild: no dose adjustment Moderate, severe and Child-Pugh B/C: 50% dose reduction Zurth et al. Child-Pugh B: compared to healthy subjects, C _{max} increased 1·5-fold and AUC ₀₋₄₈ increased 1·9-fold.	Child-Pugh A or mild: no dose adjustment is needed Child-Pugh B/C or moderate/severe: 50% of the original dose	Nebuqa label ¹ SPC Nebuqa ² Zurth <i>et al.</i> ⁵⁸
61	Dasatinib	Dasatinib is metabolised in the liver. Dasatinib and its metabolites are predominantly excreted in feces (85%, 19% unchanged) with minimal excretion in urine (4%, 0·1% unchanged).	EMA/FDA: CLcr had no clinically relevant effect on the pharmacokinetics HD: not studied	Renal impairment: no dose adjustment is needed HD: no need for dose adjustment is expected	EMA/FDA: No initial dose adjustment is needed, although caution is recommended Child-Pugh-A: not studied Child-Pugh B: 8% decrease in mean AUC Child-Pugh C: 28% decrease in mean AUC	Hepatic impairment: no dose adjustment is needed, although caution is recommended	Sprycel label ¹ SPC Sprycel ²
62	Daunorubicin	Daunorubicin is metabolised in the liver. The metabolite daunorubicinol contributes to the clinical effect. Daunorubicin and its metabolites are excreted in both urine (25%) and feces (40%)	MHRA: Serum creatinine 105-265 μ mol/L: 75% serum creatinine > 265 μ mol/L: 50% Krashin et al. HD: 50% of the dose (30 mg/m ² resulted in a comparable AUC of that in patients with 45mg/m ² without renal impairment.	GFR 30-50 ml/min: 75% of the original dose GFR < 30 ml/min: 50% of the original dose HD: 50% of the original dose	MHRA: Serum bilirubin 20-50 μ mol/L: 75% of the original dose Serum bilirubin > 50 μ mol/L: 50% of the original dose	Bilirubin 20-50 μ mol/L: 75% of the original dose Bilirubin > 50 μ mol/L: 50% of the original dose	SPC Daunorubicin ⁹ Krashin <i>et al.</i> ⁵⁹
63	Decitabine	Decitabine is converted intracellularly to its active	EMA/FDA: Renal impairment: not	Renal impairment: no need for dose adjustment at	EMA/FDA: Hepatic impairment: not	Hepatic impairment: no need for dose adjustment	Dacogen label ¹ SPC Dacogen ²

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
		metabolite. Decitabine is metabolised by cytidine deaminase in, among others, the liver and kidneys. Decitabine and its metabolites are excreted in urine (90%, 4% unchanged).	studied. Exposure not likely to be affected in patients with impaired renal function (EMA). Levine <i>et al.</i> Retrospective safety data: higher incidence of grade ≥ 3 cardiac and respiratory toxicities in group with CLcr < 60ml/min compared to CLcr ≥ 60 ml/min.	start is expected, close monitoring for toxicity is recommended HD: not recommended	studied	is expected	Levine <i>et al.</i> ⁶⁰
64	Decitabine/ cedazuridine	Decitabine is primarily metabolised by cytidine deaminase and physicochemical degradation. Cedazuridine is primarily metabolised by physicochemical degradation. Cedazuridine is mainly excreted in feces (51%, 27% unchanged) and urine (46%, 21% unchanged).	FDA: CLcr ≥ 60 ml/min: no dose adjustment CLcr 30-59 ml/min: no dose adjustment, monitor patients CLcr < 30 ml/min: no data available	GFR ≥ 60 ml/min: no dose adjustment is needed GFR 30-59 ml/min: no dose adjustment is needed, consider monitoring GFR < 30 ml/min: not recommended HD: not recommended	FDA: Mild: no dose adjustment Moderate and severe: no data available	Mild: no dose adjustment is needed Moderate and severe: not recommended	Inqovi label ¹
65	Dinutuximab (-beta)	Dinutuximab(-beta) is catabolised by proteolytic degradation to smaller peptides. No renal or hepatic clearance.	EMA: dinutuxumab-beta FDA: dinutuxumab eGFR < 70 ml/min/1.73m ² : not studied HD: not studied	Renal impairment: no need for dose adjustment is expected HD: no need for dose adjustment is expected	EMA: dinutuxumab-beta FDA: dinutuxumab Not studied in patients with hepatic impairment	Hepatic impairment: no need for dose adjustment is expected.	Unituxin label ¹ SPC Qarziba ²
66	Docetaxel	Docetaxel is primarily metabolised by CYP-mediated oxidative metabolism. Docetaxel is mainly excreted in feces (75%) and to a lesser extent with urine (6%), mostly as metabolites.	EMA/FDA: Renal impairment: not studied Dimopoulos <i>et al.</i> Full dose was tolerated in 11 patients with CLcr < 10-39 ml/min (median 28 ml/min). Hochegger <i>et al.</i> HD: not dialysed	Renal impairment: no need for dose adjustment is expected HD: no need for dose adjustment is expected	EMA: AST and/or ALT > 1.5 x ULN with AP > 2.5 x ULN: reduce to 75 mg/m ² ALT and AST > 3.5 x ULN with AP > 6 x ULN and/or serum bilirubin > ULN: only use on strict indication FDA: Bilirubin > ULN or AST and/or ALT > 1.5x ULN with AP > 2.5x ULN: avoid use	AST and/or ALT > 1.5-5 x ULN concomitant with AP > 2.5 – 5 x ULN and normal bilirubin: consider 75% of the original dose AST or ALT > 5-10 x ULN concomitant with AP < 6 x ULN and/or bilirubin ≤ 1.1 -1.5 x ULN: consider 50% of the original dose Bilirubin > 1.5 x ULN or AST/ALT > 10 x ULN or AP	Taxotere label ¹ SPC taxotere ² Dimopoulos <i>et al.</i> ⁶¹ Hochegger <i>et al.</i> ⁶² Bruno <i>et al.</i> ⁶³ Syn <i>et al.</i> ⁶⁴ Minami <i>et al.</i> ⁶⁵ Eckmann <i>et al.</i> ⁶⁶

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
					Bruno <i>et al.</i> PopPK: 27% decrease in CL in patients with ALT or AST > 1.5 X ULN and AP > 2.5 X ULN Syn <i>et al.</i> AP, AST and/or AST ≤ 5 x ULN and bilirubin < 1 x ULN: 75% of the original dose Any AP, and AST or ALT ≤ 5-10 x ULN and/or bilirubin ≤ 1-1.5x ULN: 50% of the original dose resulted in comparable AUC_{0-inf}. Minami <i>et al.</i> popPK: AP > 2.5 x ULN and AST/ALT > 2.5 - 5.0 x ULN 22% decrease in CL, suggesting a 20% dose reduction AP > 2.5 x ULN and AST/ALT > 5.0 - 20.0 x ULN 38% decrease in CL, suggesting a 40% dose reduction. Eckmann <i>et al.</i> A dose of 25 mg/m² (25% of the original dose) in patients with bilirubin 1.5-3 x ULN and ALT/AST 2.5 – 5 x ULN and AP ≥ 2.5 X ULN due to liver metastases resulted in significantly lower AUC compared to patients with normal hepatic function. (1.7 mg/L/h compared to 4.81 mg/L/h)	> 6 x ULN: not recommended	
67	Dostarlimab	Dostarlimab is catabolised by proteolytic degradation to smaller peptides. No renal or hepatic clearance.	EMA: CLcr ≥ 30 ml/min: no dose adjustment CLcr < 30 ml/min: limited data available HD: limited data available FDA: Renal impairment: no clinically significant effect on PK of dostarlimab	Renal impairment: no dose adjustment is needed HD: no need for dose adjustment is expected	EMA: Mild and moderate: no dose adjustment Severe : limited data available FDA: Hepatic impairment: no clinically significant effect on PK of dostarlimab	Mild and moderate: no dose adjustment is needed Severe: no need for dose adjustment is expected	Jemperli label ¹ SPC Jemperli ²

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
68	Doxorubicin	Doxorubicin is metabolised in the liver. Doxorubicinol is the main active metabolite. Doxorubicin and its metabolites are mainly excreted biliary in feces (40%-50%) and to a lesser extent in urine (5-12%).	FDA: Renal impairment: no advice given MHRA eGFR < 10 ml/min: 75% of the dose Yoshida <i>et al.</i> HD: AUC of doxorubicin and doxorubicinol increased 1.5 and 3-fold respectively in HD-patients.	GFR > 10 ml/min: no dose adjustment is needed GFR < 10 ml/min: no need for dose adjustment is expected HD: 75% of the original dose may be considered	FDA/ MHRA: Serum bilirubin 20-50 µmol/L: 50% of the original dose Serum bilirubin 50 µmol/L – 85.5 µmol/L : 25% of the original dose Serum bilirubin > 85.5 µmol/L: contraindicated (FDA) Child-Pugh C: contraindicated	Bilirubin 20-50 µmol/L: 50% of the original dose Bilirubin 51 – 86 µmol/L : 25% of the original dose Bilirubin > 86 µmol/L or Child-Pugh C: not recommended	Doxorubicin label ¹ SPC Doxorubicin ⁹ Yoshinda <i>et al.</i> ⁶⁷
69	Liposomal doxorubicin (Myocet®)	Doxorubicin is metabolised in the liver. Doxorubicinol is the main active metabolite. Doxorubicin and its metabolites are mainly excreted biliary in feces (40%-50%) and to a lesser extent in urine (5-12%). With the liposomal formulation total doxorubicin plasma levels are higher compared to conventional doxorubicin, but peak plasma levels of free doxorubicin are lower.	EMA: No dose adjustment is needed	Renal impairment: no need for dose adjustment is expected HD: no need for dose adjustment is expected	EMA: Bilirubin < ULN and normal AST: no dose adjustment Bilirubin < ULN and raised AST: consider a 25% dose reduction Bilirubin > ULN but < 50 µmol/L: 50% dose reduction Bilirubin > 50 µmol/L: avoid if possible, otherwise 75% dose reduction	AST > ULN: 75% of the original dose Bilirubin 20-50 µmol/L: 50% of the original dose Bilirubin 51 – 86 µmol/L : 25% of the original dose Bilirubin > 86 µmol/L or Child-Pugh C: not recommended	SPC Myocet liposomal ²
70	Pegylated liposomal doxorubicin (Doxil, Caelyx®)	Doxorubicin is metabolised in the liver. Doxorubicinol is the main active metabolite. Doxorubicin and its metabolites are mainly excreted biliary in feces (40%-50%) and to a lesser extent in urine (5-12%). With the pegylated liposomal formulation total doxorubicin plasma levels and AUC are higher compared to conventional doxorubicin.	FDA: No information EMA: CLcr ≥ 30 ml/min: doxorubicine clearance is not influenced by renal function CLcr < 30 ml/min: not studied	Renal impairment: no need for dose adjustment is expected HD: no need for dose adjustment is expected	FDA: Bilirubin ≥ 1.2 mg/dL: a dose reduction is needed EMA: Bilirubin ≥ 1.2-3.0 mg/dl: 75% of the original dose Bilirubin > 3.0 mg/dl: 50% of the original dose	Bilirubin > 20 – 50 µmol/L: 75% of the original dose Bilirubin 51-86 µmol/L: 50% of the original dose Bilirubin > 86 µmol/L: not recommended	Doxil label ¹ SPC Caelyx ²
71	Durvalumab	Durvalumab is catabolised by proteolytic degradation to smaller peptides. No renal or hepatic clearance.	EMA/FDA: CLcr: ≥ 30 ml/min: no dose adjustment is needed CLcr < 30 ml/min: not studied	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected	EMA/FDA: Mild: no dose adjustment is needed Moderate and severe: not studied	Mild: No dose adjustment is needed Moderate and severe: no	Imfinzi label ¹ SPC Imfinzi ²

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
			HD: not studied	HD: no need for dose adjustment is expected		need for dose adjustment is expected	
72	Duvelisib	Duvelisib is primarily metabolised by CYP3A4. Its major metabolite, IPI-656, is pharmacologically inactive. Duvelisib is mainly excreted in feces (79%, 11% unchanged) and 14% is excreted in urine (1% unchanged).	EMA: CLcr 23-80 ml/min: no dose adjustment CLcr < 23 ml/min and HD: no data available FDA: CLcr 23-80 ml/min: no clinically significant effect on exposure of duvelisib	GFR 23-80 ml/min: no dose adjustment is needed GFR < 23 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	EMA/FDA: Child Pugh Class A, B and C: no dose adjustment	Hepatic impairment: no dose adjustment is needed	Copiktra label ¹ SPC Copiktra ²
73	Elotuzumab	Elotuzumab is catabolised by proteolytic degradation to smaller peptides. No renal or hepatic clearance.	EMA/FDA: Renal impairment/HD: no dose adjustment needed Berdeja <i>et al.</i> No statistically significant AUC _{0-inf} differences between patients with CLcr ≥ 90 ml/min and patients with CLcr < 30 ml/min or ESRD with HD. Not dialysed	Renal impairment: no dose adjustment is needed HD: no dose adjustment is needed	EMA/FDA: Mild: no dose adjustment is needed. Moderate and severe: not studied.	Mild: No dose adjustment is needed Moderate and severe: no need for dose adjustment is expected	Empliciti label ¹ SPC Empliciti ² Berdeja <i>et al.</i> ⁶⁸
74	Enasidenib	Enasidenib is metabolised in the liver. The metabolite AGI-16903 contributes to the clinical effect. Enasidenib is mainly excreted in feces (89%, 34% unchanged) and to a lesser extent in urine (11%, 0-4% unchanged).	FDA: CLcr ≥ 30 ml/min: no clinically meaningful effect on PK CLcr < 30 ml/min: not studied	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	FDA: Mild (TB ≤ ULN & AST > ULN or TB 1-1.5x ULN & any AST): no clinically meaningful effect on PK Moderate and severe: not studied	Mild: No dose adjustment is needed Moderate: 50% of the original dose may be considered Severe: not recommended	Idhifa label ¹
75	Encorafenib	Encorafenib is metabolised in the liver. Encorafenib and its metabolites are excreted in feces (47%, 5% unchanged) and urine (47%, 2% unchanged).	EMA/FDA: CLcr 30-90 ml/min: no dose adjustment CLcr < 30 ml/min: not studied HD: not studied	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min without hepatic impairment: no need for dose adjustment is expected HD without hepatic impairment: no need for dose adjustment is expected	FDA: Child-Pugh A: no dose adjustment Child-Pugh B and C: not studied EMA: Child-Pugh A: 67% of original dose (300 mg QD) Child-Pugh B/C: no dose recommendation	Child-Pugh A: 67% of original dose (300 mg QD) Child-Pugh B/C: not recommended	Braftovi label ¹ SPC Braftovi ²
76	Enfortumab vedotin	The monoclonal antibody portion is expected to undergo proteolysis by	EMA: CLcr ≥ 15 ml/min: no dose adjustment	GFR ≥ 15 ml/min: no dose adjustment is needed GFR < 15 ml/min: no need for	EMA: Mild: no dose adjustment Moderate and severe: no data	Mild: no dose adjustment is needed Child-Pugh B/C or	Padcev label ¹ SPC Padcev ²

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
		ubiquitous proteolytic enzymes to small peptides and individual amino acids. Only a small fraction of MMAE released from enfortumab is metabolised, mainly by CYP3A4. MMAE is excreted mainly in feces and to a lesser extent in urine.	CLcr < 15 ml/min and HD: no data available FDA: Renal impairment: no dose adjustment	dose adjustment is expected HD: no need for dose adjustment is expected	available FDA: Mild: no dose adjustment Child-Pugh B and C or moderate and severe: avoid use	moderate/severe: not recommended	
77	Entrectinib	Entrectinib is primarily metabolised by CYP3A4 (~76%) into the equipotent metabolite M5. Entrectinib and M5 are mainly excreted in feces (83%; 36% unchanged and 22% as M5), with minimal excretion in urine (3%).	EMA/FDA: CLcr ≥ 30 ml/min: no dose adjustment CLcr < 30 ml/min: not studied HD: no data available	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: not recommended	EMA/FDA: Mild: no dose adjustment Moderate and severe: not studied	Mild: no dose adjustment is needed Moderate and severe: consider starting with a 50% lower dose and increase the dose if tolerated.	Rozlytrek label ¹ SPC Rozlytrek ²
78	Enzalutamide	Enzalutamide is metabolised in the liver. The N-desmethyl metabolite contributes to the clinical effect. Enzalutamide and its metabolites are mainly excreted in urine (71%) and to a lesser extent in feces (14%), mostly as inactive metabolites.	EMA/FDA: CLcr ≥ 30 ml/min: no dose adjustment CLcr < 30 ml/min: not studied HD: not studied, unlikely to be dialysable	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	EMA/FDA: Child-Pugh A, B and C: no dose adjustment Krauwinkel et al. Sum of active moieties: Child-Pugh A: AUC _{0-inf} 113% (90% CI 89-143) Child-Pugh B: AUC _{0-inf} 118% (90% CI 96-145) Child-Pugh C: AUC _{0-inf} 104% (90% CI 86-124)	Hepatic impairment: no dose adjustment is needed	Xtandi label ¹ SPC Xtandi ² Krauwinkel <i>et al.</i> ⁶⁹
79	Epirubicin	Epirubicin is extensively and rapidly metabolised in the liver. Epirubicinol is the main active metabolite. Epirubicin and its metabolites are mainly excreted in feces (34%) and to a lesser extent in urine (27%).	FDA/MHRA: Serum creatinine < 5 mg/dL: no clinically relevant effect on PK, no dose adjustment Serum creatinine > 5 mg/dL: not studied, consider dose reduction HD: not studied (FDA) not dialysed (MHRA) Gori et al. HD: 30 mg/m ² weekly was tolerated	GFR ≥ 10 ml/min: no dose adjustment is needed GFR < 10 ml/min: no need for dose adjustment is expected. HD: no need for dose adjustment is expected, consider weekly schedule	FDA: Bilirubin 1-2-3 mg/dL or AST 2-4 ULN: 50% of the original dose Bilirubin > 3 mg/dL or AST > 4x ULN: 25% of the original dose MHRA: Elevated bilirubin/AST: lower doses are recommended Severe: contraindicated Twelves et al. 25 mg/m ² once weekly was tolerated in breast cancer patients with liver	Bilirubin 21-51 µmol/L or AST 2-4 x ULN: consider 50% of the original dose Bilirubin > 51 µmol/L or AST > 4x ULN: consider 25% of the original dose Bilirubin > 86 µmol/L or Child-Pugh C: not recommended	Ellence label ¹ SPC Epirubicin ⁹ Gori <i>et al.</i> ⁷⁰ Dobbs <i>et al.</i> ⁷¹ Twelves <i>et al.</i> ⁷²

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
					metastases and AST > 2 x ULN or bilirubin > ULN Dobbs et al. Proposed dosing scheme ranging from 20-90 mg/m ² based on AST levels and target AUC.		
80	Erdafitinib	Erdafitinib is primarily metabolised by CYP2C9 and CYP3A4. Erdafitinib is mainly excreted in feces (69%, 19% unchanged) and 19% is excreted in urine (13% unchanged)	FDA: eGFR ≥ 30 ml/min/1.73m ² : no dose adjustment eGFR < 30 ml/min/1.73m ² : no data available HD: no data available	eGFR ≥ 30 ml/min: no dose adjustment is needed eGFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	FDA: Child-Pugh A/B: no dose adjustment Child-Pugh C: limited data available	Child-Pugh A/B: no dose adjustment is needed Child-Pugh C: not recommended	Balversa label ¹
81	Eribulin	Eribulin is minimally metabolised. Eribulin is predominantly excreted in feces (82%) and to a lesser extent in urine (9%), mostly unchanged.	FDA: CLcr 15- 49 ml/min: 1.1 mg/m ² EMA: CLcr < 50 ml/min: dose reduction may be needed Tan et al. CLcr 15-29 ml/min and 30-50 ml/min: AUC _{0-inf} 1.49 (90% CI 0.9-2.45) HD: not studied	GFR > 50 ml/min: no dose adjustment is needed GFR < 50 ml/min: 80% of the original dose HD: 80% of the original dose may be considered	FDA: Child-Pugh A: 1.1 mg/m ² Child-Pugh B: 0.7 mg/m ² Child-Pugh C: not studied EMA: Hepatic impairment due to liver metastases: Child-Pugh A: 0.97 mg/m ² Child-Pugh B: 0.62 mg/m ² Child-Pugh C: not studied Devriese et al. Child-Pugh A: AUC _{0-inf} 1.75 (90% CI 1.15-2.66) Child-Pugh B: AUC _{0-inf} 2.48 (90% CI 1.57-3.92)	Child-Pugh A: 80% of the original dose Child-Pugh B: 50% of the original dose Child-Pugh C: not recommended	Halaven Label ¹ SPC Halaven ² Tan et al. ⁷³ Devriese et al. ⁷⁴
82	Erlotinib	Erlotinib is metabolised in the liver. Erlotinib and its metabolites are predominantly excreted as metabolites in feces (>90%) with minimal excretion in urine (9%).	FDA: Renal impairment: not studied EMA: CLcr ≥ 30 ml/min: not studied, no dose adjustment CLcr < 30 ml/min: not studied, not recommended Miller et al. Similar clearance in patients with renal impairment (1.6-5	Renal impairment: no need for dose adjustment is expected HD: no need for dose adjustment is expected	FDA: Increased frequency of monitoring is required in patients with bilirubin > 3 x ULN EMA: Severe: not recommended O'Bryant et al. Child-Pugh B: AUC _{0-last} 92% (90%CI 69.1-123.2) Miller et al.	Direct bilirubin > 17 µmol/L or AST ≥ 3x ULN: consider a starting dose of 50%, increase if tolerated	Tarceva label ¹ Tarceva SPC ² O'Bryant et al. ⁷⁵ Togashi et al. ⁷⁶ Miller et al. ⁷⁷

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
			mg/dl) and patients with normal renal function Togashi <i>et al.</i> HD: similar PK, not dialysed.		Reduced clearance in patients with hepatic impairment (AST ≥ 3 x ULN and normal direct bilirubin or direct bilirubin 1.0-7.0 mg/dl with any AST). Recommended starting dose of 75mg QD (50% of the original dose).		
83	Etoposide (intravenous)	Etoposide is metabolised in the liver, among others to the active catechol metabolite. Etoposide and its metabolites are excreted in urine (56%, 45% unchanged) and in feces (44%).	FDA/MHRA: CLcr > 50 ml/min: no dose adjustment CLcr 15-50 ml/min: 75% of the original dose CLcr < 15 ml/min: not studied, consider further dose reduction HD: not dialysed (MHRA) Watanabe <i>et al.</i> Similar etoposide PK parameters in 5 patients on HD compared to controls. Etoposide has low dialysability, full dose was tolerated.	GFR > 50 ml/min: no dose adjustment is needed GFR 10-50 ml/min: 75% of the original dose, increase if tolerated HD: not dialysed, consider 75% of the original dose	FDA: Not reported. Total body clearance correlated with albumin concentration. MHRA: Total body clearance of etoposide is not reduced in adult patients with liver dysfunction Stewart <i>et al.</i> Patients with bilirubin ≥ 1mg/dL compared to patients with bilirubin < 1mg/dl: similar total clearance, increased unbound fraction, decreased unbound clearance.	Bilirubin < 50 µmol/L and normal albumin and normal renal function: no need for dose adjustment is expected Bilirubin ≥ 50 µmol/L or decreased albumin levels: consider 50% of the dose, increase if tolerated	Etophos label ¹ SPC Etophos ⁹ Stewart <i>et al.</i> ⁷⁸ Watanabe <i>et al.</i> ⁴⁴
84	Everolimus	Everolimus is metabolised in the liver. Its metabolites are mainly excreted in feces (80%) and to a lesser extent in urine (5%).	EMA/FDA: Renal impairment: no dose adjustment HD: not studied Thiery-Vuillemin <i>et al.</i> HD: not dialysed	Renal impairment: no dose adjustment is needed HD: no need for dose adjustment is expected	EMA/FDA: (original dose 10 mg QD) Child-Pugh A: 7.5 mg QD Child-Pugh B: 5 mg QD Child-Pugh C: 2.5 mg QD Peveling-Oberhag <i>et al.</i> Child-Pugh A: AUC _{0-inf} 1.84 (90%CI: 1.36-2.50) Child-Pugh B: AUC _{0-inf} 3.15 (90%CI: 2.36-4.21) Child-Pugh C: AUC _{0-inf} 3.64 (90%CI: 2.64-5.00)	Child-Pugh A: 75% of the original dose Child-Pugh B: 50% of the original dose Child-Pugh C: 25% of the original dose	Afinitor label ¹ SPC Afinitor ² Thiery-Vuillemin <i>et al.</i> ⁷⁹ Peveling-Oberhag <i>et al.</i> ⁸⁰ Kovarik <i>et al.</i> ⁸¹
85	Exemestane	Exemestane is extensively metabolised in the liver. Exemestane and its metabolites are excreted in urine (42%) and feces (42%), mostly as metabolites.	FDA/MHRA: Although renal impairment increases exposure to exemestane, no dose adjustment is necessary Jannuzzo <i>et al.</i>	Renal impairment: due to large therapeutic index no dose adjustment is needed HD: no need for dose adjustment is expected	FDA/MHRA: Child-Pugh A: not studied Child-Pugh B and C: although hepatic impairment increases exposure to exemestane, no dose adjustment is necessary	Hepatic impairment: Due to large therapeutic index no dose adjustment is needed	Aromasin label ¹ SPC Aromasin ⁹ Januzzo <i>et al.</i> ⁸²

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
			CLcr $\leq$ 60 ml/min/1.73 ² : 2 to 3-fold increase in AUC _{0-inf} compared with CLcr > 60 ml/min/1.73m ²		<i>Jannuzzo et al.</i> Child-Pugh B and C: 2-3 fold increase in AUC _{0-inf} compared with normal hepatic function		
86	Fedratinib	Fedratinib is predominantly metabolised by CYP3A4, in vitro. CYP2C19 and FMOs play a minor role in the metabolism. Fedratinib is mainly excreted in feces (77%, 23% unchanged) and to a lesser extent in urine (5%, 3% unchanged).	EMA: CLcr 30-59 ml/min: AUC_{0-inf} 1.5-fold increase compared to subjects with normal renal function; no dose adjustment is needed CLcr 15-29 ml/min: AUC_{0-inf} 1.9-fold increase compared to subjects with normal renal function; reduce dose to 200 mg FDA: CLcr $\geq$ 30 ml/min: no dose adjustment CLcr 15-29 ml/min: reduce dose to 200 mg Ogasawara et al. Fedratinib C_{max} and AUC_{0-inf} increased by approximately 1.5-fold in subjects with moderate renal impairment (CLcr 30 – 50 ml/min) and by nearly 1.9-fold in those with severe (15 – 29 ml/min) renal impairment compared with healthy subjects with normal renal function. Patients with severe renal impairment (CLcr 15 – 29 ml/min): reduce dose to 200 mg.	GFR $\geq$ 30 ml/min: no dose adjustment is needed GFR 15-30 ml/min and HD: 50% of the original dose	EMA/FDA: Child-Pugh A/B or mild and moderate: no dose adjustment Child-Pugh C and severe: use should be avoided	Child-Pugh A/B or mild/moderate: no dose adjustment is needed Child-Pugh C and severe: not recommended	Inrebic label ¹ SPC Inrebic ² Ogasawara et al. ⁸³
87	Fludarabine	Fludarabine is dephosphorylated in plasma to the primary metabolite F-ara-A, which is converted intracellularly to its active metabolite. Fludarabine and its metabolites are mainly excreted in urine (40-60%).	FDA: CLcr $\geq$ 80 ml/min: no dose adjustment CLcr 50-79 ml/min: 20 mg/m² CLcr 30-49 ml/min: 15 mg/m² CLcr < 30 ml/min: do not administer HD: not studied	GFR > 70 ml/min: no dose adjustment is needed GFR 30-70 ml/min: 80% of the original dose GFR < 30 ml/min: not recommended HD: 80% of the original dose. Start dialysis 12h after administration.	MHRA/FDA: Not studied	Hepatic impairment: no need for dose adjustment is expected	Fludarabine phosphate Sandoz label ¹ SPC Fludara ⁹ Lichtman et al. ⁸⁴ Kielstein et al. ⁸⁵

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
			MHRA: CLcr 30-70 ml/min: reduce up to 50% of the original dose CLcr < 30 ml/min: contraindicated Lichtman <i>et al.</i> The following dose adjustments resulted in similar F-ara-A exposure (AUC_{0-24h}) levels: CLcr > 70 ml/min/1.73m²: 25 mg/m² CLcr 30-70 ml/min/1.73 m²: 20 mg/m² CLcr < 30 ml/min/1.73m²: 15 mg/m² Kielstein <i>et al.</i> HD: average dialysis clearance was 25% of clearance in patients with normal renal function (dialysis 12h after administration of 40mg/m²).				
88	Fluorouracil	Fluorouracil (FU) is converted intracellularly mainly by DPD to inactive metabolites. A small part of FU is excreted unchanged in urine (15%). The remainder is metabolised in the liver. Metabolites are mainly excreted in urine.	FDA: No advice given MHRA: Renal impairment: dose should be reduced by 33-50%. Fleming <i>et al.</i> full dose (2600 mg/m²) was tolerated in patients with creatinine 1.6-2.6 mg/dL. No correlation between creatinine level and 5-FU clearance. Rengelshausen <i>et al.</i> HD: not dialysed. PK of 5-FU comparable to patients with	Renal impairment: no need for dose adjustment is expected HD: no need for dose adjustment is expected	FDA: No advice given MHRA: Hepatic impairment: dose should be reduced by 33-50%. Fleming <i>et al.</i> Full dose (2600 mg/m² over 24h) was tolerated in patients with bilirubin 1.5-5 mg/dL or > 5 mg/dL. No correlation between bilirubin level and 5-FU clearance.	Mild and moderate (without renal impairment): no need for dose adjustment is expected Severe: not recommended	Fluorouracil, injection USP ¹ Fluorouracil 25 mg/ml injection Hospira Uk Ltd ⁹ Rengelshausen <i>et al.</i> ⁸⁶ Fleming <i>et al.</i> ⁸⁷

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
			normal renal function. Higher levels of the potentially toxic metabolite fluoro-beta-alanine were observed.				
89	Flutamide	Flutamide is metabolised in the liver. The metabolite 2-hydroxyflutamide contributes to the clinical effect. Flutamide and its metabolites are excreted in urine (45%) and to a lesser extent in feces (2%).	MHRA: Renal impairment: not studied, use with caution HD: not studied Anjum <i>et al.</i> No difference in flutamide and hydroxyflutamide AUC between groups with varying degrees of renal function (range: HD/CLcr < 5ml/min – CLcr > 80 ml/min). HD: not dialysed	Renal impairment: no need for dose adjustment is expected HD: no need for dose adjustment is expected	MHRA: Transaminase 2-3 x ULN: not recommended	Treatment in patients with hepatic impairment is not recommended due to liver toxicity	Flutamide 250 mg tablets ⁹ Anjum <i>et al.</i> ⁸⁸
90	Fulvestrant	Fulvestrant is metabolised in the liver. Fulvestrant and its metabolites are mainly excreted in feces (90%) with minimal renal excretion (<1%).	EMA/FDA: CLcr ≥ 30 ml/min: no dose adjustment (EMA), no advice given (FDA) CLcr < 30 ml/min: not studied HD: not studied	GFR ≥ 30ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	FDA: Child-Pugh A: no dose adjustment Child-Pugh B: 250 mg Child-Pugh C: not studied EMA: Child-Pugh A/B: no dose adjustment Child-Pugh C: not studied, contraindicated	Child-Pugh A: no dose adjustment Child-Pugh B: 50% of the original dose (250mg) Child-Pugh C: not recommended due to risk of hepatotoxicity	Faslodex label ¹ SPC Faslodex ²
91	Futibatinib	Futibatinib is extensively metabolised in the liver and is mainly excreted in feces (91%, negligible unchanged), and to a lesser extent in urine (9%, negligible unchanged).	FDA: CLcr ≥ 30 ml/min: no clinically meaningful differences in futibatinib PK CLcr 15-29 ml/min: not studied HD: not studied	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	FDA: Mild: no clinically meaningful differences in futibatinib PK Moderate and severe: not studied	Mild: no dose adjustment is needed Moderate and severe: not recommended	Lytgobi label ¹
92	Gefitinib	Gefitinib is metabolised in the liver. Gefitinib and its metabolites are predominantly excreted in feces (86%) with minimal excretion in urine (< 4%).	EMA/FDA: CLcr > 20 ml/min: no clinically relevant effect on PK. No dose adjustment (EMA) Shinagawa <i>et al.</i> Not dialysed	Renal impairment: no need for dose adjustment is expected HD: no need for dose adjustment is expected	EMA/FDA: Hepatic impairment due to liver metastases: PK not altered Child Pugh A, B or C due to cirrhosis: increased plasma exposure (40, 263 and 166% respectively).	Hepatic impairment due to metastasis and Child Pugh A: no dose adjustment is needed. Child-Pugh B and C: 50% of the original dose	Iressa label ¹ SPC Iressa ² Shinagawa <i>et al.</i> ⁸⁹ Horak <i>et al.</i> ⁹⁰

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
					Horak <i>et al.</i> Child-Pugh A: AUC_{0-inf}: 1.40 Child-Pugh B: AUC_{0-inf}: 3.63 Child-Pugh C: AUC_{0-inf}: 2.66 Hepatic impairment due to liver metastases: no significant difference in PK parameters		
93	Gemcitabine	Gemcitabine is converted intracellularly to active metabolites. Gemcitabine is also metabolised by cytidine deaminase in the liver, kidney, blood and other tissues. Gemcitabine and its metabolites are predominantly excreted in urine (92-98%, 10% unchanged).	MHRA/FDA: Renal impairment: not studied. GFR 30-80 ml/min: no significant effect on PK (MHRA) Venook <i>et al.</i> No statistically significant difference in gemcitabine PK in patients with renal impairment, however tolerance might be decreased. Kiani <i>et al.</i> HD: no apparent gemcitabine PK differences in patient on HD receiving standard dose compared to reported data. Tenfold AUC increase of non-toxic metabolite 2',2'-difluorodeoxyuridine, which can be effectively dialysed. Start HD 6-12 h after administration.	GFR ≥ 30ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected. Start HD 6-12 h after administration.	MHRA/FDA: Not studied Venook <i>et al.</i> No statistically significant differences in gemcitabine PK in patients with TB ≤ 1.6mg/dL and AST ≤ 2xULN or bilirubin 1.6 - 7.0 mg/dL. However increased risk for hepatotoxicity in patients with elevated bilirubin. Joerger <i>et al.</i> Hepatic impairment (cohorts mild/moderate/severe) associated with lower clearance, not with DLT. Teusink <i>et al.</i> Retrospective safety data: full dose can be given safely in patients with severe hepatic impairment (TB ≥ 4.5 mg/dL)	TB < 27 µmol/L: no dose adjustment is needed TB ≥ 27 µmol/L: either start at 80% of the original dose and increase the dose if tolerated or start with full dose with active monitoring	Gemzar label¹ SPC Gemzar⁹ Venook <i>et al.</i>⁸¹ Kiani <i>et al.</i>⁹² Joerger <i>et al.</i>³⁴ Teusink <i>et al.</i>⁹³
94	Gemtuzumab ozogamicin	Gemtuzumab is catabolised by proteolytic degradation to smaller peptides. No renal or hepatic clearance. The metabolic pathway of gemtuzumab ozogamicin is anticipated to be the release of N-acetyl-gamma-calicheamicin dimethylhydrazide by hydrolytic cleavage, which is further metabolised via non-enzymatic reduction.	EMA/FDA: CLcr ≥ 30 ml/min: no dose adjustment CLcr < 30 ml/min: not studied	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30ml/min: no need for dose adjustment is expected. HD: no need for dose adjustment is expected	FDA: Mild: no dose adjustment Moderate and severe: not studied EMA: Bilirubin ≤ 2 × ULN and AST/ALT ≤ 2.5 × ULN: no dose adjustment Bilirubin > 2 × ULN and AST/ALT > 2.5 × ULN: postpone until recovery	Mild: no dose adjustment is needed Moderate/severe: no need for dose adjustment is expected	Mylotarg label¹ SPC Mylotarg²

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
95	Gilteritinib	Gilteritinib is primarily metabolised by CYP3A4. Gilteritinib is mainly excreted in feces (64.5%) and to a lesser extent in urine (16.4%).	EMA/FDA: CLCr $\geq$ 30 ml/min: no dose adjustment CLCr < 30 ml/min: no data available	GFR $\geq$ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	EMA/FDA: Child-Pugh A/B or mild and moderate: no dose adjustment Child-Pugh C and severe: no data available	Child-Pugh A/B or mild/moderate: no dose adjustment is needed Child-Pugh C and severe: not recommended	Xospata label ¹ SPC Xospata ²
96	Glasdegib	Glasdegib is <i>in vitro</i> primarily metabolised by CYP3A4. CYP2C8 and UGT1A9 play a minor role in the metabolism of glasdegib. Glasdegib is mainly excreted in urine (48.9%, 17.2% unchanged) and in feces (41.7%, 19.5% unchanged).	EMA/FDA: Renal impairment: no dose adjustment is needed HD: no data available	GFR $\geq$ 60 ml/min: no dose adjustment is needed GFR < 60 ml/min: no dose adjustment is needed. HD: not recommended	EMA/FDA: Mild, moderate or severe: no dose adjustment	Hepatic impairment: no dose adjustment is needed	Daurismo label ¹ SPC Daurismo ²
97	Hydroxycarbamide (Hydroxyurea)	Hydroxycarbamide is for up to 60% metabolised in the liver. Hydroxycarbamide and its metabolites are excreted in urine (up to 80%).	FDA: CLCr < 60 ml/min: 50% of the original dose HD: 50% of the original dose following dialysis EMA: CLCr > 60 ml/min: no dose adjustment CLCr 30-60 ml/min: 50% of the original dose CLCr < 30 ml/min: not recommended Yan <i>et al.</i> CLCr $\geq$ 60 ml/min: AUC _{0-inf} 188% CLCr 30-59 ml/min: AUC _{0-inf} 170% CLCr 15-29 ml/min: AUC _{0-inf} 162% CLCr < 15 ml/min: AUC _{0-inf} 180% HD: AUC _{0-inf} 152%	GFR $\geq$ 60 ml/min: no dose adjustment is needed GFR < 60 ml/min: 50% of the original dose HD: 50% of the original dose following HD	FDA/ MHRA: Not studied	No need for dose adjustment is expected Monitor for haematological toxicity	Siklos label ¹ SPC Hydrea ² Yan <i>et al.</i> ⁹⁴
98	Ibrutinib	Ibrutinib is metabolised in the liver. The metabolite PCI-45227 contributes to the clinical effect. Ibrutinib and its metabolites are predominantly excreted in feces (80%, 1% unchanged)	FDA: CLCr > 25 ml/min: no dose adjustment CLCr $\leq$ 25 ml/min: not studied HD: not studied	Renal impairment: no dose adjustment is needed. HD: no need for dose adjustment is expected	EMA/FDA: Child-Pugh A: 280 mg (EMA) 140 mg (FDA) Child-Pugh B: 140 mg (EMA) 70 mg (FDA) Child-Pugh C: avoid	Child-Pugh A: 50% of the dose Child-Pugh B: 12.5% of the dose. Child-Pugh C: not recommended	Imbruvica label ¹ SPC Imbruvica ² Filanovsky <i>et al.</i> ⁹⁵ de Jong <i>et al.</i> ⁹⁶

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
		and with minimally in urine (<10%).	EMA: CLcr > 30 ml/min: no dose adjustment CLcr ≤ 30 ml/min: administer only if benefits outweigh the risks; closely monitor patient Filanovsky <i>et al.</i> Full dose (560 mg) was tolerated in a patient with CLcr 13 ml/min.		De Jong <i>et al.</i> Child-Pugh A: AUC _{0-inf} 265·20% (90% CI 138·34-508·41) Child-Pugh B: AUC _{0-inf} 795·84%(90% CI 456·87-1386·31) Child-Pugh C: AUC _{0-inf} 956·46%(90% CI 529·69-1691·15)		
99	Idarubicin	Idarubicin is extensively metabolised in the liver. Idarubicinol is the main active metabolite. Idarubicin and its metabolites are excreted in feces and urine, mostly as idarubicinol.	FDA Creatinine > ULN: consider dose reduction HD: not studied, unlikely to be dialysed MHRA Severe (creatinine > 2mg/dL): contraindicated Tsuchiya <i>et al.</i> HD: 67% of the original dose was tolerated and effective	GFR ≥ 30 ml/min: no need for dose adjustment is expected GFR < 30 ml/min: consider 67% of the original dose HD: consider 67% of the original dose	FDA : Bilirubin > ULN: consider dose reduction Bilirubin > 5 mg/dL: not recommended Patients with bilirubin 2·6-5 mg/dL received 50% of the original dose MHRA: Bilirubin ≥1·2-2 mg/dL: 50% of the original dose Severe (bilirubin > 2 mg/dL): contraindicated	Bilirubin 45 - 86 µmol/L: 50% of the original dose Bilirubin > 86 µmol/L: not recommended	Idamycin PSF label ¹ SPC Zavedos ⁹ Tsuchiya <i>et al.</i> ⁹⁷
100	Idelalisib	Idelalisib is metabolised in the liver. Idelalisib and its metabolites are mainly excreted in feces (78%, 12% unchanged) and to a lesser extent in urine (15%, 23% unchanged).	EMA/FDA: CLcr ≥ 15 ml/min: no dose adjustment is needed HD: not studied Jin <i>et al.</i> CLcr 15-29 ml/min: AUC _{0-inf} 127% (90% CI 92-176)	Renal impairment: No dose adjustment is needed HD: no need for dose adjustment is expected	FDA ALT or AST or bilirubin > ULN: no dose adjustment AST or ALT > 2·5 x ULN or bilirubin > 1·5 x ULN: limited information EMA: Child-Pugh A/B: no dose adjustment, intensified monitoring Child-Pugh C: limited information Jin <i>et al.</i> Child-Pugh B: AUC _{0-inf} 158% (90% CI 125-199%) Child-Pugh C: AUC _{0-inf} 159% (90%CI 121-208%)	Child-Pugh A or B: no dose adjustment is needed Child-Pugh C: start with 50% of the original dose (150 mg QD), increase if tolerated	Zydelig label ¹ SPC Zydelig ² Jin <i>et al.</i> ⁹⁸ Jin <i>et al.</i> ⁹⁹
101	Ifosfamide	Ifosfamide (prodrug) is metabolised in the liver to its active metabolites, one of which is the cytotoxic and	FDA: Not studied, monitor for toxicity and consider dose reduction.	GFR ≥ 50 ml/min: no dose adjustment is needed GFR < 50 ml/min or HD: not recommended	FDA: Not studied, give cautiously MHRA	Mild and moderate: no need for dose adjustment is expected. *	Ifex label ¹ SPC Ifosfamide injection 1 g ⁹ Carlson <i>et al.</i> ¹⁰⁰

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
		urotoxic acrolein.	HD: dialysed		Hepatic impairment: contraindicated	Severe: not recommended, due to risk of reduced efficacy* *due to limited information extrapolated from cyclophosphamide	
102	Imatinib	Imatinib is metabolised in the liver. The active metabolite CGP74588 contributes to the clinical effect. Imatinib and its metabolites are predominantly excreted in feces (68%, 20% unchanged) and to a lesser extent in urine (13%, 5% unchanged).	FDA: CLcr ≥ 60 ml/min: no dose adjustment CLcr 40-59 ml/min: no dose adjustment, max 600 mg CLcr 20-39 ml/min: 50% of the dose, max 400 mg CLcr < 20 ml/min: 100 mg EMA: Renal impairment or HD: minimum of 400 mg/day as starting dose Gibbons <i>et al.</i> CLcr 40-59 ml/min and CLcr 20-39 ml/min: significantly greater AUC _{0-inf} compared to normal renal function, no increase in toxicity. No requirement for initial dose adjustment in these patients. Pappas <i>et al.</i> HD: no change in imatinib and CGP74588 PK compared to normal renal function.	Renal impairment: no dose adjustment is needed HD: no dose adjustment is needed	FDA: Mild and moderate: no dose adjustment Severe: 75% of the original dose EMA: Hepatic impairment: minimum of 400 mg/day as starting dose Ramanathan <i>et al.</i> Mild and moderate: no change in AUC severe: approximately a 1.5 increase of AUC for imatinib and CGP74588,	Hepatic impairment: no dose adjustment is needed	Gleevec label ¹ Glivec SPC ² Gibbons <i>et al.</i> ¹⁰¹ Pappas <i>et al.</i> ¹⁰² Ramanathan <i>et al.</i> ¹⁰³
103	Infigratinib	Infigratinib is primarily metabolised by CYP3A4 (~94%). Infigratinib is mainly excreted in feces (77%, 3-4% unchanged) and to a lesser extent in urine (7-2%, 1-9% unchanged).	FDA: CLcr ≥ 30 ml/min: reduce dose to 100 mg QD for 21 days, followed by 7 days off therapy (28-day cycles) CLcr < 30 ml/min: no data available HD: no data available	GFR ≥ 30 ml/min: 80% of the original dose (100 mg QD) for 21 days, followed by 7 days off therapy (28-day cycles) GFR < 30 ml/min: not recommended HD: not recommended	FDA: Mild: 100 mg QD for 21 days, followed by 7 days off therapy (28-day cycles) Moderate: 75 mg QD for 21 days, followed by 7 days off therapy (28-day cycles) Severe: no data available	Mild: 80% of the original dose (100 mg QD) for 21 days, followed by 7 days off therapy (28-day cycles) Moderate: 60% of the original dose (75 mg QD) for 21 days, followed by 7 days off therapy (28-day cycles) Severe: not recommended	Truseltiq label ¹
104	Inotuzumab ozogamicin	Inotuzumab is catabolised by proteolytic degradation to smaller peptides. No renal or hepatic clearance.	EMA/FDA: CLcr ≥ 15 ml/min: no change in clearance HD: not studied	Renal impairment: no dose adjustment is needed HD: no need for dose	EMA/FDA: Mild: no dose adjustment Moderate and severe: not studied	Hepatic impairment: no need for dose adjustment is expected	Besponsa label ¹ SPC Besponsa ²

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
		N-acetyl- gamma-calicheamicin dimethylhydrazide is metabolised via non-enzymatic reduction.		adjustment is expected	Serious ongoing hepatic liver disease (e.g. cirrhosis): contraindicated		
105	Ipilimumab	Ipilimumab is catabolised by proteolytic degradation to smaller peptides. No renal or hepatic clearance.	EMA/FDA: CLcr ≥ 30 ml/min: no dose adjustment CLcr < 30 ml/min: no dose adjustment (FDA) not studied (EMA)	Renal impairment: no dose adjustment is needed HD: no need for dose adjustment is expected	EMA/FDA: Mild: no dose adjustment Moderate and severe: not studied	Hepatic impairment: no need for dose adjustment is expected	Yervoy label ¹ SPC Yervoy ²
106	Irinotecan	Irinotecan (prodrug) is converted in the liver to its active metabolite SN-38. SN-38 is glucuronidated to the inactive glucuronide metabolite SN-38G. Irinotecan and its metabolites are excreted in urine (11-20% unchanged) and in feces.	FDA: Renal impairment: not studied, use with caution HD: not recommended MHRA: Not recommended in renal impairment. Czock <i>et al.</i>, Stemmler <i>et al.</i> (weekly) HD: minimally dialysed, low clearance of SN-38. Dose escalation from 50 mg/m ² to 80 mg/m ² was tolerated. Fujita <i>et al.</i> (weekly/2-weekly) HD: SN-38 is partly dialysed (27-50% depending on the dialysis membrane). Elimination of SN-38 is significantly delayed in patients with renal failure. Venook <i>et al.</i> (3-weekly) No significant difference in irinotecan or its metabolites PK parameters for patients with CLcr 21-60 ml/min compared to patients with prior pelvic radiotherapy and	GFR ≥ 10 ml/min: no need for dose adjustment is expected GRF < 10 ml/min: start with 50-66% of the original dose, increase if tolerated HD: start with 50-66% of the original dose, increase if tolerated	FDA: Use with caution, not studied in patients with bilirubin > 2 mg/dl or transaminase > 3 x ULN (or transaminase > 5 x ULN in case of liver metastases). MHRA (3-weekly): Bilirubin < 1.5 x ULN: no dose adjustment Bilirubin 1.5 -3 x ULN: 200 mg/m ² . Bilirubin > 3 x ULN: contraindicated Raymond <i>et al.</i> (3-weekly) Reduced irinotecan clearance in hepatic impairment. Hyperbilirubinemia is associated with exponential decrease in clearance and increase in dose normalized AUC. Dose advice: bilirubin < 1.5 x ULN: 350 mg/m ² , bilirubin ≥ 1.5 to 3 x ULN: 200 mg/m ² . Schaaf <i>et al.</i> (weekly) Bilirubin 1.5-3.0 x ULN and ALT/AST ≤ 5.0 x ULN or bilirubin ≤ 1.5 x ULN and ALT/AST 5.1-20.0 x ULN: 60 mg/m ² . Bilirubin 3.1-5.0 x ULN and ALT/AST ≤ 5.0 x ULN 50	3-weekly Bilirubin ≥ 1.5 to 3 x ULN: 200 mg/m ² Bilirubin > 3 x ULN: not recommended Weekly Bilirubin 1.5-3.0 x ULN and ALT/AST ≤ 5.0 x ULN or bilirubin ≤ 1.5 x ULN and ALT/AST 5.1-20.0 x ULN: 60 mg/m ² Bilirubin 3.1-5.0 x ULN and ALT/AST ≤ 5.0 x ULN: 50 mg/m ² Bilirubin 1.5-3.0 x ULN and ALT/AST 5.1-20.0 x ULN: 40mg/m ²	Camptosar label ¹ SPC Campto ⁹ Czock <i>et al.</i> ¹⁰⁴ Stemmler <i>et al.</i> ¹⁰⁵ Fujita <i>et al.</i> ¹⁰⁶ Raymond <i>et al.</i> ¹⁰⁷ Schaaf <i>et al.</i> ¹⁰⁸ Venook <i>et al.</i> ¹⁰⁹

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
			creatinine < 1.5mg/dL.		mg/m ² ; bilirubin 1.5-3.0 x ULN and ALT/AST 5.1-20.0 x ULN: 40 mg/m ² . Similar SN-38 exposure and observed toxicities with these dose reductions compared to patients with normal liver function (despite lower irinotecan AUC _{0-24h}).		
107	Isatuximab	Isatuximab is catabolised by proteolytic degradation to smaller peptides. No renal or hepatic clearance.	EMA/FDA: CLcr ≥ 30 ml/min: no dose adjustment CLcr < 30 ml/min: no dose adjustment	Renal impairment: no dose adjustment is needed HD: no need for dose adjustment is expected	EMA/FDA: Mild: no dose adjustment Moderate and severe: not studied	Hepatic impairment: no dose adjustment is needed	Sarclisa label ¹ SPC Sarclisa ²
108	Ivosidenib	Only a limited part of ivosidenib is metabolised in the by CYP3A4. Ivosidenib is mainly excreted in feces (77%, 67% unchanged), and to a lesser extent in urine (17%, 10% unchanged).	FDA: eGFR ≥ 30 ml/min/1.73m ² : no dose adjustment eGFR < 30 ml/min/1.73m ² : no data available HD: no data available	eGFR ≥ 30 ml/min: no dose adjustment is needed eGFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	FDA: Child-Pugh A/B: no dose adjustment Child-Pugh C: no data available Fan et al. Child-Pugh A/B: a single dose of 500 mg ivosidenib was well tolerated. No increased risk compared to matched participants with normal hepatic function.	Child-Pugh A/B: no dose adjustment is needed Child-Pugh C: not recommended	Tibsovo label ¹ Fan et al. ¹¹⁰
109	Ixabepilone	Ixabepilone is extensively metabolised in the liver. Ixabepilone and its metabolites are predominantly excreted in feces (65%) and to a lesser extent in urine (21%), mostly as inactive metabolites.	FDA: CLcr > 30 ml/min: no meaningful effect on PK CLcr ≤ 30 ml/min: not studied	GFR > 30 ml/min: no dose adjustment is needed GFR ≤ 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	FDA: Monotherapy AST and ALT ≤ 2.5 x ULN and bilirubin ≤ ULN: 40 mg/m ² AST and ALT ≤ 10 x ULN and bilirubin ≤ 1.5 x ULN: 32 mg/m ² AST and ALT ≤ 10 x ULN and bilirubin > 1.5 x ULN - ≤ 3 x ULN: 20 mg/m ² , max 30 mg/m ² AST or ALT > 10 x ULN or bilirubin > 3 x ULN: not recommended Combined with capecitabine AST or ALT ≤ 2.5 x ULN and bilirubin ≤ 1 x ULN: No dose adjustment is needed AST or ALT > 2.5 x ULN or bilirubin > 1 x ULN:	Hepatic impairment: Adjust the dose according to FDA recommendations	Ixempra label ¹

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
					contraindicated		
110	Ixazomib	Ixazomib is metabolised in the liver. Ixazomib and its metabolites are predominantly excreted in feces (62%) and to a lesser extent in urine (22%, <3.5% unchanged).	EMA/FDA: CLcr $\geq$ 30 ml/min: no dose adjustment CLcr < 30 ml/min: 3 mg QD HD: 3 mg QD, not dialysed Gupta et al. CLcr < 30 ml/min or HD: AUC _{0-last} : 1.39 (90% 1.04-1.86), not dialysed.	GFR > 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: 75% of the original dose HD: 75% of the original dose	EMA/FDA: Mild: no dose adjustment Moderate and severe: 3 mg QD Gupta et al. Moderate (2.3 mg): dose-normalized AUC _{0-last} 1.27 (90% CI 1.27-2.11) Severe (1.5 mg): dose-normalized AUC _{0-last} 1.13 (90% CI 0.69-1.84)	Mild: no dose adjustment is needed Moderate and severe: 75% of the original dose	Ninlaro label ¹ SPC Ninlaro ² Gupta et al. ¹¹¹ Gupta et al. ¹¹²
111	Lapatinib	Lapatinib is metabolised in the liver. Lapatinib is predominantly excreted in feces (27% unchanged). Less than 2% is eliminated in urine.	EMA/FDA: CLcr $\geq$ 30 ml/min: no dose adjustment CLcr < 30 ml/min: not studied HD: unlikely to be dialysed Pai et al.: Following a 250 mg QD dose in end-stage renal disease patients on maintenance HD, PK parameters were comparable with those in healthy subjects. Renal impairment and HD seemed not to affect lapatinib pharmacokinetics.	GFR $\geq$ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	FDA: Child-Pugh A: not studied, no dose adjustment Child-Pugh B: 14% increase in AUC, no dose adjustment Child-Pugh C: 63% increase in AUC: 750 mg QD (HER2-positive metastatic breast cancer) or 1000 mg QD (hormone receptor and HER2-positive breast cancer) EMA: Child-Pugh A: not studied Child-Pugh B: 56% increase in AUC Child-Pugh C: 85% increase in AUC	Child-Pugh A/B: no dose adjustment is needed Child-Pugh C: 750mg QD (HER2 positive metastatic breast cancer) or 1000 mg QD (hormone receptor and HER2-positive breast cancer)	Tykerb label ¹ SPC Tyverb ² Pai et al. ¹¹³
112	Larotrectinib	Larotrectinib is predominantly metabolised by CYP3A4. Larotrectinib and its metabolites are mainly excreted in feces (58%, 5% unchanged) and urine (39%, 20% unchanged).	EMA/FDA: Renal impairment: no dose adjustment HD: 1.5-fold increase in AUC _{0-inf} ; no dose adjustment recommended	Renal impairment: no dose adjustment is needed HD: no need for dose adjustment is expected	EMA/FDA: Mild: no dose adjustment is needed Moderate and severe: 50% dose reduction Child-Pugh A: 1.3-fold increase in AUC _{0-inf} Child-Pugh B: 2-fold increase in AUC _{0-inf} Child-Pugh-C: 3.2-fold increase in AUC _{0-inf}	Child-Pugh A: no dose adjustment is needed Child-Pugh B/C: 50% of original dose	Vitrakvi label ¹ SPC Vitrakvi ²
113	Lenalidomide	Lenalidomide is not metabolised by CYP enzymes in humans. Lenalidomide is mainly excreted in urine (90%, 82% unchanged) and	EMA/FDA: Lenalidomide is substantially excreted by the kidney. Therefore care should be taken in dose selection and	GFR $\geq$ 50 ml/min: no dose adjustment is needed GFR < 50 ml/min dose reductions per indication according to drug label	EMA/FDA Lenalidomide has not formally been studied in patients with hepatic impairment	Hepatic impairment: no need for dose adjustment is expected	Revlimid label ¹ SPC Revlimid ²

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
		minorly in feces (4%).	monitoring of renal function is advised in patients with renal impairment.	HD: dose reductions per indication according to the drug label			
114	Lenvatinib	Lenvatinib is metabolised in the liver. Lenvatinib and its metabolites are mainly excreted in feces (64%) and to a lesser extent in urine (24%), with approximately 2% as intact Lenvatinib.	EMA/FDA: CLcr ≥ 30 ml/min: no dose adjustment CLcr < 30 ml/min: Renal cell carcinoma (RCC): 10 mg QD; differentiated thyroid carcinoma (DTC): 14 mg QD; endometrial carcinoma (EC): 10 mg QD; hepatocellular carcinoma (HCC): not studied (EMA) HD: not studied (FDA), not recommended (EMA)	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: 50 % of the original dose (RCC and EC 10 mg QD, DTC: 14 mg QD) HD: 50% of the original dose may be considered	EMA/FDA: Child-Pugh A/B: no dose adjustment Child-Pugh C: RCC and EC 10 mg QD, DTC 14 mg QD, HCC not recommended (EMA) Shumaker <i>et al.</i> Child-Pugh A: AUC _{0-inf} 1·2 (90% CI 0·8-1·8) Child-Pugh B: AUC _{0-inf} 1·1 (90% CI 0·7-1·6) Child-Pugh C: AUC _{0-inf} 1·8 (90% CI 1·2-2·7)	Child-Pugh A/B: no dose adjustment is needed Child-Pugh C: 50% of the original dose (RCC and EC 10 mg QD, DTC 14 mg QD)	Lenvima label ¹ SPC Lenvima ² SPC Kispix ² Shumaker <i>et al.</i> ¹¹⁴
115	Letrozole	Letrozole is metabolised in the liver. Letrozole and its metabolites are mainly excreted in urine (90%, 6% unchanged).	FDA/MHRA: CLcr ≥ 10 ml/min: no dose adjustment HD: not studied	Renal impairment: no dose adjustment is needed HD: no need for dose adjustment is expected	FDA: Child-Pugh A/B: no dose adjustment Child-Pugh C/cirrhosis: 50% (2·5 mg every other day) MHRA: Child-Pugh A/B: no dose adjustment Child-Pugh C: 95% increase in AUC, administer with caution	Child-Pugh A/B: no dose adjustment is needed Child-Pugh C: 50% of the original dose (2·5mg every other day)	Femara label ¹ SPC Femara ⁹
116	Lomustine	Lomustine is rapidly metabolised to its active metabolites. Its metabolites are mainly excreted in urine.	FDA: Renal impairment: not studied HD: not studied MHRA: CLcr < 30 ml/min: contraindicated Kintzel <i>et al.</i> CLcr 60 ml/min: 75% of the original dose CLcr 45 ml/min: 70% of the original dose CLcr 30 ml/min: not recommended	GFR > 50 ml/min: no dose adjustment is needed GFR 30-50 ml/min: 75% of the original dose GFR < 30 ml/min: not recommended HD: not recommended	FDA/ MHRA: Hepatic impairment: not studied	Mild and moderate: no need for dose adjustment is expected Severe: not recommended	Gleostine label ¹ SPC lomustine medac ⁹ Kintzel <i>et al.</i> ⁴²
117	Loncastuximab tesirine	The monoclonal antibody portion (loncastuximab) is	FDA: CLcr ≥ 30 ml/min: no clinically	GFR ≥ 30 ml/min: no dose adjustment is needed	FDA: Mild: no dose adjustment	Mild: no dose adjustment is needed	Zynlonta label ¹

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
		expected to undergo proteolytic degradation to smaller peptides. No renal or hepatic elimination. Tesirine (SG3199) is metabolised by CYP3A4/5. Tesirine is expected to be minimally renally excreted.	significant differences in PK CLcr 15-29 ml/min: not studied HD: not studied	GFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	Moderate and severe: not studied	Moderate and severe: not recommended	
118	Lorlatinib	Lorlatinib is <i>in vitro</i> primarily metabolised by CYP3A4 and UGT1A4, with minor contribution of CYP2C8, CYP2C19, CYP3A5 and UGT1A3. The major metabolite is inactive. Unchanged lorlatinib was the major component in plasma (44%). 47.7% (<1% unchanged) was recovered in urine and 40.9% (9.1% unchanged) is recovered in feces.	EMA/FDA: CLcr ≥ 30 ml/min: no dose adjustment CLcr < 30 ml/min and HD: not studied and therefore not recommended	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no dose adjustment expected though monitor for toxicity due to potentially increased exposure HD: not recommended	EMA/FDA: Mild: no dose adjustment Moderate and severe: not studied and therefore not recommended	Mild: no dose adjustment is needed Moderate: no dose adjustment expected though monitor for toxicity due to potentially increased exposure Severe: not recommended	Lorviqua label ¹ SPC Lorviqua ²
119	Lurbinectedin	Lurbinectedin is metabolised by CYP3A4, <i>in vitro</i> . Lurbinectedin is mainly excreted in feces (89%, < 0.2 unchanged) and to a lesser extent in urine (6%, 1% unchanged).	FDA: CLcr ≥ 30 ml/min: no dose adjustment CLcr < 30 ml/min: no data available	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	FDA: Mild: no dose adjustment Moderate and severe: no data available	Mild: no dose adjustment is needed Moderate and severe: not recommended	Zepzelca label ¹
120	Margetuximab	Margetuximab is catabolised by proteolytic degradation to smaller peptides. No renal or hepatic clearance.	FDA: CLcr ≥ 30 ml/min: no dose adjustment CLcr < 30 ml/min: no data available	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	FDA: Mild: no dose adjustment Moderate and severe: no data available	Mild: no dose adjustment is needed Moderate and severe: no need for dose adjustment is expected	Margenza label ¹
121	Melphalan	Melphalan is hydrolyzed in plasma to inactive metabolites. Approximately 10% is excreted in urine unchanged.	FDA/MHRA Oral: no dose advice given HD: not dialysed FDA: (IV) Consider 50% of the dose if Blood Urea Nitrogen ≥ 30mg/dL for palliative treatment	Conditioning treatment Renal impairment/HD: no need for dose adjustment is expected Palliative treatment GFR 30-50 ml/min: consider 50% of the dose GFR < 30 ml/min or HD: not recommended	FDA/MHRA: Hepatic impairment: not studied	Hepatic impairment: no need for dose adjustment is expected	Evomela/Alkeran label ¹ SPC Alkeran/Melphalan hydrochloride ⁹ Kergueris <i>et al.</i> ¹¹⁵

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
			MHRA: (IV) CLcr 30-50 ml/min: 50% of the original dose CLcr < 30 ml/min: high-dose melphalan contraindicated Kergueris et al. PK parameters correlated with creatinine clearance. Renal impairment did not result in a large decrease in CL compared to inter-individual variation in CL				
122	Melphalan flufenamide	Melphalan flufenamide is rapidly distributed to peripheral tissue with no late redistribution back to plasma. Melphalan flufenamide is metabolised in tissue to desethyl-melphalan flufenamide and melphalan. Renal and hepatic excretion of unchanged melphalan flufenamide is negligible	EMA: eGFR > 45 ml/min/1.73m ² : no dose adjustment eGFR 30-45 ml/min/1.73m ² : dose adjustment to 30 mg (75% of original dose) eGFR < 30 ml/min/1.73m ² : no data available FDA CLcr 45-89 ml/min: no dose adjustment CLcr 15-44 ml/min: no data available	eGFR > 45 ml/min 1.73m ² : no dose adjustment is needed eGFR 30-45 ml/min: 75% of the original dose eGFR < 30 ml/min: not recommended HD: not recommended	EMA/FDA: Mild: no dose adjustment Moderate and severe: no data available	Mild: no dose adjustment is needed Moderate and severe: no need for dose adjustment is expected	Pepaxti label ¹ SPC Pepaxti ²
123	Mercaptopurine	Mercaptopurine (prodrug) is metabolised in the liver to form among others, active 6- thioguanine nucleotides. The main elimination route of 6- mercaptopurine is by metabolism. Xanthine oxidase converts 6- mercaptopurine into the inactive metabolite 6- thiouric acid, which is excreted in urine. About 46% of het dose is excreted in urine (approximately 7% unchanged)	EMA/FDA: Not studied, consider dose reduction, starting at the low end of dosing range, or increasing the dosing interval to 36-48 hours. HD: no clearance expected	GFR ≥ 30 ml/min: no need for dose adjustment is expected GFR < 30 ml/min: increase dosing interval to 48 hours HD: not recommended	EMA/FDA: Not studied, consider dose reduction, starting at the low end of dosing range.	Mild : no need for dose adjustment is expected Moderate: consider starting with a lower dose or increase dosing interval. Severe: not recommended	Purinethol/Purixan label ¹ SPC Xaluprine ²
124	Methotrexate	Methotrexate is partly metabolised in the liver. Methotrexate and its metabolites are mainly excreted in urine by	FDA Reduced clearance in renal impairment. No dose advice given.	GFR ≥ 50 ml/min: no dose adjustment is needed GFR 20-50 ml/min: 50% of the original dose GFR < 20 ml/min not	FDA No advice given MHRA: Bilirubin > 5 mg/dL:	Hepatic impairment: no need for dose adjustment is expected Bilirubin > 86	Methotrexate injection USP label ¹ Methotrexate concentration for solution for infusion ⁹

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
		glomerular filtration and active tubular secretion (80-90% unchanged). Excretion in feces is minimal (10% or less).	MHRA: CLcr > 50 ml/min: no dose adjustment CLcr 20-50 ml/min: 50% of the dose CLcr < 20 ml/min: not recommended Conventional HD and peritoneal dialysis: not dialysed Wall <i>et al.</i> HD: approximately 63% of infused methotrexate removed by 6 hours of high-flux dialysis initiated 1 hour after administration	recommended. If unavoidable consider HD HD: not recommended, if unavoidable 50% of the original dose, can be dialysed with daily high flux dialysis.	contraindicated	µmol/L: avoid use	Wall <i>et al.</i> ¹¹⁶
125	Midostaurin	Midostaurin is metabolised in the liver. The metabolites CGP62221 and CGP52421 contribute to the clinical effect. Midostaurin and its metabolites are predominantly excreted in feces (78-95%, mostly as metabolites) and to a minimal extent in urine (5%).	EMA/FDA: CLcr ≥ 30 ml/min: no clinically meaningful effect on PK, no dose adjustment CLcr < 30 ml/min: not studied Tollkuci <i>et al.</i> HD: full dose was tolerated and effective	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	FDA: Mild and moderate: no clinically meaningful effect on PK Severe: not studied EMA: Child-Pugh A/B: no dose adjustment Child-Pugh C: not studied	Mild and moderate: no dose adjustment is needed Severe: not recommended	Rydapt Label ¹ SPC Rydapt ² Tollkuci <i>et al.</i> ¹¹⁷
126	Mirvetuximab soravtansine-gynx	The monoclonal antibody portion of mirvetuximab soravtansine-gynx is expected to be metabolised into small peptides by catabolic pathways. Unconjugated DM4 (the small molecule) and S-methyl-DM4 undergo metabolism by CYP3A4. S-methyl DM4 and DM4-sulfo-SPDB-lysine were detected in urine within 24 hours of infusion as the main metabolites.	FDA: CLcr ≥ 30 ml/min: no dose adjustment is recommended CLcr < 30 ml/min: not studied.	GFR ≥ 30 ml/min: no dose adjustment is needed. GFR < 30 ml/min: not recommended.	FDA: Mild (TB ≤ ULN and AST > ULN or TB > 1 to 1.5 times ULN and any AST): no dose adjustment needed. Moderate or severe (TB > 1.5 ULN): avoid use.	Mild: no need for dose adjustment. Moderate and severe: not recommended.	Mirvetuximab soravtansine-gynx label ¹
127	Mitomycin	Mitomycin is metabolised and inactivated in the liver but also in other tissues. Excretion is mainly in feces	MHRA: Renal impairment: not studied	GFR ≥ 30 ml/min: no need for dose adjustment is expected GFR < 30 ml/min: not	MHRA: Hepatic impairment: not studied	Mild and moderate: no need for dose adjustment is expected Severe: consider 50% of	Jelcyto label ¹ Mitomycin-C Kyowa SPC ⁹

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
		and to a lesser extent in urine (approximately 10% unchanged)	FDA: GFR < 30 ml/min: no data available, avoid use	recommended HD: not recommended due to nephrotoxicity		the original dose	
128	Mitotane	Mitotane is metabolised in the liver to a water soluble metabolite. Its metabolites are slowly excreted in urine (10%) and a variable amount (1-17%) in feces.	FDA: Renal impairment: no advice given EMA: CLcr ≥ 30 ml/min: exercise caution, monitor mitotane plasma levels CLcr < 30 ml/min: not recommended	Renal impairment: no need for dose adjustment is expected HD: no need for dose adjustment is expected	EMA/FDA: Hepatic impairment: not studied, use with caution Monitor mitotane plasma levels (EMA) Severe: not recommended (EMA)	Mild and moderate: no need for dose adjustment is expected. Severe: not recommended	Lysodren label ¹ SPC Lysodren ²
129	Mitoxantrone	Mitoxantrone is metabolised in the liver. Mitoxantrone and its metabolites are slowly excreted in feces (18%) and urine (10%, of which 65% unchanged).	MHRA: Renal impairment: not studied, use with caution HD: not studied Boros et al. HD: not dialysed	Renal impairment: no need for dose adjustment is expected HD: no need for dose adjustment is expected	MHRA: Hepatic impairment: not studied, use with caution Savaraj et al. Total clearance in patients with liver dysfunction or ascites was less than 50% of that observed in patients without liver dysfunction or ascites.	Mild and moderate: no need for dose adjustment is expected Severe: consider 50% of the original dose	SPC Mitoxantrone 2 mg/ml concentrate for solution for infusion (Accord Healthcare Limited) ⁹ Boros et al. ¹¹⁸ Savaraj et al. ¹¹⁹
130	Mobocertinib	Mobocertinib is metabolised in the liver by CYP3A to equipotent metabolites. Mobocertinib is mainly excreted in feces (76%, 6% unchanged), and to a lesser extent in urine (4%, 1% unchanged)	FDA: eGFR ≥ 30 ml/min/1.73m ² : no dose adjustment eGFR < 30 ml/min/1.73m ² : not studied	eGFR ≥ 30 ml/min: no dose adjustment is needed eGFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	FDA: Mild and moderate: no dose adjustment Severe: not studied	Mild and moderate: no dose adjustment is needed Severe: not recommended	Exkivity label ¹
131	Mogamulizumab	Mogamulizumab is catabolised by proteolytic degradation to smaller peptides. No renal or hepatic clearance.	EMA/FDA: Renal impairment: no clinically significant PK changes Yoshihara et al. HD: not dialysed, no dose adjustment is needed	Renal impairment: no dose adjustment is needed HD: no dose adjustment is needed	EMA/FDA: Mild and moderate: no clinically significant changes in PK Severe: not studied	Mild and moderate: no dose adjustment is needed Severe: no need for dose adjustment is expected	Potelegeo label ¹ SPC Poteligeo ² Yoshihara et al. ¹²⁰
132	Mosunetuzumab	Mosunetuzumab is expected to be catabolised by proteolytic degradation to smaller peptides. No renal or hepatic clearance.	EMA/FDA: CLcr ≥ 30 ml/min: no dose adjustment CLcr < 30 ml/min: not studied HD: not studied	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected	EMA/FDA: Mild: no dose adjustment Moderate and severe: not studied	Mild: no dose adjustment is needed Moderate and severe: no need for dose adjustment is expected	Lunsumio label ¹ SPC Lunsumio ²

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
				HD: no need for dose adjustment is expected			
133	Necitumumab	Necitumumab is catabolised by proteolytic degradation to smaller peptides. No renal or hepatic clearance.	FDA: CLcr: ≥ 11 ml/min: No influence on exposure	Renal impairment: no dose adjustment is needed HD: no need for dose adjustment is expected	FDA: Mild and moderate: no influence on exposure Severe: not studied	Mild and moderate: no dose adjustment is needed Severe: no need for dose adjustment is expected	Label Portrazza ¹
134	Nelarabine	Nelarabine (prodrug) is metabolised by adenosine deaminase to its metabolite (ara-G), which is intracellularly phosphorylated to the active metabolite (ara-GTP) Nelarabine (5-10%) and ara-G (20-30%) are partially eliminated in urine.	EMA/FDA: CLcr ≥ 50 ml/min: no dose adjustment CLcr < 50 ml/min: not studied HD: not studied	Renal impairment: no need for dose adjustment is expected. HD: no need for dose adjustment is expected	EMA/FDA: Hepatic impairment: not studied	Hepatic impairment: no need for dose adjustment is expected	Arranon label ¹ Atriance SPC ²
135	Neratinib	Neratinib is metabolised in the liver. The metabolites M3, M6, M7 and M11 contribute to the clinical effect. Neratinib and its metabolites are predominantly excreted in feces (97.1%) with minimal excretion in urine (1.1%).	FDA: Renal impairment: no clinically significant effect on PK HD: not studied EMA: CLcr ≥ 30 ml/min: no dose adjustment CLcr < 30 ml/min or HD: not studied	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	EMA/FDA: Child-Pugh A/B: no dose adjustment Child-Pugh C: 2-8-fold increase of AUC 80 mg QD (33% of the original dose) (FDA), not recommended (EMA).	Child-Pugh A/B: no dose adjustment is needed Child-Pugh C: 33% of the original dose	Nerlynx label ¹ SPC Nerlynx ²
136	Nilotinib	Nilotinib is metabolised in the liver. Nilotinib and its metabolites are predominantly excreted in feces (93-94%, 69% unchanged).	EMA/FDA: Renal impairment: not studied Onaka et al. HD: not dialysed, dose adjustment AUC similar to previously reported in patients with normal renal function	Renal impairment: no need for dose adjustment is expected HD: no need for dose adjustment is expected	FDA: Newly diagnosed Ph+ Chronic Myelogenous Leukemia (CML) Child-Pugh A-C: start at 200 mg BID, max 300 mg BID Resistant or chronic phase Ph+ CML Child-Pugh A-B: start at 300 mg BID, max 400 mg BID Child-Pugh C: start at 200 mg BID, max 400 mg BID EMA: No dose adjustment is needed	Hepatic impairment: no dose adjustment is needed	Tasigna label ¹ Tasigna SPC ² Onaka et al. ¹²¹ Yin et al. ¹²²

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
					Yin et al. Child-Pugh A: AUC _{0-inf} : 1.35 (90% CI 0.91-2.02) Child-Pugh B: AUC _{0-inf} : 1.35 (90% CI 0.89-2.07) Child-Pugh C: AUC _{0-inf} : 1.19 (90% CI 0.80-1.78)		
137	Nilutamide	Nilutamide is extensively metabolised in the liver, less than 2% is excreted unchanged. Two metabolites contribute to the clinical effect. The metabolites of nilutamide are slowly excreted in urine (62%) with minimal fecal elimination	FDA: Renal impairment: not studied HD: not studied	Renal impairment: no need for dose adjustment is expected HD: no need for dose adjustment is expected	FDA: Hepatic impairment: not studied Severe: contraindicated	Mild and moderate: no need for dose adjustment is expected Severe: not recommended due to risk of hepatotoxicity	Nilandron label ¹
138	Nintedanib	Nintedanib is metabolised in the liver, mainly to inactive metabolites. Nintedanib and its metabolites are predominantly excreted in feces/bile (93.4%) with minimal renal excretion (<1%).	EMA: CLcr ≥ 30 ml/min: no dose adjustment CLcr < 30 ml/min: not studied HD: not studied	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected.	EMA: Child-Pugh A: no dose adjustment Child-Pugh B and C: not recommended Marzin et al. Child-Pugh A: AUC _{0-inf} : 215.4% (90% CI 121-384%) Child-Pugh B : AUC _{0-inf} : 867.1% (90% CI 573-1312%) Okusaka et al. Slightly higher exposure (37% increase) in patients with Child-Pugh score 7 compared to patients with score 5-6. MTD 200 mg BID for both groups.	Child-Pugh A: consider 50% of the original dose Child-Pugh B and C: not recommended	SPC Vargatef ² Marzin et al. ¹²³ Okusaka et al. ¹²⁴
139	Niraparib	Niraparib is metabolised via amide hydrolysis by carboxylesterases forming the inactive metabolite M1. Niraparib is eliminated by hepatobiliary (38.8%) and renal routes (47.5%). In urine niraparib was mainly recovered as metabolites, in the feces primarily as unchanged niraparib	EMA/FDA: CLcr ≥ 30 ml/min: no dose adjustment CLcr < 30ml/min: no data available HD: no data available	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	FDA: Mild: no dose adjustment Moderate: 200 mg QD Severe: not studied EMA: Mild: no dose adjustment Moderate: recommended starting dose 200 mg QD (33% dose reduction) Severe: no data available Akce et al. Moderate: AUC _{0-inf} : 1.5639 (90% CI 1.0618-2.3034)	Mild: no dose adjustment is needed Moderate and severe: 66% of the original dose	Zejula label ¹ SPC Zejula ² Akce et al. ¹²⁵

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
140	Nivolumab	Nivolumab is catabolised by proteolytic degradation to smaller peptides. No renal or hepatic clearance.	EMA/FDA: GFR ≥ 30 ml/min: no dose adjustment GFR < 30 ml/min: no dose adjustment (FDA), not studied (EMA)	Renal impairment: no dose adjustment is needed HD: no need for dose adjustment is expected	EMA/FDA: Mild: no dose adjustment Moderate: no dose adjustment (FDA), not studied (EMA) Severe: not studied	Mild and moderate: no dose adjustment is needed Severe: no need for dose adjustment is expected	Opdivo label ¹ SPC Opdivo ²
141	Nivolumab/relatlimab	Nivolumab and relatlimab are catabolised by proteolytic degradation to smaller peptides. No renal or hepatic clearance.	EMA: CLcr ≥ 30 ml/min: no dose adjustment CLcr < 30 ml/min: limited data available FDA: eGFR ≥ 30 ml/min/1.73m ² : no dose adjustment eGFR < 30 ml/min/1.73m ² : no data available	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	EMA/FDA: Mild and moderate: no dose adjustment Severe: limited data available	Mild and moderate: no dose adjustment is needed Severe: no need for dose adjustment is expected	Opdualag label ¹ SPC Opdivo ²
142	Obinutuzumab	Obinutuzumab is catabolised by proteolytic degradation to smaller peptides. No renal or hepatic clearance.	FDA: No effect of baseline CLcr on PK. EMA: CLcr ≥ 30 ml/min: no dose adjustment CLcr < 30ml/min: not studied	Renal impairment: no dose adjustment is needed HD: no need for dose adjustment is expected	EMA/FDA: Not studied in patients with hepatic impairment	Hepatic impairment: no need for dose adjustment is expected	Label Gazyva ¹ SPC Gazyvaro ²
143	Ofatumumab	Ofatumumab is catabolised by proteolytic degradation to smaller peptides. No renal or hepatic clearance.	EMA/FDA: CLcr ≥ 30 ml/min: no dose adjustment CLcr < 30 ml/min: not studied	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	EMA/FDA: Hepatic impairment: not studied	Hepatic impairment: no need for dose adjustment is expected	Label Arzerra ¹ SPC Arzerra ²
144	Olaparib	Olaparib is extensively metabolised in the liver. Olaparib and its metabolites are excreted both in urine (approximately 44%) and feces (approximately 42%), mostly as metabolites.	EMA/FDA: CLcr 51-80 ml/min: no dose adjustment CLcr 31-50 ml/min: 200 mg BID CLcr < 30 ml/min: not studied, not recommended (EMA) HD: not studied Pilla Reddy et al. CLcr < 30 ml/min: PBPK predicted AUC ratio 2.21 (90% CI 2.19–2.22) Rolfo et al.	GFR > 50 ml/min: no dose adjustment GFR 30-50 ml/min: approximately 70 % of the original dose (200mg BID) GFR < 30 ml/min: consider 50% of the dose HD: consider 50% of the original dose	EMA/FDA: Child-Pugh A/B: no dose adjustment is needed Child-Pugh C: not studied, not recommended (EMA) Pilla Reddy et al. Child-Pugh C: PBPK predicted AUC ratio between 1.06 (90% CI 1.03 - 1.08) and 3.88 (3.74 - 4.02) Rolfo et al. Based on a PK assessment, no safety signals were detected in patients with mild/moderate	Child-Pugh A/B: no dose adjustment is needed Child-Pugh C: consider 50% of the original dose	Lynparza label ¹ SPC Lynparza ² Pilla Reddy et al. ¹²⁶ Baum et al. ¹²⁷ Rolfo et al. ¹²⁸ Rolfo et al. ¹²⁹

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
			CLcr 60-89 ml/min: AUC ratio 1.24 (90% CI 1.06-1.47) CLcr 30-59 ml/min: AUC ratio 1.44 (90% CI 1.10-1.89) Baum <i>et al.</i> A dose of 200 mg BID was well tolerated by one patient with HD.		hepatic impairment.		
145	Olaratumab	Olaratumab is catabolised by proteolytic degradation to smaller peptides. No renal or hepatic clearance.	FDA: CLcr ≥ 30 ml/min: no clinically important effect on PK CLcr < 30 ml/min: not studied HD: not studied	Renal impairment: no need for dose adjustment is expected HD: no need for dose adjustment is expected	FDA: Mild and moderate: no clinically important effect on PK Severe: not studied	Mild and moderate: no need for dose adjustment is expected Severe: no need for dose adjustment is expected	Label Lartruvo ¹
146	Olutasidenib	Olutasidenib is primarily (90%) metabolised by cytochrome P450(CYP)3A4, with minor contributions from CYP2C8, CYP2C9, CYP1A2, and CYP2C19. Approximately 75% of olutasidenib was recovered in feces (35% unchanged) and 17% in the urine (1% unchanged).	FDA: CLcr ≥ 30 ml/min: no dosage modification is recommended. CLcr < 30 ml/min or HD: not studied.	GFR ≥ 30 ml/min: no dose adjustment is needed. GFR <30 ml/min or HD: no need for dose adjustment is expected.	FDA: Mild and moderate: no dose modification is recommended. Severe: not studied.	Mild and moderate: no need for dose adjustment. Severe: not recommended.	Olutasidenib label ¹
147	Omacetaxine mepesuccinate	Omacetaxine mepesuccinate is primarily metabolised by plasma-esterases with little hepatic metabolism. Omacetaxine and its metabolites are excreted in feces (44%) and urine (37%).	FDA: Renal impairment: not studied HD: not studied	Renal impairment: no need for dose adjustment is expected HD: no need for dose adjustment is expected	FDA: Hepatic impairment: not studied	Hepatic impairment: no need for dose adjustment is expected	Synribo label ¹
148	Osimertinib	Osimertinib is metabolised in the liver. Two metabolites (AZ7550 and AZ5104) contribute to the pharmacological effect. Osimertinib is primarily excreted in feces (68%, 1.2% unchanged) and to a lesser extent in urine (14%, 0.8% unchanged), mostly as metabolites.	EMA/FDA: CLcr ≥ 15 ml/min: no dose adjustment CLcr < 15 ml/min: not studied HD: not studied Tamura <i>et al.</i> HD: not dialysed, full dose was tolerated. Vishwanathan <i>et al.</i> No dose adjustment is required for patients with	Renal impairment: no dose adjustment is needed HD: no need for dose adjustment is expected	EMA/FDA: Mild or moderate or Child-Pugh A/B: no dose adjustment Severe or Child-Pugh C: not studied	Mild and moderate or Child-Pugh A/B: no dose adjustment Severe or Child-Pugh C: 50% of the original dose may be considered	Tagrisso label ¹ SPC Tagrisso ² Tamura <i>et al.</i> ¹³⁰ Vishwanathan <i>et al.</i> ¹³¹

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
			CrCL < 30 ml/min				
149	Oxaliplatin	Oxaliplatin is not metabolised. It is highly protein bound (>90%). Oxaliplatin is mainly excreted in urine (54%) and minimally in feces (<3%).	FDA/MHRA CLcr 30-80 ml/min: no dose adjustment CLcr < 30 ml/min: 65 mg/m² (FDA), contraindicated (MHRA) Gori et al., Watayo et al. HD: administration of 50% of the original dose with HD directly or 1.5 hours after administration resulted in AUC comparable to normal renal function. Takimoto et al. Decreased CLcr correlated strongly with decrease in clearance of plasma ultrafiltrable platinum ($r^2 = 0.765$), no corresponding increase in toxicity was observed in patients with normal, mild (CLcr 40-59 ml/min) and moderate (CLcr 20-39 ml/min) renal function.	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: consider 50% of the original dose HD: consider 50% of the original dose, HD within 1.5 hour after administration.	FDA/MHRA: Hepatic impairment: not studied Synold et al. Mild, moderate, severe and liver transplantation: full dose (130 mg/m²) was tolerated, platinum clearance was not correlated with any liver function variable (bilirubin, AST or AP).	Hepatic impairment: No dose adjustment is needed	Eloxatin label¹ SPC Eloxatin⁹ Gori et al.¹³² Watayo et al.¹³³ Takimoto et al.¹³⁴ Synold et al.¹³⁵
150	Nab-paclitaxel	Nab-paclitaxel is a nanoparticle albumin-bound form of paclitaxel. Paclitaxel is metabolised in the liver. Paclitaxel and its metabolites are mainly excreted in feces (approximately 20%) and minimally in urine (4%, < 1% unchanged).	EMA/FDA: CLcr ≥ 30 ml/min: no dose adjustment required CLcr < 30 ml/min: insufficient data, no advise given	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected.	FDA: Mild: no dose adjustment required Moderate and severe: metastatic breast carcinoma (MBC) 77% of original dose (200mg/m²), non-small cell lung cancer (NSCLC) 80% of original dose (80mg/m²), pancreatic adenocarcinoma not recommended Bilirubin > 5 x ULN or AST > 10 x ULN: not recommended EMA: Mild: No dose adjustment required Moderate and severe: 80% of original	Mild: no dose adjustment is needed Moderate and severe: MBC or NSCLC: approximately 80% of original dose, pancreatic adenocarcinoma: contraindicated Bilirubin > 5 x ULN or AST > 10 x ULN: contraindicated	Abraxane label¹ SPC Abraxane² Biakhov et al.¹³⁶

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
					dose (MBC 200mg/m², NSCLC 80 mg/m²), pancreatic adenocarcinoma insufficient data, not recommended Bilirubin > 5 x ULN or AST > 10 x ULN: insufficient data, not recommended Biakhov <i>et al.</i> The recommended modification schema of solvent-based paclitaxel was tested for nab-paclitaxel and resulted in an acceptable safety and pharmacokinetic profile (bilirubin ≤ 1.25 x ULN: 100% of the dose; bilirubin 1.26-2 x ULN: 80% of the dose; bilirubin 2.01-5 x ULN: 50% of the dose).		
151	Paclitaxel	Paclitaxel is metabolised in the liver by CYP2C8 and CYP3A4. Paclitaxel and its metabolites are predominantly excreted in feces (71%) and to a lesser extent in urine (14%).	FDA: No advise given MHRA: Renal impairment: not studied, no dose advise given HD: pharmacokinetic properties in one patient undergoing HD in range with non-dialysis patients Tomita <i>et al.</i> Paclitaxel is not dialysed. AUC and C_{max} were comparable to values reported in patients with normal renal function. Gelderblom <i>et al.</i> 1.5-2-fold higher paclitaxel AUC value in a patient with CLcr 20 ml/min compared to values reported in patients with normal renal function. However, no major hematological toxicity was observed.	Renal impairment: no need for dose adjustment is expected HD: no need for dose adjustment is expected	FDA: 24-hour infusion: Transaminase < 2 x ULN and bilirubin ≤ 1.5 mg/dL: no dose reduction (135 mg/m²) Transaminase 2-10 x ULN and bilirubin ≤ 1.5 mg/dL: 74% of original dose (100mg/m²) Transaminase < 10 x ULN and bilirubin 1.6-7.5 mg/dL: 37% of original dose (50 mg/m²) Transaminase ≥ 10 x ULN or bilirubin > 7.5 mg/dL: not recommended 3-hour infusion: Transaminase < 10 x ULN and bilirubin ≤ 1.25 x ULN: no dose reduction (175 mg/m²) Transaminase < 10 x ULN and bilirubin 1.26-2 x ULN: 77% of original dose (135mg/m²) Transaminase < 10 x ULN and bilirubin 2.01-5xULN: 51% of original dose (90mg/m²) Transaminase ≥	24-hour infusion: Transaminases < 2 x ULN and bilirubin ≤ 26 µmol/l: no dose adjustment is needed (135mg/m²) Transaminases 2-10 x ULN and bilirubin ≤ 26 µmol/l: 74% of original dose (100mg/m²) Transaminases < 10 x ULN and bilirubin 27-128 µmol/l: 37% of original dose (50mg/m²) Transaminases ≥ 10 x ULN or bilirubin > 128 µmol/l: contraindicated 1 to 3-hour infusion (regardless of interval): Transaminases < 10xULN and bilirubin ≤ 1.25xULN: no dose reduction.	Taxol label¹ Paclitaxel SPC⁹ Briasoulis <i>et al.</i>¹³⁷ Tomita <i>et al.</i>¹³⁸ Gelderblom <i>et al.</i>¹³⁹ Joerger <i>et al.</i>¹⁴⁰

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
					10 x ULN or bilirubin > 5 x ULN: not recommended MHRA: Mild and moderate: not studied, no dose advise given Severe: contraindicated Briasoulis <i>et al.</i> 70mg/m² as 1 hour infusion every 2 weeks safe in 9 patients with severe hepatic dysfunction (transaminase > 10xULN or bilirubin > 5xULN), despite altered pharmacokinetics. Joerger <i>et al.</i> TB concentrations were a significant predictor of paclitaxel elimination capacity (P=0.002). Patients with ALT/AST < 10 x ULN and bilirubin 2.1-3.5 x ULN initially treated with 135mg/m² or ALT/AST < 10 x ULN and bilirubin 3.6-10 x ULN initially treated with 110mg/m² (3-hour infusions) had significantly lower AUC and higher incidence of hematological toxicity compared to patient with bilirubin < 2 x ULN initially treated with 175 mg/m².	Transaminases < 10xULN and bilirubin 1.26-2xULN: 75% of original dose. Transaminases < 10 x ULN and bilirubin 2.01-5 x ULN: 50% of original dose. Transaminases ≥ 10 x ULN or bilirubin > 5 x ULN: contraindicated.	
152	Palbociclib	Palbociclib is metabolised in the liver. Palbociclib and its metabolites are mainly excreted in feces (74.1%) and to a lesser extent in urine (17.5%), mostly as metabolites.	EMA/FDA: CLcr ≥ 15 ml/min: no dose adjustment HD: not studied Yu <i>et al.</i> No dose adjustment is required in patients with a CLcr > 30 ml/min	Renal impairment: no dose adjustment is needed HD: no need for dose adjustment is expected	EMA/FDA: Child-Pugh A/B: no dose adjustment Child-Pugh C: 75 mg QD for 21 days	Child-Pugh A/B: no dose adjustment is needed Child-Pugh C: 60% of the original dose	Ibrance label¹ SPC Ibrance² Yu <i>et al.</i>¹⁴¹
153	Panitumumab	Panitumumab is catabolised by proteolytic	EMA/FDA: CLcr: ≥ 30 ml/min: no	Renal impairment: no need for dose adjustment is	EMA/FDA: Mild and moderate: no	Mild and moderate: no dose adjustment is	Vectibix label¹ SPC Vectibix²

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
		degradation to smaller peptides. No renal or hepatic clearance.	clinically important effect on PK CLcr < 30 ml/min: not studied	expected HD: no need for dose adjustment is expected	clinically important effect on PK Severe: not studied Krens <i>et al.</i> Child-Pugh B: no clinically significant deviations in AUC and CL.	needed Severe: no need for dose adjustment is expected	Krens <i>et al.</i> ¹⁴²
154	Panobinostat	Panobinostat is extensively metabolised in the liver. Panobinostat and its metabolites are excreted in both feces (44- 77%) and urine (29-51%).	EMA/FDA: CLcr ≥ 30 ml/min: no dose adjustment is needed CLcr < 30 ml/min or HD: not studied Sharma <i>et al.</i> Panobinostat AUC _{0-inf} geometric mean ratios compared to CLcr> 80ml/min: CLcr 50-79 ml/min: 0.67 (90% CI 0.39-1.17) CLcr 30-49 ml/min: 1.05 (90% CI 0.58-1.91) CLcr < 30 ml/min: 0.63 (0.33-1.20) Sekiguchi <i>et al.</i> HD: dialysable. Elimination of panobinostat by HD 14.1-36.3%.	Renal impairment: no need for dose adjustment is expected. HD: no need for dose adjustment is expected.	EMA/FDA: Mild: 75% of original dose (15mg) Moderate: 50% of original dose (10mg) Severe: avoid use Slingerland <i>et al.</i> Panobinostat exposure (AUC _{0-inf}) increased by 43% in patients with mild hepatic impairment and by 105% in moderate hepatic impairment	Mild: 75% of original dose Moderate: 50% of original dose Severe: not recommended	Farydak label ¹ SPC Farydak ² Sharma <i>et al.</i> ¹⁴³ Slingerland <i>et al.</i> ¹⁴⁴ Sekiguchi <i>et al.</i> ¹⁴⁵
155	Pazopanib	Pazopanib is metabolised in the liver. Pazopanib and its metabolites are predominantly excreted in feces. Renal elimination is less than 4%.	EMA/FDA: CLcr ≥ 30 ml/min: no dose adjustment CLcr < 30 ml/min: not studied HD: not studied, unlikely to be dialysed	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	EMA/FDA: Mild: no dose adjustment Moderate: 25% of the dose (200 mg QD) as MTD Severe: not recommended Shibata <i>et al.</i> Mild: (MTD 800 mg QD): AUC _{0-24h} 87% Moderate (MTD 200 mg QD): AUC _{0-24h} 29% Severe (MTD 200 mg QD): AUC _{0-24h} 15%	Mild: no dose adjustment is needed Moderate: select alternative therapy if possible. If not possible start with 25% of the original dose, titrate up to a C _{trough} > 20 mg/L Severe: not recommended	Votrient label ¹ SPC Votrient ² Shibata <i>et al.</i> ¹⁴⁶
156	Pegaspargase	Pegylated L-asparaginase is degraded by proteolytic degradation. No renal or hepatic clearance.	FDA: No advise given EMA:	Renal impairment: no dose adjustment is needed HD: no need for dose	FDA: No advise given EMA:	Hepatic impairment: no dose adjustment is needed	Oncaspar label ¹ SPC Oncaspar ²

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
			Renal impairment: no dose adjustment is needed	adjustment is expected	No dose adjustment is needed		
157	Pembrolizumab	Pembrolizumab is catabolised by proteolytic degradation to smaller peptides. No renal or hepatic clearance.	EMA/FDA: eGFR: ≥ 15 ml/min/1.73m ² : no clinically important effect on clearance HD: not studied	Renal impairment: no dose adjustment is needed HD: no need for dose adjustment is expected	EMA/FDA: Mild: no clinically important effect on clearance (FDA), no dose adjustment (EMA) Moderate and severe: not studied	Mild: no dose adjustment is needed Moderate and severe: no need for dose adjustment is expected	Keytruda label ¹ SPC Keytruda ²
158	Pemetrexed	Pemetrexed undergoes intracellular polyglutamation and is primarily excreted unchanged in urine (70-90%). Hepatic metabolism is minimal.	EMA/FDA: CLcr ≥ 45 ml/min: no dose adjustment CLcr < 45 ml/min: no dose recommendations (FDA), not recommended (EMA) Hill et al. CLcr 30-45 ml/min: 80% of dose was tolerated without grade ≥ 3 hematological toxicity Mita et al. Increased drug exposures in patients with renal impairment, GFR ≥ 40 ml/min: no dose adjustment needed Brandes et al. HD: not dialysed De Rouw et al. Pemetrexed clearance was increased 30-fold (from 1.00 L/h to 3.01 L/h) during high-flux HD Boosman et al. eGFR < 45 ml/min: 51.0-92.6% probability of severe neutropenia under standard dose of 500 mg/m ² eGFR 20 ml/min: at a dose of 20mg a 13-fold lower AUC was observed in these patients compared to patients with a renal function of 90 ml/min.	CLcr ≥ 45 ml/min: no dose adjustment is needed. CLcr < 45 ml/min and HD: not recommended	EMA/FDA: Not studied in patients with hepatic impairment	Mild and moderate: no need for dose adjustment is expected Severe: not recommended, based on the risk of pemetrexed induced liver dysfunction	Alimta label ¹ SPC Alimta ² Mita et al. ¹⁴⁷ Brandes et al. ¹⁴⁸ Hill et al. ¹⁴⁹ Boosman et al. ¹⁵⁰ De Rouw et al. ¹⁵¹

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
159	Pemigatinib	Pemigatinib is in vitro mainly metabolised by CYP3A4. The major drug-related moiety in plasma is unchanged pemigatinib. Pemigatinib is mainly excreted in feces (82·4%, 1·4% unchanged), and to a lesser extent in urine (12·6%, 1·0% unchanged).	EMA: GFR ≥ 30 ml/min: no dose adjustment GFR < 30 ml/min: reduce dose of patients on 13·5 mg QD to 9 mg QD; reduce dose of patients on 9 mg QD to 4·5 mg QD HD: no dose adjustment FDA: GFR ≥ 30 ml/min: no dose adjustment GFR < 30 ml/min: no data available HD: no data available Ji <i>et al.</i> Severe: clinically significant increase in AUC (59%) compared with healthy subjects ESRD on HD: AUC not significantly different from healthy subjects	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: reduce dose from 13·5 mg QD to 9 mg QD and from 9 mg QD to 4·5 mg QD HD: no dose adjustment is needed	EMA: Child-Pugh A/B or mild and moderate: no dose adjustment Child-Pugh C or severe: reduce dose of patients on 13·5 mg QD to 9 mg QD; reduce dose of patients on 9 mg QD to 4·5 mg QD FDA: Hepatic impairment: no dose adjustment Ji <i>et al.</i> Mild and moderate: no dose adjustment Severe: clinically significant increase in AUC (74%) compared with healthy subjects, indicating a need for dose reduction. Pemigatinib was well tolerated as a single 9 mg dose in patients with severe hepatic impairment.	Child-Pugh A/B or mild/moderate: no dose adjustment is needed Child-Pugh C or severe: reduce dose from 13·5 mg QD to 9 mg QD and from 9 mg QD to 4·5 mg QD	Pemazyre label ¹ SPC Pemazyre ² Ji <i>et al.</i> ¹⁵²
160	Pentostatin	Only a small amount of pentostatin is metabolised. Pentostatin is predominantly excreted unchanged in urine (90%).	MHRA: Ambiguous advice: CLcr < 60 ml/min: contraindicated. However a study with 13 renally impaired patients suggest the following dose adjustments: CLcr 40-59 ml/min: 75% of original dose (3 mg/m²) CLcr 35-39 ml/min: 50% of original dose (2 mg/m²) Lathia <i>et al.</i> Pentostatin AUC_{0-inf} was comparable when treated with 4 mg/m² in patients with CLcr > 60 ml/min, 3 mg/m² in patients with CLcr 41-60 ml/min and 2 mg/m² in one patient with CLcr 35- 40	GFR 40-59 ml/min: 75% of original dose GFR 35-39 ml/min: 50% of original dose GFR < 35 ml/min: not recommended HD: not recommended. If unavoidable consider 50% of the original dose, start HD 1-2 h after administration	MHRA: Limited experience, treat with caution	Hepatic impairment: No need for dose adjustments is expected	SPC Nipent ⁹ Lathia <i>et al.</i> ¹⁵³

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
			mg/m ² .				
161	Pertuzumab	Pertuzumab is catabolised by proteolytic degradation to smaller peptides. No renal or hepatic clearance.	EMA/FDA: CLcr ≥ 30 ml/min: No dose adjustment is needed CLcr < 30 ml/min: not studied	Renal impairment: no dose adjustment is needed HD: no need of dose adjustment is expected	EMA/FDA: Not studied in patients with hepatic impairment	Hepatic impairment: no need of dose adjustment is expected	Perjeta label ¹ SPC Perjeta ²
162	Pexidartinib	Pexidartinib is primarily metabolised by CYP3A4 and UGT1A4 to inactive metabolites. Pexidartinib is mainly excreted in feces (65%, 44% unchanged) and to a lesser extent in urine (27%, not unchanged).	FDA: CLcr ≥ 15 ml/min: increased exposure by 30%, adjust dose to 200 mg in the morning and 400 mg in the evening	GFR ≤ 90 ml/min: 75% of original dose (200 mg orally in the morning, 400 mg orally in the evening) HD: not recommended	FDA: Mild: no dose adjustment Moderate: 50% of the original dose Severe: no data available	Mild: no dose adjustment is needed Moderate: 50% of the original dose Severe: not recommended	Turalio label ¹
163	Pixantrone	Only a small amount of pixantrone is metabolised. Pixantrone is mainly excreted unchanged in bile with minimal excretion in urine (<10%).	EMA: Use with caution in patients with renal impairment	Renal impairment or HD: no need for dose adjustment is expected	EMA: Mild and moderate: use with caution Severe: not recommended	Mild and moderate: no need for dose adjustment is expected Severe: not recommended	SPC Pixuvri ²
164	Polatuzumab vedotin	Polatuzumab vedotin is expected to undergo catabolism to small peptides, amino acids, unconjugated MMAE, and unconjugated MMAE-related catabolites. MMAE is a substrate for CYP3A4. MMAE is mainly excreted in feces and minorly in urine.	EMA/FDA: CLcr ≥ 30 ml/min: no dose adjustment CLcr < 30ml/min: no data available HD: no data available	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	EMA/FDA: Mild: no dose adjustment Moderate and severe: not recommended	Mild: no dose adjustment is needed Moderate and severe: not recommended	Polivy label ¹ SPC Polivy ²
165	Ponatinib	Ponatinib is metabolised in the liver. Ponatinib and its metabolites are predominantly excreted in feces (87%) and to a minimal extent in urine (5%).	FDA: Renal impairment: not studied EMA: CLcr ≥ 50 ml/min: no dose adjustment needed CLcr < 50 ml/min/ESRD: caution is recommended	GFR ≥ 50 ml/min: no dose adjustment is needed GFR < 50 ml/min or HD: no need for dose adjustment is expected	FDA: Child-Pugh A/B/C: 67% of original dose (30mg QD) EMA: No dose reduction needed for hepatic impairment Narasimhan et al. No major differences in ponatinib exposure were observed for Child-Pugh A (AUC _{0-inf} 122-8%) Child-Pugh B (AUC _{0-inf} 90-6%) or Child-Pugh	Child-Pugh A to C: No need for dose adjustment is expected	FDA label Iclusig ¹ SPC Iclusig ² Narasimhan et al. ¹⁵⁴

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
					C (AUC _{0-inf} 79-4%) respectively.		
166	Pomalidomide	Pomalidomide is metabolised by hydrolysis or hydroxylation with subsequent glucuronidation. Hydroxylation is predominantly via CYP1A2 and CYP3A4. Pomalidomide is mainly excreted in urine (73%, 2% unchanged) and to a lesser extent in feces (15%, 8% unchanged).	EMA: Renal impairment: no dose adjustment is needed HD: no dose adjustment is needed. Take dose following haemodialysis FDA: CLcr ≥ 30 ml/min: no dose adjustment is needed CLcr < 30 ml/min: reduce dose to 3 mg (25% dose reduction) HD: reduce dose to 3mg (25% dose reduction). Take dose following haemodialysis	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: 75% of the original dose HD: 75% of the original dose. Take dose following haemodialysis	EMA: Child-Pugh A to C: no starting dose adjustment is needed. Monitor closely for adverse events, dose reduction should be used as needed FDA: Child-Pugh A/B: reduce dose to 3 mg (25% dose reduction) Child-Pugh C: reduce dose to 2 mg (50% dose reduction) Li et al. GMR (%) of pomalidomide AUC was 151·2% (mild), 157·5% (moderate) and 171·5% (severe) vs. healthy subjects. Mild and moderate: reduce dose to 3 mg (25% dose reduction) Severe: reduce dose to 2 mg (50% dose reduction)	Child-Pugh A/B: 75% of the original dose Child-Pugh C: 50% of the original dose	Pomalyst label ¹ SPC Imnovid ² Li et al. ¹⁵⁵
167	Pralatrexate	Pralatrexate is minimally metabolised. Pralatrexate is mainly excreted unchanged in urine (39%) and to a lesser extent in feces (34%: unchanged and metabolites). On average, 10% of a total dose is exhaled.	FDA: eGFR ≥ 30 ml/min/1·73m ² : no dose reduction needed eGFR 15-29 ml/min/1·73m ² : 50% of the original dose (15 mg/m ²) eGFR < 15 ml/min/1·73m ² or HD: (relatively) contraindicated Kelly et al. Comparable AUC _{0-inf} between cohorts with eGFR ≥ 90 ml/min, eGFR 60-89 ml/min, eGFR 30-59 ml/min treated with 30 mg/m ² and a cohort with eGFR 15-29 ml/min treated with 15 mg/m ²	GFR ≥ 30 ml/min: no dose adjustment is needed GFR 15-29 ml/min: 50% of the original dose (15 mg/m ²) GFR < 15 ml/min: not recommended HD: not recommended	FDA: Not studied (excluded patients with bilirubin ≥ 1·5 mg/dl and AST/ALT ≥ 2·5 x ULN)	Hepatic impairment: No need for dose adjustments is expected.	Folotyn label ¹ Kelly et al. ¹⁵⁶
168	Pralsetinib	Pralsetinib is primarily metabolised by CYP3A4 and UGT1A4. CYP2D6 and CYP1A2 play a minor role in	EMA/FDA: Renal impairment: no dose adjustment	Renal impairment: no dose adjustment is needed HD: no need for dose	EMA/FDA: Mild: no dose adjustment Moderate and severe: not recommended	Mild: no dose adjustment is needed Moderate and severe: not	Gavreto label ¹ SPC Gavreto ²

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
		the metabolism. Pralsetinib is mainly excreted in feces (72.5%, 66% unchanged) and in urine (6.1%, 4.8% unchanged).		adjustment is expected		recommended	
169	Procarbazine	Procarbazine (prodrug) is rapidly metabolised after administration, primarily in the liver and kidneys, into reactive metabolites. Procarbazine and its metabolites are predominantly excreted in urine (70%, 5% unchanged). Some of procarbazine metabolites are excreted via the lungs.	MHRA: CLcr < 10 ml/min: contraindicated	GFR ≥ 10 ml/min: no dose adjustment is needed GFR < 10 ml/min: not recommended HD: not recommended	MHRA: Severe hepatic impairment: contraindicated	Hepatic impairment: No need for dose adjustments is expected	SPC Procarbazine ⁹
170	Raltitrexed	Raltitrexed undergoes intracellular polyglutamation and is primarily excreted unchanged in urine (40-50%) and to a lesser extent in feces (15%).	MHRA: CLcr > 65 ml/min: no dose adjustment CLcr 55-65 ml/min: 75%, 4 weeks interval CLcr 25-54 ml/min: 50%, 4 weeks interval CLcr < 25 ml/min: contraindicated Judson <i>et al.</i> CLcr 25-65 ml/min: AUC _{0-inf} : 1.97 (95% CI 1.36-2.84), compared to CLcr >65 ml/min	GFR > 65 ml/min: no dose adjustment GFR 55-65 ml/min: 75% of the original, 4 weeks interval GFR 25-54 ml/min: 50% of the original dose, 4 weeks interval GFR < 25 ml/min: not recommended HD: not recommended	MHRA: Mild and moderate: no dose adjustment Severe: not studied	Mild and moderate: no dose adjustment is needed Severe: not recommended, based on the risk of raltitrexed induced liver dysfunction	SPC Tomudex ⁹ Judson <i>et al.</i> ¹⁵⁷
171	Ramucirumab	Ramucirumab is catabolised by proteolytic degradation to smaller peptides. No renal or hepatic clearance.	EMA/FDA CLcr ≥ 15 ml/min: no dose adjustment	Renal impairment: no need for dose adjustment HD: no need for dose adjustment is expected	EMA/FDA: Mild and moderate: no dose adjustment needed Severe: not studied Child-Pugh B and C cirrhosis: clinical deterioration is reported (FDA)	Mild and moderate: no dose adjustment is needed Severe: no need for dose adjustment is expected Child-Pugh B and C cirrhosis: not recommended	Cyramza label ¹ SPC Cyramza ²
172	Regorafenib	Regorafenib is metabolised in the liver. The M-2 and M-5 metabolite contribute to the clinical effect. Regorafenib and its metabolites are	EMA/FDA: Renal impairment: no dose adjustment recommended HD: not studied	Renal impairment: no dose adjustment is needed HD: no need for dose adjustment is expected	FDA: Mild and moderate: no dose adjustment recommended, close monitoring Severe: not studied, not	Mild, moderate or Child-Pugh A: no dose adjustment is needed Child-Pugh B: no need for dose adjustment is expected	Stivarga label ¹ SPC Stivarga ²

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
		predominantly excreted in feces (71%, 47% unchanged) and to a lesser extent in urine (19%).			recommended EMA: Child-Pugh A: no dose adjustment is needed Child-Pugh B: limited data indicate similar exposure Child-Pugh C: not studied	Child-Pugh C: not recommended	
173	Ribociclib	Ribociclib is metabolised in the liver. Ribociclib and its metabolites are primarily excreted in feces (69%) and to a lesser extent in urine (23%), predominantly as metabolites.	EMA/FDA: eGFR $\geq$ 30 ml/min/1.73m ² : no dose adjustment eGFR 15-30 ml/min/1.73m ² : 33% of the original starting dose (200 mg QD)	GFR $\geq$ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: 33% of the original starting dose (200 mg QD) HD: not recommended	EMA/FDA: Child-Pugh A: no dose adjustment needed Child-Pugh B: 1.32-fold increase in AUC _{0-inf} ; 400 mg QD Child-Pugh C: 1.29-fold increase in AUC _{0-inf} ; 400 mg QD	Child-Pugh A: no dose adjustment is needed Child-Pugh B: 67% of the original dose Child-Pugh C: 67% of the original dose	Kisqali label ¹ SPC Kisqali ²
174	Ripretinib	Ripretinib is primarily metabolised by CYP3A4 into the active metabolite DP-5439. Ripretinib is mainly excreted in feces (34% as ripretinib; 6% as DP-5439). Excretion by urine was < 1%.	EMA: CLcr $\geq$ 30 ml/min: no dose adjustment CLcr < 30 ml/min: no dosing recommendation can be made FDA: CLcr $\geq$ 30 ml/min: no dose adjustment CLcr < 30 ml/min: not studied	GFR $\geq$ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	FDA: Mild: no dose adjustment Moderate and severe: not studied EMA: Child-Pugh A or mild: no dose adjustment Child-Pugh B and C or moderate and severe: not studied	Child-Pugh A or mild: no dose adjustment is needed Child-Pugh B/C or moderate/severe: not recommended	Qinlock label ¹ SPC Qinlock ²
175	Rituximab	Rituximab is catabolised by proteolytic degradation to smaller peptides. No renal or hepatic clearance.	EMA/FDA: Renal impairment: not studied Jillella et al. HD: not dialysed, comparable plasma levels	Renal impairment: no need for dose adjustment is expected HD: no dose adjustment is needed	EMA/FDA: Hepatic impairment: not studied	Hepatic impairment: no need for dose adjustment is expected	Rituxan label ¹ SPC MabThera ² Jillella et al. ¹⁵⁸
176	Romidepsin	Romidepsin is extensively metabolised in the liver. Romidepsin's route of excretion is unknown.	FDA: CLcr $\geq$ 15 ml/min: pharmacokinetics not affected. CLcr < 15 ml/min or HD: not studied	Renal impairment or HD: no need for dose adjustment is expected	FDA: Mild: no dose adjustment Moderate: 7 mg/m ² (50% of original dose) Severe: 5 mg/m ² (~33% of original dose)	Mild: no need for dose adjustment is expected Moderate: consider 50% of starting dose (7 mg/m ²) Severe: consider ~33% of starting dose (5 mg/m ²)	Istodax label ¹
177	Rucaparib	Rucaparib is <i>in vitro</i> primarily metabolised by CYP2D6 and to a lesser extent by CYP1A2 and	EMA/FDA: CLcr $\geq$ 30 ml/min: no dose adjustment CLcr < 30 ml/min and HD: not	GFR $\geq$ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected	EMA/FDA: Mild: no dose adjustment Moderate: no dose adjustment but careful	Mild and moderate: no dose adjustment is needed Severe: not	Rubraca label ¹ SPC Rubraca ² Grechko et al. ¹⁵⁹

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
		CYP3A4. Unchanged rucaparib accounts for the largest fraction on plasma (64%), the most abundant metabolite M324 counts for 19%. Rucaparib is mainly excreted in feces (72%) with minor excretion in urine (17%).	studied and therefore not recommended	HD: no need for dose adjustment is expected	monitoring for hepatic function and adverse reactions Severe: not studied and therefore not recommended Grechko et al. Moderate: slightly higher AUC _{0-inf} compared to normal hepatic function (GMR 1.446, 90% CI 0.668-3.131)	recommended	
178	Ruxolitinib (for myelofibrosis)	Ruxolitinib is metabolised in the liver. Two metabolites of ruxolitinib are active and contribute for approximately 18% to the clinical effect. Ruxolitinib and its metabolites are mainly excreted in urine (74%) and to a lesser extent in feces (22%), mostly as metabolites.	FDA: CLcr 15-59 ml/min and platelet count > 150x10 ⁹ /L: no dose adjustment CLcr 15-59 ml/min and platelet count 100-150x10 ⁹ /L: 10 mg BID CLcr 15-59 ml/min and platelet count 50 – 99x10 ⁹ /L: 5 mg QD CLcr 15-59 ml/min and platelet count < 50 x 10 ⁹ /L: avoid HD with platelet count 100-200x10 ⁹ /L: 15 mg after dialysis, on dialysis days HD with platelet count >200x 10 ⁹ /L: 20 mg after dialysis, on dialysis days EMA: CLcr ≥ 30 ml/min: no dose adjustment CLcr < 30 ml/min: approximately 50% of the dose based on platelet count HD with platelet count 100-200x10 ⁹ /L: 15 mg QD after dialysis HD with platelet count >200x 10 ⁹ /L: 20 mg QD or 10 mg BID after dialysis Chen et al. eGFR 50-80 ml/min/1.73m ² : AUC _{0-inf} 1.10 (90% CI 0.90-	Renal impairment: Adjust the dose according to FDA recommendations	FDA: Child-Pugh A-C and platelet count: > 150 x10 ⁹ /L: no dose adjustment 100-150 x10 ⁹ /L: 10 mg BID 50-100 x10 ⁹ /L: 5 mg QD < 50 x 10 ⁹ /L: avoid EMA: Child-Pugh A-C: approximately 50% of the original daily dose based on platelet count, divided in two doses Chen et al. Child-Pugh A: AUC _{0-inf} 1.87(90% CI 1.29-2.71) Child-Pugh B: AUC _{0-inf} 1.28 (90% CI 0.88-1.85) Child-Pugh C: AUC _{0-inf} 1.65(90% CI 1.14-2.40)	Child-Pugh A to C: Adjust the dose according to FDA recommendations	Jakafi label ¹ SPC Jakavi ² Chen et al. ¹⁶⁰

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
			1:36) eGFR 30-49 ml/min/1.73m ² : AUC _{0-inf} 1.22 (90% CI 0.99-1.50) eGFR < 30 ml/min/1.73m ² : AUC _{0-inf} 1.03 (90% CI 0.84-1.27) HD: AUC _{0-inf} 0.93 (90% CI 0.72-1.19)				
179	Sacituzumab govitecan	The monoclonal antibody portion is expected to undergo proteolysis by ubiquitous proteolytic enzymes to small peptides and individual amino acids. SN-38, the small molecule moiety, is metabolised via UGT1A.	EMA: CLcr ≥ 60 ml/min: no dose adjustment CLcr < 60 ml/min: no data available FDA: Renal impairment: no data available	GFR ≥ 60 ml/min: no dose adjustment is needed GFR < 60 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	EMA/FDA: Mild: similar exposure to patients with normal hepatic function, no dose adjustment Moderate and severe: no data available, not recommended	Mild: no dose adjustment is needed Moderate and severe: no need for dose adjustment is expected	Trodelvy label ¹ SPC Trodelvy ²
180	Selinexor	Selinexor is metabolised by CYP3A4, multiple UGTs and glutathione S-transferases. Hepatic clearance is presumably the main route of elimination.	EMA: CLcr ≥ 15 ml/min: no dose adjustment is needed CLcr < 15 ml/min: no data available FDA: CLcr ≥ 15 ml/min: no dose adjustment CLcr < 15 ml/min: no data available HD: no data available	GFR ≥ 15 ml/min: no dose adjustment is needed GFR < 15 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	EMA: Mild: no dose adjustment Moderate and severe: No data available FDA: Mild: no dose adjustment Moderate and severe: no data available	Mild: no dose adjustment is needed Moderate and severe: not recommended	Xpovio label ¹ SPC Nexpovio ² Bader <i>et al.</i> ¹⁶¹
181	Selpercatinib	Selpercatinib is mainly metabolised by CYP3A4. Tucatinib is mainly excreted in feces (69%, 14% unchanged) and to a lesser extent in urine (24%, 11.5% unchanged).	EMA: eGFR ≥ 15 ml/min: no dose adjustment ESRD/HD: no data available FDA: CLcr ≥ 30 ml/min: no dose adjustment CLcr < 30 ml/min: no data available	GFR ≥ 15 ml/min: no dose adjustment is needed GFR < 15 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	EMA: Child-Pugh A/B: no dose adjustment Child-Pugh C: AUC _{0-inf} increased by 77% compared to normal hepatic function. Dose modification is recommended FDA: Mild and moderate (AUC _{0-inf} increased with 7% and 32%): no dose adjustment Severe (AUC _{0-in} increased with 77%): reduce the dosage of selpercatinib to 80 mg BID	Child-Pugh A/B or mild/moderate: no dose adjustment is needed Child-Pugh C or severe: 50% of starting dose.	Retevmo label ¹ SPC Retevmo ²
182	Sonidegib	Sonidegib is metabolised in	FDA	Renal impairment: no need	FDA	Hepatic impairment: no	Odomzo label ¹

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
		the liver. Sonidegib and its metabolites are predominantly excreted in feces (93.4%, 88.7% unchanged) and to a lesser extent in urine (1.95%).	CLcr $\geq$ 30 ml/min: no effect on steady-state exposure EMA CLcr $\geq$ 30 ml/min: dose adjustment probably not required. CLcr < 30 ml/min: not studied	for dose adjustment is expected HD: no need for dose adjustment is expected.	Child-Pugh A/B/C: no effect on steady-state exposure EMA No dose adjustment needed Horsmans <i>et al.</i> Child-Pugh A: AUC _{0-inf} 0.599 (90% CI 0.335-1.07) Child-Pugh B: AUC _{0-inf} 0.776 (90% CI 0.391-1.54) Child-Pugh C: AUC _{0-inf} 0.916 (90% CI 0.462-1.82)	dose adjustment is needed	SPC Odomzo ² Horsmans <i>et al.</i> ¹⁶²
183	Sorafenib	Sorafenib is metabolised in the liver. The active metabolite sorafenib N-oxide contributes to the clinical effect. Sorafenib and its metabolites are predominantly excreted in feces (77%, 51% unchanged) and to a lesser extent in urine (19%). No unchanged sorafenib is found in urine.	EMA/FDA: Renal impairment: no dose adjustment is needed HD: not studied Miller <i>et al.</i> No relationship between sorafenib AUC and varying degrees of renal impairment or HD was observed. Dose reduction to 200 mg BID and 200 mg QD for CLcr 20-39 ml/min and HD, respectively were given due to less tolerability. Kennoki <i>et al.</i> Not dialysed. An increased incidence of adverse events was observed in patients with haemodialysis, however AUC ₀₋₁₀ was lower than reported values in patients with normal renal function.	GFR > 40 ml/min: no dose adjustment is needed GFR 20-39 ml/min: 200 mg BID, dose-escalation based on tolerability GFR < 20 ml/min or HD: 200 mg QD, dose-escalation based on tolerability	EMA/FDA: Child-Pugh A/B: no dose adjustment needed Child-Pugh C: not studied Miller <i>et al.</i> No significant relationship between sorafenib AUC and varying degrees of hepatic impairment (mild, moderate, severe, very severe). Dose reduction recommended in moderate-severe hepatic dysfunction due to less tolerability.	Child-Pugh A/B: no dose adjustment is needed Child-Pugh C: starting dose of 200mg QD, dose-escalation based on tolerability	FDA label Nexavar ¹ SPC Nexavar ² Miller <i>et al.</i> ¹⁶³ Kennoki <i>et al.</i> ¹⁶⁴
184	Sotorasib	Sotorasib is primarily metabolised by non-enzymatic conjugation and oxidation to inactive metabolites by CYP2C8, CYP3A4 and CYP3A5. Sotorasib is mainly excreted in feces (74%) and to a lesser extent in urine (6%, 1% unchanged).	EMA: CLcr $\geq$ 60 ml/min: no dose adjustment CLcr < 60 ml/min: no data available FDA: eGFR $\geq$ 30 ml/min/1.73m ² : no clinically meaningful differences	GFR $\geq$ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	EMA: Mild: no dose adjustment Moderate and severe: not recommended FDA: Mild: no dose adjustment Moderate and severe: no data available	Mild: no dose adjustment is needed Moderate and severe: not recommended	Lumakras label ¹ SPC Lumykras ²

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
			eGFR < 30 ml/min/1.73m ² : no data available				
185	Streptozocin	Streptozocin is cleared rapidly from the plasma, its metabolites have markedly longer half-life's. In vitro data suggests no involvement of CYP enzymes in streptozocin degradation. Streptozocin and its metabolites are predominantly excreted in urine (30% of the dose as nitrosurea containing metabolites, 10-20% as parent compound) and to a minimal extent in feces (<1%).	MHRA: GFR 45-60 ml/min: 50% of original dose GFR 31-44 ml/min: evaluation risk/benefits GFR ≤ 30 ml/min: contraindicated	GFR 46-60 ml/min: 50% of original dose GFR 31-45 ml/min: not recommended, if unavoidable consider 25% of the original dose. GFR ≤ 30 ml/min or HD: not recommended	MHRA: Consider dose reduction	Hepatic impairment: no need for dose adjustment is expected	Zanosar SPC ⁹
186	Sunitinib	Sunitinib is metabolised in the liver. The active metabolite N-desmethylsunitinib contributes to the clinical effect. Sunitinib and its metabolites are predominantly excreted in feces (61%) and to a lesser extent in urine (16%).	FDA: Renal impairment: no dose adjustment needed HD: no initial dose adjustment needed, consider dose increase up to 2-fold based on tolerability and safety due to 47% lower sunitinib exposure in patients on HD EMA: Renal impairment/HD: no dose adjustment needed Khosravan <i>et al.</i> Sunitinib geometric mean ratio: CLcr < 30 ml/min: 86% (90% CI: 61-120%) HD: 53% (90% CI: 37-74%) Izzedine <i>et al.</i> Sunitinib PK in two dialysed patients were comparable to patients with normal renal function. Sunitinib is not dialysed.	Renal impairment: no dose adjustment is needed HD: no initial dose adjustment is needed, increase dose based on sunitinib + active metabolite C _{trough} levels	FDA: Child-Pugh A/B: no dose adjustment needed Child-Pugh C: not studied EMA Child-Pugh A/B: no dose adjustment needed Child-Pugh C: not recommended Bello <i>et al</i> Child-Pugh A: AUC _{0-inf} 1.03 (90%CI: 0.80-1.33) Child-Pugh B: AUC _{0-inf} 1.03 (90% CI: 0.80-1.32)	Child-Pugh A/B: no dose adjustment is needed Child-Pugh C: consider 75% of the original dose, increase if tolerated	Sutent label ¹ SPC Sutent ² Khosravan <i>et al.</i> ¹⁶⁵ Izzedine <i>et al.</i> ¹⁶⁶ Bello <i>et al.</i> ¹⁶⁷
187	Tafasitamab	Tafasitamab is catabolised by proteolytic degradation to smaller peptides. No renal or	EMA/FDA: CLcr ≥ 30 ml/min: no dose adjustment	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need	EMA/FDA: Mild: no dose adjustment Moderate and severe: no	Mild: no dose adjustment is needed	Monjuvi label ¹ SPC Minjuvi ²

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
		hepatic clearance.	CL _{cr} < 30 ml/min: no data available	for dose adjustment is expected HD: no need for dose adjustment is expected	data available	Moderate and severe: no need for dose adjustment is expected	
188	Tamoxifen	Tamoxifen is extensively metabolised in the liver to several active metabolites which significantly contribute to the therapeutic effect, with N-desmethyl tamoxifen as major metabolite. Tamoxifen and its metabolites are predominantly excreted in feces.	FDA/MHRA: no advise given Langenegger <i>et al.</i> In HD patients: tamoxifen and N-desmethyl tamoxifen plasma levels were lower than expected, but within therapeutic range	Renal impairment or HD: no need for dose adjustment is expected	FDA/MHRA: not studied Floren <i>et al.</i> Tamoxifen dose was adjusted based on tamoxifen and N-desmethyltamoxifen levels in a patient with acute hepatic decompensation (TB 340 µmol/L, AST 99 UI/L, INR 3.0) after transjugular intrahepatic portosystemic shunt placement.	Mild/ moderate: no dose adjustment is needed Severe: not recommended	Nolvadex label ¹ SPC Nolvadex ⁹ Langenegger <i>et al.</i> ¹⁰ Floren <i>et al.</i> ¹⁶⁸
189	Tagraxofusp	Tagraxofusp is catabolised by proteolytic degradation to smaller peptides. No renal or hepatic clearance.	EMA: No data available FDA: eGFR ≥ 30 ml/min/1.73m ² : no dose adjustment eGFR < 30 ml/min/1.73m ² : no data available	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min/: no need for dose adjustment is expected HD: no need for dose adjustment is expected	EMA: No data available FDA: Mild and moderate: no dose adjustment Severe: no data available	Mild and moderate: no dose adjustment is needed Severe: no need for dose adjustment is expected	Elzonris label ¹ SPC Elzonris ²
190	Talazoparib	Talazoparib undergoes minimal hepatic metabolism. Renal elimination through passive diffusion and active secretion is the primary route of excretion (69%, 55% unchanged) with 20% (14% unchanged) recovered in feces.	FDA: CL _{cr} ≥ 60 ml/min: no dose adjustment CL _{cr} 30-59 ml/min: 25% dose reduction CL _{cr} < 30 ml/min: not studied HD: not studied EMA: CL _{cr} ≥ 60 ml/min: no dose adjustment CL _{cr} 30-59 ml/min: 25% dose reduction CL _{cr} 15-29 ml/min: 50% dose reduction CL _{cr} < 15 ml/min: not studied HD: not studied Yu <i>et al.</i> CL _{cr} ≥ 60 ml/min: Cl/F -15.2% CL _{cr} 30-59 ml/min:	GFR ≥ 60 ml/min: no dose adjustment (1 mg) GFR 30-59 ml/min: 25% reduction of original dose GFR 15-29 ml/min: 50% dose reduction (0.5 mg) GFR < 15 ml/min: 50% of the original dose may be considered HD: 50% of the original dose may be considered.	FDA: Mild: no dose adjustment Moderate and severe: not studied EMA: Mild: no dose adjustment Moderate and severe: not studied, only use when the benefit outweighs the potential risk, and the patient should be carefully monitored for hepatic function and adverse events	Mild: no dose adjustment is needed Moderate and severe: no need for dose adjustment is expected	Talzenna label ¹ SPC Talzenna ² Yu <i>et al.</i> ¹⁶⁹

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
			CI/F -38.2% CLcr < 30 ml/min: insufficient data				
191	Tazemetostat	Tazemetostat is metabolised by CYP3A to inactive metabolites. Tazemetostat is mainly excreted in feces (79%), and to a lesser extent in urine (15%)	FDA: Renal impairment: no dose adjustment	Renal impairment: no dose adjustment is needed HD: no need for dose adjustment is expected	FDA: Mild: no dose adjustment Moderate and severe: no data available	Mild: no dose adjustment is needed Moderate and severe: not recommended	Tazverik label ¹
192	Tebentafusp	Tebentafusp is expected to be catabolised by proteolytic degradation to smaller peptides. Although the metabolic pathway of tebentafusp has not been characterized, no renal or hepatic clearance is expected.	EMA: CLcr ≥ 30 ml/min: no dose adjustment CLcr < 30 ml/min: no data available FDA: CLcr ≥ 30 ml/min: no clinically significant differences in tebentafusp PK CLcr < 30 ml/min: no data available	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	EMA: No dose adjustment on ALT/AST levels FDA: Mild: no dose adjustment is needed Moderate and severe: no data available	Mild: no dose adjustment is needed Moderate and severe: no need for dose adjustment is expected	Kimmtrak label ¹ SPC Kimmtrak ²
193	Tegafur/gimeracil/oteracil	Tegafur is a prodrug, which is converted in the liver to the active metabolite 5-FU. 5-FU is converted intracellularly to inactive metabolites by DPD. Tegafur and its metabolites are excreted in urine (83-91%, of which 3-8-4-2% unchanged).	EMA CLcr 51-80 ml/min: no dose adjustment CLcr 30-50 ml/min: 80% of original dose (20 mg/m ² BID) CLcr: < 30 ml/min: not recommended due to increased adverse events HD: not studied Booka et al. Moderate correlation between 5-FU AUC _{0-24h} and CLcr in 16 patients with varying degrees of renal impairment. Tomiyama et al. Comparable 5-FU AUC _{0-24h} in a patient undergoing HD receiving 40mg and reported 5-FU AUC _{0-24h} in patients receiving 100mg.	GFR > 50 ml/min: no dose adjustment is needed GFR 30-50 ml/min: 80% of original dose (20mg/m ² BID) GFR < 30 ml/min or HD: 40% of the original dose (20 mg/m ² QD)	EMA: No dose adjustment recommended Yoon et al. Mild: 80mg/m ² /day Moderate: 70 mg/m ² /day Severe: 50 mg/m ² /day	Hepatic impairment: no dose adjustment is needed	Teysono SPC ² Booka et al. ¹⁷⁰ Tomiyama et al. ¹⁷¹
194	Temozolomide	Temozolomide is spontaneously hydrolyzed,	FDA:	GFR ≥ 36 ml/min: no dose adjustment is needed	FDA:	Child-Pugh A/B: no dose adjustment is needed	Temodar label ¹ SPC Temodal ²

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
		primarily to the active 3-methyl(triazene-1-yl)imidazole-4-carboxamide (MTIC). Temozolomide and its metabolites are predominantly excreted in urine (37-7%, 5-10% unchanged) and minimally in feces (0-8%).	CLcr $\geq$ 36 ml/min: no dose adjustment needed CLcr < 36 ml/min: no dose advice given, exercise caution HD: not studied EMA: Renal impairment: dose reductions probably not necessary. Exercise caution.	GFR < 36 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment expected	Child-Pugh A/B: no dose adjustment needed Child-Pugh C: no dose advise given, exercise caution EMA: Mild and moderate: no dose adjustment needed Severe: dose reductions probably not necessary	Child-Pugh C: no need for dose adjustment is expected	
195	Temsirolimus	Temsirolimus is mainly metabolised in the liver. The principle metabolite is sirolimus, which is equally potent as temsirolimus. Temsirolimus and its metabolites are predominantly excreted in feces (78%) and to a lesser extent in urine (4-6%).	EMA/FDA: Renal impairment: no dose adjustment recommended HD: not studied Lunardi <i>et al.</i> (Tem)sirolimus pharmacokinetics not significantly altered by haemodialysis compared to controls with normal renal function	Renal impairment: no dose adjustment is needed HD: no need for dose adjustment is expected	FDA: Bilirubin 1-1.5 x ULN or AST > ULN but bilirubin $\leq$ ULN): 60% of original dose (15mg/week) Bilirubin > 1.5xULN: contraindicated EMA: Renal cell carcinoma (RCC), if platelet count $\geq 100 \times 10^9$ /l: Mild and moderate or Child-Pugh A/B: no dose adjustment is needed Severe or Child-Pugh C: 40% of original dose (10 mg/week) Mantel cell lymphoma (MCL): Mild: no dose adjustment recommended Moderate and severe: contraindicated	RCC Mild or moderate: no dose adjustment is needed Severe: 40% of the original dose MCL Mild: no dose adjustment Moderate and severe: not recommended	Torisel label ¹ SPC Torisel ² Lunardi <i>et al.</i> ¹⁷²
196	Teniposide	Teniposide is metabolised in the liver. Teniposide and its metabolites are predominantly excreted in urine (44%, of which 4-12% as unchanged parent compound) and to a lesser extent in feces (0-10%).	FDA: Insufficient data, dose adjustment may be necessary.	Renal impairment: no need for dose adjustment is expected HD: no need for dose adjustment is expected	FDA: Insufficient data, dose adjustment may be necessary	Mild and moderate: no need for dose adjustment is expected Severe: not recommended	Vumon label ¹
197	Tepotinib	Tepotinib is metabolised in the liver by CYP3A4 and CYP2C8. Tepotinib is mainly	EMA: CLcr $\geq$ 30 ml/min: no dose adjustment	GFR $\geq$ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for	EMA: Child-Pugh A/B or mild and moderate: no dose adjustment	Child-Pugh A/B or mild/moderate: no dose adjustment is needed	Tepmetko label ¹ SPC Tepmetko ²

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
		excreted in feces (~78%, 45% unchanged), and to a lesser extent in urine (13-6%, 7% unchanged).	CLcr < 30 ml/min: no data available, not recommended FDA: CLcr ≥ 30 ml/min: no dose adjustment CLcr < 30 ml/min: no data available	dose adjustment is expected HD: no need for dose adjustment is expected	Child-Pugh C and severe: no data available FDA: Child-Pugh A/B or mild and moderate: no dose adjustment Child-Pugh C and severe: no data available	Child-Pugh C and severe: not recommended	
198	Thalidomide	Thalidomide is primarily metabolised by non-enzymatic hydrolysis. There is minimal CYP catalyzed hepatic metabolism. Thalidomide is mainly excreted in urine (>90%), and to a lesser extent in feces.	EMA: Studies in healthy subjects suggest that thalidomide PK is not influenced to any significant extent by impaired renal function. Severe: no dose adjustment, carefully monitor for any adverse events. FDA: Renal impairment: not expected to influence drug exposure Eriksson <i>et al.</i>: No need to increase the dose due to haemodialysis, although clearance is doubled during dialysis.	Renal impairment: no dose adjustment is needed HD: no dose adjustment is needed	EMA: Studies in healthy subjects suggest that thalidomide PK is not influenced to any significant extent by impaired hepatic function. Severe: no dose adjustment, carefully monitor for any adverse events. FDA: No data available	Mild and moderate: no dose adjustment is needed Severe: no dose adjustment is needed	Thalidomide label ¹ SPC Thalidomide BMS ² Eriksson <i>et al.</i> ¹⁷³
199	Thiotepa	Thiotepa is extensively and rapidly metabolised in the liver. One of the major active metabolites is triethylene phosphoramide (TEPA). Several known metabolites are all excreted in the urine. Urinary excretion of the parent compound accounts for < 2% of the given dose, TEPA for ≤ 11% of the given dose.	FDA: CLcr 15-59 ml/min: more extensive monitoring indicated. EMA: CLcr ≥ 30 ml/min: not studied. No need for dose adjustment Ekhart <i>et al.</i>: Increased exposure (AUC) to thiotepa (+43%) and TEPA (+157%) in a patient with CLcr 38ml/min compared to AUC of reference population.	GFR ≥ 30 ml/min: no need for dose adjustment is expected GFR < 30 ml/min: consider 70% of the original dose, increase if tolerated HD: consider 70% of the original dose, increase if tolerated	FDA: Mild: similar clearance compared to normal liver function. Moderate: 1.6-1.8 fold increase of thiotepa AUC. More extensive monitoring indicated. Severe: unknown. More extensive monitoring indicated. EMA: Dose modification not recommended for transient alterations of hepatic parameters. Exercise caution in patients with pre-existing hepatic impairment,	Mild: no dose adjustment is needed Moderate: intensify monitoring Severe: not recommended	Tepadina label ¹ Tepadina SPC ² Ekhart <i>et al.</i> ¹⁷⁴

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
					especially severe		
200	Tioguanine	Tioguanine (prodrug) is extensively metabolised into several active and inactive metabolised in the liver and other tissues. Tioguanine and its metabolites are mainly excreted in urine, mostly as metabolites.	FDA: No advise given MHRA: Consider dose adjustment	Renal impairment or HD: no need for dose adjustment is expected	FDA: No advise given MHRA: Consider dose adjustment	Hepatic impairment: no need for dose adjustment is expected	Tabloid label ¹ SPC Tioguanine ⁹
201	Tisotumab vedotin	The monoclonal antibody portion (tisotumab) is expected to undergo proteolytic degradation to smaller peptides. No renal or hepatic elimination. Vedotin (MMAE) is primarily metabolised by CYP3A4. It is expected that vedotin is mainly excreted in feces and to a lesser extent in urine.	FDA: CLcr ≥ 30 ml/min: no clinically significant difference in exposure CLcr < 30 ml/min: not studied HD: not studied	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	FDA: Mild: no dose adjustment Moderate and severe: not studied, avoid use	Mild: no dose adjustment is needed Moderate and severe not recommended	Tivdak label ¹
202	Tivozanib	Only a small part of tivozanib is metabolised in the liver by CYP3A4 and CYP1A1. Tivozanib is mainly excreted in feces (79%, 26% unchanged), and to a lesser extent in urine (12%, not unchanged).	EMA: CLcr ≥ 30 ml/min: no dose adjustment CLcr < 30 ml/min or HD: no dose recommendation given FDA: CLcr ≥ 15 ml/min: no dose adjustment CLcr < 15 ml/min or HD: no data available	GFR ≥ 15 ml/min: no dose adjustment is needed GFR < 15 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	FDA: Child-Pugh A or mild: No dose adjustment Child-Pugh B or moderate: AUC _{tau} 62% increase. Reduce dose to 0.89 mg QD Child-Pugh C or severe: no data available EMA: Mild: No dose adjustment Moderate: significant increase (2.6-fold) in AUC _{0-inf} . Reduce dose to one capsule (1.34 mg) every other day Severe: significant increase (4.0-fold) in AUC _{0-inf} . Do not use tivozanib	Child-Pugh A or mild: no dose adjustment is needed Child-Pugh B or moderate: 50% of the original dose by increasing the dose interval to use every other day Child-Pugh C or severe: not recommended	Fotivda label ¹ SPC Fotivda ²
203	Topotecan	Topotecan undergoes pH dependent hydrolysis to a pharmacologically active lactone form. Topotecan is to a lesser extent eliminated (<10%) by metabolism to a N-demethylated metabolite. Topotecan and its	Intravenous: EMA/FDA: CLcr ≥ 40 ml/min: no dose adjustment needed CLcr 20-39 ml/min: 50% of original dose (0.75mg/m ²) CLcr < 20 ml/min: not studied, not recommended O'Reilly et al.	(Oral and intravenous) GFR ≥ 40 ml/min: no dose adjustment is needed GFR 20-39 ml/min: 50% of original dose GFR < 20 ml/min: not recommended, if unavoidable consider 25% of the original dose	Intravenous: FDA: no differences in pharmacokinetics in patients with hepatic impairment. EMA: Bilirubin 1.5-10 mg/dl: insufficient data to make	(Oral and intravenous) Bilirubin ≤171 µmol/l: no need for dose adjustment is expected Bilirubin >171 µmol/l: not recommended	Hycamtin label ¹ SPC Hycamtin ² O'Reilly <i>et al.</i> ¹⁷⁵ Devriese <i>et al.</i> ¹⁷⁶ O'Reilly <i>et al.</i> ¹⁷⁷ Herrington <i>et al.</i> ¹⁷⁸

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
		metabolites are predominantly excreted in urine (54%) and to a lesser extent in feces (20%).	Significantly reduced clearance of topotecan in patients with mild and moderate renal impairment: CLcr $\geq$ 60 ml/min: 0.4$\pm$0.18 L/min/m² CLcr 40-59 ml/min: 0.27$\pm$0.11 L/min/m² CLcr 20-39 ml/min: 0.14$\pm$0.05 L/min/m² Herrington <i>et al.</i> Case report, almost fourfold increase of topotecan clearance on dialysis compared to off dialysis Oral: FDA: CLcr > 50 ml/min: no dose adjustment CLcr 30-49 ml/min: 65% of original dose (1.5 mg/m²) CLcr < 30 ml/min: 26% of original dose (0.6 mg/m²) EMA: CLcr > 50 ml/min: no dose adjustment CLcr 30-49 ml/min: 83% of original dose (1.9 mg/m²) CLcr < 30 ml/min: limited data Devriese <i>et al.</i> CLcr 50-79 ml/min: AUC_{0-inf}: 1.61 (90% CI 1.14-2.28) CLcr 30-49 ml/min: AUC_{0-inf}: 2.48 (90% CI 1.72-3.56) CLcr < 30 ml/min: AUC_{0-inf}: 3.98 (2.64-6.01)	HD: not recommended, if unavoidable consider 25% of the original dose	dose recommendations Bilirubin >10 mg/dl: not recommended O'Reilly <i>et al.</i> No statistically significant pharmacokinetic differences of total topotecan or topotecan lactone between patients with normal hepatic function (bilirubin $\leq$1.2 mg/dl) and hepatic impairment (bilirubin >1.2 mg/dl). Oral: FDA: No differences in pharmacokinetics in patients with hepatic impairment. EMA: Mild and moderate (bilirubin 1.5-10 mg/dl): insufficient data to make recommendations Severe: not recommended		
204	Toremifene	Toremifene is extensively metabolised in the liver. The active metabolite N-demethyltoremifene contributes to the clinical	FDA: No dose advise given, no change in PK patients with impaired renal function	Renal impairment: no dose adjustment is needed HD: no need for dose adjustments is expected	FDA: No dose advise given, although stated mean elimination half-life of toremifene increased less	Mild and moderate : no need for dose adjustment is expected due to large therapeutic index Severe: consider starting	Fareston label ¹ SPC Fareston ² Anttila <i>et al.</i> ¹⁷⁹

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
		effect. Toremifene and its metabolites are predominantly excreted in feces and to a lesser extent in urine (approximately 10%).	EMA: Renal impairment: no dose adjustment is needed Antilla <i>et al.</i> No difference in PK in patients with renal impairment		than twofold in patients with hepatic impairment. EMA: Use with caution in patients with hepatic impairment Antilla <i>et al.</i> AUC was significantly increased in patients with hepatic impairment (bilirubin 1.5-2 x ULN) compared to normal hepatic function (28.4 ± 12.3 vs. 44.5 ± 28.9 $\mu\text{g} \cdot \text{hr/ml}$)	with 50% of the original dose, increase if tolerated	
205	Trabectedin	Trabectedin is extensively metabolised in the liver. Trabectedin and its metabolites are predominantly excreted in feces (58%) and to a lesser extent in urine (5-8%), mostly as metabolites.	EMA/FDA: CLcr ≥ 30 ml/min: no dose adjustment CLcr < 30 or HD: not studied/contraindicated Thariat <i>et al.</i> AUC _{0-inf} of normal dose trabectedin in patient on haemodialysis was 2-fold that of the control population, although within 95%CI.	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: No need for dose adjustment is expected	FDA: Moderate (bilirubin 1.5-3 x ULN and AST and ALT < 8 x ULN): 60% of original dose (0.9 mg/m ²) Severe: contraindicated EMA: Bilirubin $> \text{ULN}$: contraindicated Calvo <i>et al.</i> Hepatic impairment (bilirubin 1.5 – 3 x ULN, AST and ALT ≤ 8 x ULN): dose normalized AUC _{0-last} 1.97 (90% CI 1.20-3.22)	Mild: no need for dose adjustment is expected Moderate: 60% of original dose (0.9 mg/m ²) Severe: not recommended	Yondelis ¹ SPC Yondelis ² Thariat <i>et al.</i> ¹⁸⁰ Calvo <i>et al.</i> ¹⁸¹
206	Trametinib	Trametinib is metabolised in the liver. Trametinib and its metabolites are predominantly excreted in feces ($> 80\%$) and to a lesser extent in urine ($\leq 19\%$), mostly as metabolites.	EMA/FDA GFR ≥ 30 ml/min/1.73m ² : no dose adjustment is needed GFR < 30 ml/min/1.73m ² or HD: not studied Park <i>et al.</i> Comparable C _{max} in a dialysed patient receiving a reduced dose (1mg QD) of trametinib compared to previously reported concentrations at that dose.	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	FDA: Mild: no dose adjustment Moderate and severe: not studied EMA: Mild: no dose adjustment Moderate and severe: limited impact of moderate to severe hepatic impairment on trametinib exposure	Mild and moderate: no dose adjustment is needed Severe: consider 50% of the original dose	Mikinst label ¹ SPC Mekinst ² Park <i>et al.</i> ¹⁸⁷

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
207	Trastuzumab deruxtecan	Trastuzumab deruxtecan undergoes intracellular cleavage by lysosomal enzymes to release deruxtecan (DXd). In vitro, DXd is mainly metabolised by CYP3A4.	EMA/FDA: CLcr ≥ 30 ml/min: no dose adjustment CLcr < 30 ml/min: no data available HD: no data available	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	EMA: Mild: no dose adjustment Moderate and severe: no data available, monitor closely when administered FDA: Mild: no dose adjustment Moderate: monitor closely when administered Severe: no data available	Mild: no dose adjustment is needed Moderate: no need for dose adjustment is expected, close monitoring for toxicity is recommended Severe: not recommended	Enhertu label ¹ SPC Enhertu ²
208	Trastuzumab emtansine	Trastuzumab is catabolised by proteolytic degradation to smaller peptides. No renal or hepatic elimination. DM1 is mainly metabolised in the liver. DM1 and DM1-containing catabolites are mainly excreted in bile with minimal elimination in urine.	EMA/FDA: CLcr: ≥ 30 ml/min: No dose adjustment is needed CLcr < 30 ml/min: not studied	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	EMA/FDA: Child-Pugh A: no dose adjustment Child-Pugh B: no dose adjustment Child-Pugh C: not studied	Child-Pugh A/B: no dose adjustment is needed Child Pugh C: not recommended	Label Kadcylla ¹ SPC Kadcylla ²
209	Trastuzumab	Trastuzumab is catabolised by proteolytic degradation to smaller peptides. No renal or hepatic clearance.	EMA/FDA: CLcr: ≥ 30 ml/min: no clinically significant differences in PK HD: not studied	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	EMA/FDA: Hepatic impairment: not studied	Hepatic impairment: no need for dose adjustment is expected	Label Herceptin ¹ SPC Herceptin ²
210	Tremelimumab	Tremelimumab is thought to be cleared through proteolytic degradation and catabolism. Excretion was not studied, but expected to be cleared as small peptides or aminoacids or incorporated in the endogenous aminoacid pool.	EMA/FDA: CLcr ≥ 30 ml/min: no clinically significant effect on the PK of tremelimumab. CrCl < 30 ml/min: not studied.	GFR ≥ 30 ml/min: no dose adjustment is needed. GFR < 30 ml/min: no need for dose adjustment is expected. HD: no need for dose adjustment is expected.	EMA: Mild: no clinically significant effect on the PK of tremelimumab. Moderate: not studied. FDA: Mild to moderate: no clinically significant effect on the PK of tremelimumab. Severe: not studied.	Mild and moderate: no dose adjustment is needed. Severe: no need for dose adjustment is expected.	Imjudo label ¹ SmPC Imjudo ²
211	Treosulfan	Treosulfan (prodrug) is spontaneously converted to an active monoepoxide	MHRA: Renal impairment: careful monitoring of blood counts	GFR ≥ 50 ml/min: no need for dose adjustment is expected GFR < 50ml/min: consider the	MHRA: no advise given	Hepatic impairment: no need for dose adjustment is expected, however due to limited knowledge about	SPC treosulfan ⁹

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
		intermediate and finally to L- diepoxibutane. Treosulfan is renally excreted, with cumulative renal elimination of 5-49% of unchanged treosulfan.		use of busulfan and dose according to busulfan plasma levels HD: not recommended		treosulfan pharmacokinetics careful monitoring is advised.	
212	Trifluridine/tipiracil	Trifluridine and tipiracil are not metabolised by CYP enzymes. Trifluridine is primarily metabolised by TPase and excreted in urine as the inactive metabolite TPY. Trifluridine is excreted in feces (3%). Tipiracil is excreted in feces (50%).	EMA/FDA: CLcr ≥ 30 ml/min: no dose adjustment CLcr < 30 ml/min: reduce dose to 20 mg/m ² BID HD: no data available Saif <i>et al.</i> CLcr ≥ 30 ml/min: safe and tolerable at the recommended dose of 35 mg/m ² BID CLcr < 30 ml/min: safe and tolerable at a reduced dose of 20 mg/m ² BID	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: reduce dose according to drug label, based on BSA HD: not recommended	EMA: Mild: no dose adjustment Moderate: not recommended FDA: Mild: no dose adjustment Moderate and severe: no data available Saif <i>et al.</i> Mild: no dose adjustment Moderate and severe: not recommended, due to grade 3 or 4 increased blood bilirubin	Mild: no dose adjustment is needed Moderate and severe: not recommended	Lonsurf label ¹ SPC Lonsurf ² Saif <i>et al.</i> ¹⁸² Saif <i>et al.</i> ¹⁸³
213	Tucatinib	Tucatinib is primarily metabolised by CYP2C8 and to a lesser extent by CYP3A4. Tucatinib is mainly excreted in feces (85·8%, 15·9% unchanged) and to a lesser extent in urine (4·1%).	EMA: CLcr < 90 ml/min: no dose adjustment FDA: CLcr ≥ 30 ml/min: no dose adjustment CLcr < 30 ml/min: no data available	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	EMA/FDA: Child-Pugh A/B or mild and moderate: no dose adjustment Child-Pugh C or severe: 1·6-fold increase AUC _{0-inf} compared to subjects with normal hepatic function. Reduced starting dose of 200 mg orally BID is recommended.	Child-Pugh A/B or mild/moderate: no dose adjustment is needed Child-Pugh C or severe: 66% of the original dose	Tukysa label ¹ SPC Tukysa ²
214	Vandetanib	Vandetanib is partly metabolised in the liver. Vandetanib and its active metabolites are excreted in urine (44%) and feces (25%).	EMA: CLcr ≥ 50 ml/min: no dose adjustment CLcr 30-50 ml/min: reduce dose to 200 mg QD (67% of the original dose) CLcr < 30 ml/min: not recommended FDA: CLcr ≥ 60 ml/min: no dose adjustment	GFR > 50 ml/min: no dose adjustment is needed GFR 30 - 50 ml/min: 67% of the original dose GFR < 30 ml/min: 50% of the dose may be considered HD: 50% of the dose may be considered	EMA/FDA: Child-Pugh A-C did not affect vandetanib exposure. Bilirubin > 1·5 x ULN: not recommended FDA: Mild: no dose adjustment Moderate and severe: not recommended Weil <i>et al.</i>	Hepatic impairment: no dose adjustment is needed	Caprelsa label ¹ SPC Caprelsa ² Weil <i>et al.</i> ¹⁸⁴

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
			CLcr 15-59 ml/min: reduce dose to 200 mg QD (67% of the original dose) Weil <i>et al.</i> CLcr 50-81 ml/min: AUC _{0-inf} 1.46 (90% CI 1.24-1.72) CLcr 30-49 ml/min: AUC _{0-inf} 1.62 (90% CI 1.31-1.99) CLcr <30 ml/min: AUC _{0-inf} 1.79 (90% CI 1.39-2.31)		Child-Pugh A: AUC _{0-inf} 1.04 (90% CI 0.86-1.26) Child-Pugh B: AUC _{0-inf} 0.94 (90% CI 0.78-1.15) Child-Pugh C: AUC _{0-inf} 0.93 (90% CI 0.76-1.14)		
215	Vemurafenib	Vemurafenib is only partly metabolised in the liver. Vemurafenib is predominantly excreted unchanged in feces (94%) and in minimal amounts (<1%) in urine.	FDA: CLcr ≥ 60 ml/min: no dose adjustment is needed CLcr 30-59 ml/min: no dose adjustment is needed CLcr < 30 ml/min: not sufficiently studied EMA: CLcr > 40 ml/min: no dose adjustment is needed CLcr ≤ 30 ml/min: limited data available.	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	FDA: Mild and moderate (TB <3 x ULN): no dose adjustment recommended Severe: limited data EMA: No need for dose adjustment in patients with hepatic impairment. Close monitoring warranted in moderate and severe hepatic impairment.	Mild and moderate: no dose adjustment is needed Severe: no need for dose adjustment is expected, monitor liver biochemistry twice a week.	Vemurafenib label ¹ SPC Zelboraf ²
216	Venetoclax	Venetoclax is primarily metabolised by CYP3A4, <i>in vitro</i> . Venetoclax is mainly eliminated in feces (>99.9%, 20-8% unchanged) and to a lesser extent in urine (<0.1%).	EMA: CLcr ≥ 15 ml/min: no dose adjustment CLcr < 15 ml/min: no data available FDA: CLcr ≥ 30-80 ml/min: no dose adjustment CLcr < 30 ml/min: no data available HD: no data available	GFR ≥ 15 ml/min: no dose adjustment is needed. GFR < 15 ml/min: no need for dose adjustment is expected. Monitor closely due to increased risk of TLS HD: no need for dose adjustment is expected. Monitor closely due to increased risk of TLS	EMA: Child-Pugh A/B, and mild and moderate: no dose adjustment Severe: reduce dose with at least 50% FDA: Mild and moderate: no dose adjustment Severe: no data available Salem <i>et al.</i> Mild: AUC _{0-inf} ratio of central values estimate: 1.261 (90% CI 0.808-1.970) Child-Pugh B: AUC _{0-inf} : 1.396 (90% CI 0.869-2.242) Child-Pugh C: AUC _{0-inf} : 2.700 (90% CI 1.625-4.487) Mild and moderate: no dose adjustment Severe: Reduce dose with at	Child-Pugh A/B and mild/moderate: no dose adjustment is needed Child-Pugh C and severe: 50% of the original dose	Vendexta label ¹ SPC Venclyxto ² Salem <i>et al.</i> ¹⁸⁵

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
					least 50%		
217	Vinblastine sulfate	Vinblastine is extensively metabolised in the liver to the more active desacetylvinblastine. It is excreted slowly in urine and feces.	MHRA: Renal impairment: no dose adjustment is needed	Renal impairment: no dose adjustment is needed HD: no need for dose adjustment is expected	MHRA: direct serum bilirubin > 3 mg/dl: 50% dose reduction is recommended.	Bilirubin > 51 µmol/L: 50% of the original dose	SPC vinblastine sulphate ⁹
218	Vincristine sulfate	Vincristine is metabolised in the liver. Vincristine and its metabolites are mainly excreted in feces (80%) and to a lesser extent in urine (10-20%).	FDA/MHRA: Renal impairment: not studied	Renal impairment: no need for dose adjustment is expected HD: no need for dose adjustment is expected	FDA/MHRA: Direct serum bilirubin >3 mg/dl: 50% dose reduction is recommended. MHRA: Direct serum bilirubin >3 mg/dl: 50% dose reduction is recommended.	Bilirubin > 51 µmol/L: 50% of original dose	Vincristine sulfate label ¹ SPC vincristine sulfate ⁹
219	Vincristine sulfate liposomal	Liposomal-encapsulated formulation of vincristine sulfate. Vincristine is metabolised in the liver. Vincristine and its metabolites are mainly excreted in feces (80%) and to a lesser extent in urine (10-20%).	FDA/MHRA: Renal impairment: not studied	Renal impairment: no need for dose adjustment is expected HD: no need for dose adjustment is expected	FDA (liposomal vincristine) Child-Pugh A: not studied Child-Pugh B: AUC and C _{max} were comparable to normal hepatic function Child-Pugh C: not studied Bedikian <i>et al</i>: After adjustment for dose differences, no statistically significant AUC _{0-inf} differences between patients with hepatic impairment (6 patients with Child-Pugh B and one with Child-Pugh C) and patients with normal liver function were observed (p=0.81).	Child-Pugh A/B: no dose adjustment is needed Child-Pugh C: consider a 50% dose reduction	Marqibo label ¹ Bedikian <i>et al</i> . ¹⁸⁶
220	Vinflunine	Vinflunine is metabolised in the liver. The active metabolite 4-O-deacetylvinflunine contributes to the clinical effect. Vinflunine and its metabolites are mainly excreted in feces (67%) and to a lesser extent in urine (33%).	EMA: CLcr > 60 ml/min: no dose adjustment CLcr 40-60 ml/min: 87.5% of the original dose (280 mg/m ²) CLcr 20-39 ml/min: 78% of the original dose (250 mg/m ²) Isambert <i>et al</i>. Geometric mean ratio of clearance: CLcr 40-60 ml/min: 0.88 (90% CI 0.78-0.98)	GFR > 60 ml/min: no dose adjustment is needed GFR 40-60 ml/min: 87.5% of the original dose (280 mg/m ²) GFR 20-39 ml/min: 78% of the original dose (250 mg/m ²) HD: 50% of the original dose (160 mg/m ²)	EMA: Child-Pugh A or prothrombin ≥ 60% of the normal value and bilirubin 1.5-3 x ULN and at least one of the following: transaminases > ULN and/or GGT > 5 x ULN: 78% of the original dose (250 mg/m ²) Child-Pugh B or prothrombin ≥ 50% of the normal value and bilirubin > 3 x ULN and transaminases > ULN and GGT > ULN: 62.5% of	Child-Pugh A, mild or moderate: 78% of the original dose Child-Pugh B: 62.5% of the original dose Child-Pugh C or severe: not recommended	SPC Javlor ² Isambert <i>et al</i> . ¹⁸⁷ Delord <i>et al</i> . ¹⁸⁸

	Agent	PK summary	Renal impairment		Hepatic impairment		References
			Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	
			CLcr 20-39 ml/min: 0.72 (90% CI 0.65-0.79)		the original dose (200 mg/m²) Child-Pugh C or prothrombin < 50% of the normal value or bilirubin >5xULN or isolated transaminases >2.5x ULN (≥5 only in case of liver metastases) or GGT >15 x ULN: not studied Delord <i>et al.</i> No difference in PK parameters (CL +AUC) for mild and moderate impairment*, dose adjustment solely based on safety data. Child-Pugh A/ mild-moderate*: 250 mg/m² Child-Pugh B/ moderate-severe*: 200 mg/m² * definition of mild/moderate/severe impairment as stated in the EMA advice above.		
221	Vinorelbine	Vinorelbine is metabolised in the liver. Vinorelbine and its metabolites are mainly excreted in feces (46%) and to a lesser extent in urine (18% or less).	FDA: No information MHRA: Not studied, no dose adjustment is needed	Renal impairment: no dose adjustment is needed HD: no need for dose adjustment is expected	FDA: (IV) Serum TB ≤ 2.0 mg/dl: no dose adjustment Serum TB 2.1-3.0 mg/dl: 50% of starting dose Serum TB > 3.0 mg/dl: 25% of starting dose MHRA: (IV) Mild and moderate: no dose adjustment Severe: reduced dose of 20mg/m² is recommended Oral: Mild: 60 mg/m²/week Moderate: 50 mg/m²/week Severe: not recommended	IV/Oral Mild and moderate: no dose adjustment is needed Severe: consider 66% of original dose	Navelbine label ¹ SPC Navelbine injection ⁹ SPC Navelbine 80 mg soft capsule ⁹ Kitzen <i>et al.</i> ¹⁰⁹

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
					<i>Kitzen et al.</i> No pharmacokinetic differences between patients with mild and moderate liver dysfunction compared to patients with normal hepatic function.		
222	Vismodegib	Vismodegib is metabolised in the liver. Vismodegib is mainly excreted in feces (82%) and to a lesser extent in urine (4-4%).	EMA/FDA: CLcr 30-79 ml/min: no dose adjustment CLcr < 30 ml/min: not studied HD: not studied Sbrana et al. HD: full dose was tolerated in one case report	GFR 30-79 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	EMA/FDA: Mild to severe: no dose adjustment Abou-Alfa et al. Mild: AUC _{0-24h} : 1.24 (90% CI 0.9-1.7) Moderate: AUC _{0-24h} : 1.31 (90% CI 0.9-1.8) Severe: AUC _{0-24h} : 0.86 (90% CI 0.5-1.4)	Hepatic impairment: no dose adjustment is needed	Erivedge label ¹ SPC Erivedge ² Abou-Alfa <i>et al.</i> ¹⁹⁰ Sbrana <i>et al.</i> ¹⁹¹
223	Vorinostat	Vorinostat is metabolised in the liver. Excretion is mainly through metabolism with < 1% of unchanged vorinostat excreted in urine.	FDA: Renal impairment: not studied, treat with caution HD: not studied	Renal impairment: no need for dose adjustment is expected HD: no need for dose adjustment is expected	FDA: Mild and moderate: treat with caution Severe: contraindicated Ramalingam et al. No PK- differences between patients with mild, moderate and severe hepatic impairment, dose adjustments of 300mg QD, 200mg QD and 100mg QD respectively, are solely based on safety data	Mild: 75% of the original dose Moderate: 50% of the original dose Severe: 25% of the original dose	Zolanza label ¹ Ramalingam <i>et al.</i> ¹⁹²
224	Zanubrutinib	Zanubrutinib is primarily metabolised by CYP3A enzymes. Zanubrutinib is mainly excreted in feces (87%, 38% unchanged) and minorly in urine (8%, <1% unchanged).	FDA: CLcr ≥ 15 ml/min: no dose adjustment CLcr < 15 ml/min: not studied HD: not studied EMA: CLcr ≥ 30 ml/min: no dose adjustment CLcr < 30 ml/min: not studied HD: not studied	GFR ≥ 30 ml/min: no dose adjustment is needed GFR < 30 ml/min: no need for dose adjustment is expected HD: no need for dose adjustment is expected	EMA/FDA: Child-Pugh A/B: no dose adjustment Child-Pugh C: . Adjust dose to 80 mg BID. Ou et al. Child-Pugh A: zanubrutinib total (bound + unbound) AUC _{0-inf} : 1.1 (90% CI 0.8-1.5) Child-Pugh B: zanubrutinib total AUC _{0-inf} : 1.2 (90% CI 0.9-1.6) Child-Pugh C: : zanubrutinib total AUC _{0-inf} : 2.6 (90% CI 1.2-	Child-Pugh A/B: no dose adjustment is needed Child-Pugh C: 25% of the original dose	Brukina label ¹ SPC Brukina ² Ou <i>et al.</i> ¹⁹³

			Renal impairment		Hepatic impairment		
	Agent	PK summary	Available evidence	Authors' recommendations	Available evidence	Authors' recommendations	References
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Abbreviations: 5-FU, 5-fluorouracil; ALT, alanine transaminase; AP, alkaline phosphatase; AST, aspartate transaminase; AUC_{0-inf}, area under the plasma concentration time profile of the drug of interest from time zero to infinity; AUC_{0-last}, area under the plasma concentration time profile of the drug of interest from time zero to last measured concentration; AUC_{0-24h}, area under the plasma concentration time profile of the drug of interest from time 0 to 24 hours; BID, twice daily; CI, confidence interval; CL, clearance; CL_{cr}, creatinine clearance; C_{max}, maximum concentration; C_{trough}, trough concentration; CVVH, continuous veno-venous hemofiltration; CYP, cytochrome P450; DLT, dose limiting toxicity; DPD, dihydropyrimidine-dehydrogenase; EMA, European Medicines Agency; ESRD, end-stage renal disease; FDA, Food and Drug Administration; FMO, Flavin-containing monooxygenase; (e)GFR, (estimated) glomerular filtrating rate; HD, haemodialysis; HER, human epidermal growth factor receptor 2; IV, intravenous; MHRA, Medicines and Healthcare products Regulatory Agency; MMAE, monomethylauristatin E; MMAF, monomethylauristatin F, MTD, maximum tolerated dose; PBPK, physiologically- based pharmacokinetic model; PK, pharmacokinetics; PopPK, population pharmacokinetic model; QD, once daily, SPC, Summary of Product Characteristics; t_{1/2}, half-life; TB, total bilirubin; TLS, tumor lysis syndrome; UGT, uridine 5'-diphospho-glyceronosyltransferase; ULN, upper limit of normal.

Explanation: AUC changes are presented as geometric means compared to normal renal or hepatic function, unless otherwise stated. Hepatic impairment is categorised according to Child-Pugh score or the National Cancer Institute Common Toxicity Criteria for Adverse Events, version 4.0 (CTCAEv4) and Organ Dysfunction Working Group: Mild: bilirubin >1.0-1.5 x ULN and any AST or bilirubin ≤ULN and AST >ULN; Moderate: bilirubin 1.5-3 x ULN, with any AST); Severe (bilirubin >3.0-10 x ULN, with any AST)

References

1. Drugs@FDA: FDA Approved Drug Products. 2023. <https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm> (accessed 31/03 2023).
2. European public assessment reports for human medicines. 2023. https://www.ema.europa.eu/en/medicines/field_ema_web_categories%253Aname_field/Human/ema_group_types/ema_medicine (accessed 31/03 2023).
3. Marbury T, Lawitz E, Stonerock R, et al. Single-dose pharmacokinetic studies of abiraterone acetate in men with hepatic or renal impairment. *Journal of clinical pharmacology* 2014; **54**(7): 732-41.
4. Xu Y, Izumi R, Nguyen H, et al. Evaluation of the Pharmacokinetics and Safety of a Single Dose of Acalabrutinib in Subjects With Hepatic Impairment. *Journal of clinical pharmacology* 2022; **62**(6): 812-22.
5. Wiebe S, Schnell D, Kulzer R, et al. Influence of Renal Impairment on the Pharmacokinetics of Afatinib: An Open-Label, Single-Dose Study. *European journal of drug metabolism and pharmacokinetics* 2017; **42**(3): 461-9.
6. Schnell D, Buschke S, Fuchs H, et al. Pharmacokinetics of afatinib in subjects with mild or moderate hepatic impairment. *Cancer chemotherapy and pharmacology* 2014; **74**(2): 267-75.
7. Imai H, Kaira K, Naruse I, et al. Successful afatinib treatment of advanced non-small-cell lung cancer patients undergoing hemodialysis. *Cancer chemotherapy and pharmacology* 2017; **79**(1): 209-13.
8. Morcos PN, Cleary Y, Sturm-Pellanda C, et al. Effect of Hepatic Impairment on the Pharmacokinetics of Alectinib. *Journal of clinical pharmacology* 2018.
9. Medicines Information: SPC & PILs. 2023. <https://products.mhra.gov.uk/> (accessed 12/04 2023).
10. Langenegger T, Wahl P, Schiesser D, Thurlimann B. Plasma levels of tamoxifen, N-desmethyl tamoxifen and anastrozole in a patient with metastatic breast cancer and chronic hemodialysis. *Breast cancer research and treatment* 2006; **100**(2): 177-81.
11. Firkin F, Roncolato F, Ho WK. Dose-adjusted arsenic trioxide for acute promyelocytic leukaemia in chronic renal failure. *European journal of haematology* 2015; **95**(4): 331-5.
12. Sweeney CJ, Takimoto C, Wood L, et al. A pharmacokinetic and safety study of intravenous arsenic trioxide in adult cancer patients with renal impairment. *Cancer chemotherapy and pharmacology* 2010; **66**(2): 345-56.
13. Perreault S, Moeller J, Patel K, et al. Use of arsenic trioxide in a hemodialysis-dependent patient with relapsed acute promyelocytic leukemia. *Journal of oncology pharmacy practice : official publication of the International Society of Oncology Pharmacy Practitioners* 2016; **22**(4): 646-51.
14. Hoch M, Sato M, Zack J, et al. Pharmacokinetics of Asciminib in Individuals With Hepatic or Renal Impairment. *Journal of clinical pharmacology* 2021; **61**(11): 1454-65.
15. Thiery-Vuillemin A, Orillard E, Mouillet G, et al. Hemodialysis does not impact axitinib exposure: clinical case of a patient with metastatic renal cell carcinoma. *Cancer chemotherapy and pharmacology* 2017; **79**(6): 1273-6.
16. Tortorici MA, Toh M, Rahavendran SV, et al. Influence of mild and moderate hepatic impairment on axitinib pharmacokinetics. *Investigational new drugs* 2011; **29**(6): 1370-80.
17. Laille E, Goel S, Mita AC, et al. A phase I study in patients with solid or hematologic malignancies of the dose proportionality of subcutaneous Azacitidine and its pharmacokinetics in patients with severe renal impairment. *Pharmacotherapy* 2014; **34**(5): 440-51.
18. Ham JC, Hoogendijk-van den Akker JM, Verdonck LF. A hemodialysis patient with higher-risk myelodysplastic syndrome treated with standard-dose azacitidine. *Leukemia & lymphoma* 2012; **53**(12): 2521-2.
19. Garnier-Viougeat N, Rixe O, Pintaud G, et al. Pharmacokinetics of bevacizumab in haemodialysis. *Nephrology, dialysis, transplantation : official*

publication of the European Dialysis and Transplant Association - European Renal Association 2007; **22**(3): 975.

20. Ito F, Goya N, Nakazawa H, et al. A study of plasma bicalutamide concentrations in hemodialysis patients. *Urologia internationalis* 2012; **89**(2): 162-5.
21. Crooke ST, Luft F, Broughton A, Strong J, Casson K, Einhorn L. Bleomycin serum pharmacokinetics as determined by a radioimmunoassay and a microbiologic assay in a patient with compromised renal function. *Cancer* 1977; **39**(4): 1430-4.
22. Zhu M, Wu B, Brandl C, et al. Blinatumomab, a Bispecific T-cell Engager (BiTE((R))) for CD-19 Targeted Cancer Immunotherapy: Clinical Pharmacology and Its Implications. *Clinical pharmacokinetics* 2016; **55**(10): 1271-88.
23. LoRusso PM, Venkatakrishnan K, Ramanathan RK, et al. Pharmacokinetics and safety of bortezomib in patients with advanced malignancies and varying degrees of liver dysfunction: phase I NCI Organ Dysfunction Working Group Study NCI-6432. *Clinical cancer research : an official journal of the American Association for Cancer Research* 2012; **18**(10): 2954-63.
24. Leal TB, Remick SC, Takimoto CH, et al. Dose-escalating and pharmacological study of bortezomib in adult cancer patients with impaired renal function: a National Cancer Institute Organ Dysfunction Working Group Study. *Cancer chemotherapy and pharmacology* 2011; **68**(6): 1439-47.
25. Abbas R, Hsyu PH. Clinical Pharmacokinetics and Pharmacodynamics of Bosutinib. *Clinical pharmacokinetics* 2016; **55**(10): 1191-204.
26. Abbas R, Chalon S, Leister C, El Gaaloul M, Sonnichsen D. Evaluation of the pharmacokinetics and safety of bosutinib in patients with chronic hepatic impairment and matched healthy subjects. *Cancer chemotherapy and pharmacology* 2013; **71**(1): 123-32.
27. Zhao B, Chen R, O'Connor OA, et al. Brentuximab vedotin, an antibody-drug conjugate, in patients with CD30-positive haematologic malignancies and hepatic or renal impairment. *British journal of clinical pharmacology* 2016; **82**(3): 696-705.
28. Gupta N, Hanley MJ, Kerstein D, et al. Effect of severe renal impairment on the pharmacokinetics of brigatinib. *Investigational new drugs* 2021; **39**(5): 1306-14.
29. Masauzi N, Higa T, Nakagawa S, et al. Pharmacokinetic study of busulfan in an AML patient treated with regular hemodialysis. *Annals of hematology* 1998; **77**(6): 293-4.
30. Azaro A, Rodon J, Machiels JP, et al. A phase I pharmacokinetic and safety study of cabazitaxel in adult cancer patients with normal and impaired renal function. *Cancer chemotherapy and pharmacology* 2016; **78**(6): 1185-97.
31. Sarantopoulos J, Mita AC, He A, et al. Safety and pharmacokinetics of cabazitaxel in patients with hepatic impairment: a phase I dose-escalation study. *Cancer chemotherapy and pharmacology* 2017; **79**(2): 339-51.
32. Nguyen L, Holland J, Ramies D, et al. Effect of Renal and Hepatic Impairment on the Pharmacokinetics of Cabozantinib. *Journal of clinical pharmacology* 2016; **56**(9): 1130-40.
33. Poole C, Gardiner J, Twelves C, et al. Effect of renal impairment on the pharmacokinetics and tolerability of capecitabine (Xeloda) in cancer patients. *Cancer chemotherapy and pharmacology* 2002; **49**(3): 225-34.
34. Joerger M, Huitema AD, Koeberle D, et al. Safety and pharmacology of gemcitabine and capecitabine in patients with advanced pancreatobiliary cancer and hepatic dysfunction. *Cancer chemotherapy and pharmacology* 2014; **73**(1): 113-24.
35. Twelves C, Glynne-Jones R, Cassidy J, et al. Effect of hepatic dysfunction due to liver metastases on the pharmacokinetics of capecitabine and its metabolites. *Clinical cancer research : an official journal of the American Association for Cancer Research* 1999; **5**(7): 1696-702.
36. Chen X, Cui X, Pognan N, et al. Pharmacokinetics of capmatinib in participants with hepatic impairment: A phase 1, open-label, single-dose, parallel-group study. *British journal of clinical pharmacology* 2022; **88**(1): 91-102.
37. Calvert AH, Newell DR, Gumbrell LA, et al. Carboplatin dosage: prospective evaluation of a simple formula based on renal function. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* 1989; **7**(11): 1748-56.
38. Watanabe M, Aoki Y, Tomita M, et al. Paclitaxel and carboplatin combination chemotherapy in a hemodialysis patient with advanced ovarian cancer.

Gynecologic oncology 2002; **84**(2): 335-8.

39. Badros AZ, Vij R, Martin T, et al. Carfilzomib in multiple myeloma patients with renal impairment: pharmacokinetics and safety. *Leukemia : official journal of the Leukemia Society of America, Leukemia Research Fund, UK* 2013; **27**(8): 1707-14.
40. Quach H, White D, Spencer A, et al. Pharmacokinetics and safety of carfilzomib in patients with relapsed multiple myeloma and end-stage renal disease (ESRD): an open-label, single-arm, phase I study. *Cancer chemotherapy and pharmacology* 2017; **79**(6): 1067-76.
41. Brown J, Plummer R, Bauer TM, et al. Pharmacokinetics of carfilzomib in patients with advanced malignancies and varying degrees of hepatic impairment: an open-label, single-arm, phase 1 study. *Experimental hematology & oncology* 2017; **6**: 27.
42. Kintzel PE, Dorr RT. Anticancer drug renal toxicity and elimination: dosing guidelines for altered renal function. *Cancer treatment reviews* 1995; **21**(1): 33-64.
43. Inauen R, Cathomas R, Boehm T, et al. Feasibility of using cetuximab and bevacizumab in a patient with colorectal cancer and terminal renal failure. *Oncology* 2007; **72**(3-4): 209-10.
44. Watanabe R, Takiguchi Y, Moriya T, et al. Feasibility of combination chemotherapy with cisplatin and etoposide for haemodialysis patients with lung cancer. *British journal of cancer* 2003; **88**(1): 25-30.
45. Crews KR, Wimmer PS, Hudson JQ, Howard SC, Ribeiro RC, Razzouk BI. Pharmacokinetics of 2-chlorodeoxyadenosine in a child undergoing hemofiltration and hemodialysis for acute renal failure. *Journal of pediatric hematology/oncology* 2002; **24**(8): 677-80.
46. Benitez LL, Gharibian K, Frame D, Mody R, Mora E. Clofarabine Dosing in a Patient With Acute Myeloid Leukemia on Intermittent Hemodialysis: Case Report and Review of the Literature. *Journal of pediatric hematology/oncology* 2017; **39**(6): 481-4.
47. Cheeti S, Deng Y, Chang I, et al. Effect of Hepatic Impairment on Cobimetinib Pharmacokinetics: The Complex Interplay Between Physiological Changes and Drug Characteristics. *Clin Pharmacol Drug Dev* 2021; **10**(2): 144-52.
48. Tan W, Yamazaki S, Johnson TR, et al. Effects of Renal Function on Crizotinib Pharmacokinetics: Dose Recommendations for Patients with ALK-Positive Non-Small Cell Lung Cancer. *Clinical drug investigation* 2017; **37**(4): 363-73.
49. El-Khoueiry AB, Sarantopoulos J, O'Bryant CL, et al. Evaluation of hepatic impairment on pharmacokinetics and safety of crizotinib in patients with advanced cancer. *Cancer chemotherapy and pharmacology* 2018; **81**(4): 659-70.
50. Wang LH, Lee CS, Majeske BL, Marbury TC. Clearance and recovery calculations in hemodialysis: application to plasma, red blood cells, and dialysate measurements for cyclophosphamide. *Clinical pharmacology and therapeutics* 1981; **29**(3): 365-72.
51. Haubitz M, Bohnenstengel F, Brunkhorst R, Schwab M, Hofmann U, Busse D. Cyclophosphamide pharmacokinetics and dose requirements in patients with renal insufficiency. *Kidney international* 2002; **61**(4): 1495-501.
52. Juma FD, Rogers HJ, Trounce JR. Effect of renal insufficiency on the pharmacokinetics of cyclophosphamide and some of its metabolites. *European journal of clinical pharmacology* 1981; **19**(6): 443-51.
53. Juma FD. Effect of liver failure on the pharmacokinetics of cyclophosphamide. *European journal of clinical pharmacology* 1984; **26**(5): 591-3.
54. Smith GA, Damon LE, Rugo HS, Ries CA, Linker CA. High-dose cytarabine dose modification reduces the incidence of neurotoxicity in patients with renal insufficiency. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* 1997; **15**(2): 833-9.
55. Radeski D, Cull GM, Cain M, Hackett LP, Ilett KF. Effective clearance of Ara-U the major metabolite of cytosine arabinoside (Ara-C) by hemodialysis in a patient with lymphoma and end-stage renal failure. *Cancer chemotherapy and pharmacology* 2011; **67**(4): 765-8.
56. Barker JA, Marini BL, Bixby D, Perissinotti AJ. Successful use of high-dose cytarabine in a patient with acute myeloid leukemia and severe hepatic dysfunction. *Journal of oncology pharmacy practice : official publication of the International Society of Oncology Pharmacy Practitioners* 2016; **22**(6): 811-5.
57. Park JJ, Boddy AV, Liu X, et al. Pharmacokinetics of dabrafenib in a patient with metastatic melanoma undergoing haemodialysis. *Pigment cell &*

melanoma research 2017; **30**(1): 68-71.

58. Zurth C, Nykanen P, Wilkinson G, et al. Clinical Pharmacokinetics of the Androgen Receptor Inhibitor Darolutamide in Healthy Subjects and Patients with Hepatic or Renal Impairment. *Clinical pharmacokinetics* 2022; **61**(4): 565-75.
59. Krashin E, Dolberg OJ, Hellmann I, Huitema AD, Rosing H, Ellis M. Cytosine arabinoside and daunorubicin induction therapy in a patient with acute myeloid leukemia on chronic hemodialysis. *Anti-cancer drugs* 2016; **27**(8): 800-3.
60. Levine LB, Roddy JV, Kim M, Li J, Phillips G, Walker AR. A comparison of toxicities in acute myeloid leukemia patients with and without renal impairment treated with decitabine. *Journal of oncology pharmacy practice : official publication of the International Society of Oncology Pharmacy Practitioners* 2018; **24**(4): 290-8.
61. Dimopoulos MA, Deliveliotis C, Moulopoulos LA, et al. Treatment of patients with metastatic urothelial carcinoma and impaired renal function with single-agent docetaxel. *Urology* 1998; **52**(1): 56-60.
62. Hochegger K, Lhotta K, Mayer G, Czejka M, Hilbe W. Pharmacokinetic analysis of docetaxel during haemodialysis in a patient with locally advanced non-small cell lung cancer. *Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association* 2007; **22**(1): 289-90.
63. Bruno R, Hille D, Riva A, et al. Population pharmacokinetics/pharmacodynamics of docetaxel in phase II studies in patients with cancer. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* 1998; **16**(1): 187-96.
64. Syn NL, Wang L, Wong AL, et al. Dose modifications in Asian cancer patients with hepatic dysfunction receiving weekly docetaxel: A prospective pharmacokinetic and safety study. *Cancer science* 2016; **107**(2): 173-80.
65. Minami H, Kawada K, Sasaki Y, et al. Population pharmacokinetics of docetaxel in patients with hepatic dysfunction treated in an oncology practice. *Cancer science* 2009; **100**(1): 144-9.
66. Eckmann K, Michaud LB, Rivera E, et al. Pilot study to assess toxicity and pharmacokinetics of docetaxel in patients with metastatic breast cancer and impaired liver function secondary to hepatic metastases. *Journal of oncology pharmacy practice : official publication of the International Society of Oncology Pharmacy Practitioners* 2014; **20**(2): 120-9.
67. Yoshida H, Goto M, Honda A, et al. Pharmacokinetics of doxorubicin and its active metabolite in patients with normal renal function and in patients on hemodialysis. *Cancer chemotherapy and pharmacology* 1994; **33**(6): 450-4.
68. Berdeja J, Jagannath S, Zonder J, et al. Pharmacokinetics and Safety of Elotuzumab Combined With Lenalidomide and Dexamethasone in Patients With Multiple Myeloma and Various Levels of Renal Impairment: Results of a Phase Ib Study. *Clinical lymphoma, myeloma & leukemia* 2016; **16**(3): 129-38.
69. Krauwinkel W, Noukens J, van Dijk J, et al. A comparison of the pharmacokinetics and safety of enzalutamide in subjects with hepatic impairment and matched healthy subjects. *Journal of clinical pharmacy and therapeutics* 2017; **42**(3): 268-75.
70. Gori S, Rulli A, Mosconi AM, Sidoni A, Colozza M, Crino L. Safety of epirubicin adjuvant chemotherapy in a breast cancer patient with chronic renal failure undergoing hemodialytic treatment. *Tumori* 2006; **92**(4): 364-5.
71. Dobbs NA, Twelves CJ, Gregory W, Cruickshank C, Richards MA, Rubens RD. Epirubicin in patients with liver dysfunction: development and evaluation of a novel dose modification scheme. *European journal of cancer* 2003; **39**(5): 580-6.
72. Twelves CJ, O'Reilly SM, Coleman RE, Richards MA, Rubens RD. Weekly epirubicin for breast cancer with liver metastases and abnormal liver biochemistry. *British journal of cancer* 1989; **60**(6): 938-41.
73. Tan AR, Sarantopoulos J, Lee L, et al. Pharmacokinetics of eribulin mesylate in cancer patients with normal and impaired renal function. *Cancer chemotherapy and pharmacology* 2015; **76**(5): 1051-61.
74. Devriese LA, Witteveen PO, Marchetti S, et al. Pharmacokinetics of eribulin mesylate in patients with solid tumors and hepatic impairment. *Cancer*

chemotherapy and pharmacology 2012; **70**(6): 823-32.

75. O'Bryant CL, Haluska P, Rosen L, et al. An open-label study to describe pharmacokinetic parameters of erlotinib in patients with advanced solid tumors with adequate and moderately impaired hepatic function. *Cancer chemotherapy and pharmacology* 2012; **69**(3): 605-12.

76. Togashi Y, Masago K, Fukudo M, et al. Pharmacokinetics of erlotinib and its active metabolite OSI-420 in patients with non-small cell lung cancer and chronic renal failure who are undergoing hemodialysis. *J Thorac Oncol* 2010; **5**(5): 601-5.

77. Miller AA, Murry DJ, Owzar K, et al. Phase I and pharmacokinetic study of erlotinib for solid tumors in patients with hepatic or renal dysfunction: CALGB 60101. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* 2007; **25**(21): 3055-60.

78. Stewart CF, Arbus SG, Fleming RA, Evans WE. Changes in the clearance of total and unbound etoposide in patients with liver dysfunction. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* 1990; **8**(11): 1874-9.

79. Thiery-Vuillemin A, Curtit E, Maurina T, et al. Hemodialysis does not affect everolimus pharmacokinetics: two cases of patients with metastatic renal cell cancer. *Annals of oncology : official journal of the European Society for Medical Oncology / ESMO* 2012; **23**(11): 2992-3.

80. Peveling-Oberhag J, Zeuzem S, Yong WP, et al. Effects of hepatic impairment on the pharmacokinetics of everolimus: a single-dose, open-label, parallel-group study. *Clinical therapeutics* 2013; **35**(3): 215-25.

81. Kovarik JM, Sabia HD, Figueiredo J, et al. Influence of hepatic impairment on everolimus pharmacokinetics: implications for dose adjustment. *Clinical pharmacology and therapeutics* 2001; **70**(5): 425-30.

82. Jannuzzo MG, Poggesi I, Spinelli R, Rocchetti M, Cicioni P, Buchan P. The effects of degree of hepatic or renal impairment on the pharmacokinetics of exemestane in postmenopausal women. *Cancer chemotherapy and pharmacology* 2004; **53**(6): 475-81.

83. Ogasawara K, Smith WB, Xu C, Yin J, Palmisano M, Krishna G. Pharmacokinetics and tolerability of fedratinib, an oral, selective Janus kinase 2 inhibitor, in subjects with renal or hepatic impairment. *Cancer chemotherapy and pharmacology* 2020; **85**(6): 1109-17.

84. Lichtman SM, Etcubanas E, Budman DR, et al. The pharmacokinetics and pharmacodynamics of fludarabine phosphate in patients with renal impairment: a prospective dose adjustment study. *Cancer investigation* 2002; **20**(7-8): 904-13.

85. Kielstein JT, Stadler M, Czock D, Keller F, Hertenstein B, Radermacher J. Dialysate concentration and pharmacokinetics of 2F-Ara-A in a patient with acute renal failure. *European journal of haematology* 2005; **74**(6): 533-4.

86. Rengelshausen J, Hull WE, Schwenger V, Goggelmann C, Walter-Sack I, Bommer J. Pharmacokinetics of 5-fluorouracil and its catabolites determined by 19F nuclear magnetic resonance spectroscopy for a patient on chronic hemodialysis. *American journal of kidney diseases : the official journal of the National Kidney Foundation* 2002; **39**(2): E10.

87. Fleming GF, Schilsky RL, Schumm LP, et al. Phase I and pharmacokinetic study of 24-hour infusion 5-fluorouracil and leucovorin in patients with organ dysfunction. *Annals of oncology : official journal of the European Society for Medical Oncology / ESMO* 2003; **14**(7): 1142-7.

88. Anjum S, Swan SK, Lambrecht LJ, et al. Pharmacokinetics of flutamide in patients with renal insufficiency. *British journal of clinical pharmacology* 1999; **47**(1): 43-7.

89. Shinagawa N, Yamazaki K, Asahina H, Agata J, Itoh T, Nishimura M. Gefitinib administration in a patient with lung cancer undergoing hemodialysis. *Lung cancer* 2007; **58**(3): 422-4.

90. Horak J, White J, Harris AL, et al. The effect of different etiologies of hepatic impairment on the pharmacokinetics of gefitinib. *Cancer chemotherapy and pharmacology* 2011; **68**(6): 1485-95.

91. Venook AP, Egorin MJ, Rosner GL, et al. Phase I and pharmacokinetic trial of gemcitabine in patients with hepatic or renal dysfunction: Cancer and Leukemia Group B 9565. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* 2000; **18**(14): 2780-7.

92. Kiani A, Kohne CH, Franz T, et al. Pharmacokinetics of gemcitabine in a patient with end-stage renal disease: effective clearance of its main metabolite

by standard hemodialysis treatment. *Cancer chemotherapy and pharmacology* 2003; **51**(3): 266-70.

93. Teusink AC, Hall PD. Toxicities of gemcitabine in patients with severe hepatic dysfunction. *The Annals of pharmacotherapy* 2010; **44**(4): 750-4.

94. Yan JH, Ataga K, Kaul S, et al. The influence of renal function on hydroxyurea pharmacokinetics in adults with sickle cell disease. *Journal of clinical pharmacology* 2005; **45**(4): 434-45.

95. Filanovsky K, Shvidel L. Safety and efficacy of ibrutinib in a patient with severe renal impairment. *Hematology reports* 2017; **9**(3): 7078.

96. de Jong J, Skee D, Hellemans P, et al. Single-dose pharmacokinetics of ibrutinib in subjects with varying degrees of hepatic impairment<sup/>. *Leukemia & lymphoma* 2017; **58**(1): 185-94.

97. Tsuchiya Y, Ubara Y, Suwabe T, et al. Successful treatment of acute promyelocytic leukemia in a patient on hemodialysis. *Clinical and experimental nephrology* 2011; **15**(3): 434-7.

98. Jin F, Robeson M, Zhou H, Hisoire G, Ramanathan S. The pharmacokinetics and safety of idelalisib in subjects with severe renal impairment. *Cancer chemotherapy and pharmacology* 2015; **76**(6): 1133-41.

99. Jin F, Robeson M, Zhou H, Hisoire G, Ramanathan S. The pharmacokinetics and safety of idelalisib in subjects with moderate or severe hepatic impairment. *Journal of clinical pharmacology* 2015; **55**(8): 944-52.

100. Carlson L, Goren MP, Bush DA, et al. Toxicity, pharmacokinetics, and in vitro hemodialysis clearance of ifosfamide and metabolites in an anephric pediatric patient with Wilms' tumor. *Cancer chemotherapy and pharmacology* 1998; **41**(2): 140-6.

101. Gibbons J, Egorin MJ, Ramanathan RK, et al. Phase I and pharmacokinetic study of imatinib mesylate in patients with advanced malignancies and varying degrees of renal dysfunction: a study by the National Cancer Institute Organ Dysfunction Working Group. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* 2008; **26**(4): 570-6.

102. Pappas P, Karavasilis V, Briasoulis E, Pavlidis N, Marselos M. Pharmacokinetics of imatinib mesylate in end stage renal disease. A case study. *Cancer chemotherapy and pharmacology* 2005; **56**(4): 358-60.

103. Ramanathan RK, Egorin MJ, Takimoto CH, et al. Phase I and pharmacokinetic study of imatinib mesylate in patients with advanced malignancies and varying degrees of liver dysfunction: a study by the National Cancer Institute Organ Dysfunction Working Group. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* 2008; **26**(4): 563-9.

104. Czock D, Rasche FM, Boesler B, Shipkova M, Keller F. Irinotecan in cancer patients with end-stage renal failure. *The Annals of pharmacotherapy* 2009; **43**(2): 363-9.

105. Stemmler J, Weise A, Hacker U, Heinemann V, Schalhorn A. Weekly irinotecan in a patient with metastatic colorectal cancer on hemodialysis due to chronic renal failure. *Onkologie* 2002; **25**(1): 60-3.

106. Fujita K, Sunakawa Y, Miwa K, et al. Delayed elimination of SN-38 in cancer patients with severe renal failure. *Drug metabolism and disposition: the biological fate of chemicals* 2011; **39**(2): 161-4.

107. Raymond E, Boige V, Faivre S, et al. Dosage adjustment and pharmacokinetic profile of irinotecan in cancer patients with hepatic dysfunction. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* 2002; **20**(21): 4303-12.

108. Schaaf LJ, Hammond LA, Tipping SJ, et al. Phase 1 and pharmacokinetic study of intravenous irinotecan in refractory solid tumor patients with hepatic dysfunction. *Clinical cancer research : an official journal of the American Association for Cancer Research* 2006; **12**(12): 3782-91.

109. Venook AP, Enders Klein C, Fleming G, et al. A phase I and pharmacokinetic study of irinotecan in patients with hepatic or renal dysfunction or with prior pelvic radiation: CALGB 9863. *Annals of oncology : official journal of the European Society for Medical Oncology / ESMO* 2003; **14**(12): 1783-90.

110. Fan B, Dai D, DiNardo CD, et al. Clinical pharmacokinetics and pharmacodynamics of ivosidenib in patients with advanced hematologic malignancies with an IDH1 mutation. *Cancer chemotherapy and pharmacology* 2020; **85**(5): 959-68.

111. Gupta N, Hanley MJ, Harvey RD, et al. A pharmacokinetics and safety phase 1/1b study of oral ixazomib in patients with multiple myeloma and severe renal impairment or end-stage renal disease requiring haemodialysis. *British journal of haematology* 2016; **174**(5): 748-59.
112. Gupta N, Hanley MJ, Venkatakrishnan K, et al. Pharmacokinetics of ixazomib, an oral proteasome inhibitor, in solid tumour patients with moderate or severe hepatic impairment. *British journal of clinical pharmacology* 2016; **82**(3): 728-38.
113. Pai SM, Chaikin P, Berg JK. Pharmacokinetics of Lapatinib, a Nonrenally Cleared Drug, in Patients With End-Stage Renal Disease on Maintenance Hemodialysis. *Journal of clinical pharmacology* 2019; **59**(10): 1379-83.
114. Shumaker R, Aluri J, Fan J, Martinez G, Pentikis H, Ren M. Influence of hepatic impairment on lenvatinib pharmacokinetics following single-dose oral administration. *Journal of clinical pharmacology* 2015; **55**(3): 317-27.
115. Kergueris MF, Milpied N, Moreau P, Harousseau JL, Larousse C. Pharmacokinetics of high-dose melphalan in adults: influence of renal function. *Anticancer research* 1994; **14**(6a): 2379-82.
116. Wall SM, Johansen MJ, Molony DA, DuBose TD, Jr., Jaffe N, Madden T. Effective clearance of methotrexate using high-flux hemodialysis membranes. *American journal of kidney diseases : the official journal of the National Kidney Foundation* 1996; **28**(6): 846-54.
117. Tollkuci E, Seddon A, Geswein L, Mulseh M. Midostaurin administration in two hemodialysis patients. *Journal of oncology pharmacy practice : official publication of the International Society of Oncology Pharmacy Practitioners* 2018: 1078155218801067.
118. Boros L, Cacek T, Pine RB, Battaglia AC. Distribution characteristics of mitoxantrone in a patient undergoing hemodialysis. *Cancer chemotherapy and pharmacology* 1992; **31**(1): 57-60.
119. Savaraj N, Lu K, Manuel V, Loo TL. Pharmacology of mitoxantrone in cancer patients. *Cancer chemotherapy and pharmacology* 1982; **8**(1): 113-7.
120. Yoshihara M, Kubota Y, Fukuda M, et al. Mogamulizumab treatment in a hemodialysis patient with adult T-cell leukemia/lymphoma. *Turkish journal of haematology : official journal of Turkish Society of Haematology* 2014; **31**(4): 424-5.
121. Onaka T, Takahashi N, Miura M, Yonezawa A, Imada K, Sawada K. Pharmacokinetics of nilotinib in imatinib-resistant/intolerant chronic myeloid leukemia patients on hemodialysis for chronic renal failure. *American journal of hematology* 2012; **87**(4): 451.
122. Yin OQ, Gallagher N, Tanaka C, et al. Effects of hepatic impairment on the pharmacokinetics of nilotinib: an open-label, single-dose, parallel-group study. *Clinical therapeutics* 2009; **31 Pt 2**: 2459-69.
123. Marzin K, Kretschmar G, Luedtke D, et al. Pharmacokinetics of Nintedanib in Subjects With Hepatic Impairment. *Journal of clinical pharmacology* 2017.
124. Okusaka T, Otsuka T, Ueno H, et al. Phase I study of nintedanib in Japanese patients with advanced hepatocellular carcinoma and liver impairment. *Cancer science* 2016; **107**(12): 1791-9.
125. Akce M, El-Khoueiry A, Piha-Paul SA, et al. Pharmacokinetics and safety of niraparib in patients with moderate hepatic impairment. *Cancer chemotherapy and pharmacology* 2021; **88**(5): 825-36.
126. Pilla Reddy V, Bui K, Scarfe G, Zhou D, Learoyd M. Physiologically Based Pharmacokinetic Modeling for Olaparib Dosing Recommendations: Bridging Formulations, Drug Interactions, and Patient Populations. *Clinical pharmacology and therapeutics* 2018.
127. Baum J, Zickler D, Bolbrinker J, et al. Olaparib in an ovarian cancer patient with end-stage renal disease and hemodialysis. *Cancer chemotherapy and pharmacology* 2023; **91**(4): 325-30.
128. Rolfo C, de Vos-Geelen J, Isambert N, et al. Pharmacokinetics and Safety of Olaparib in Patients with Advanced Solid Tumours and Renal Impairment. *Clinical pharmacokinetics* 2019; **58**(9): 1165-74.
129. Rolfo C, Isambert N, Italiano A, et al. Pharmacokinetics and safety of olaparib in patients with advanced solid tumours and mild or moderate hepatic impairment. *British journal of clinical pharmacology* 2020; **86**(9): 1807-18.
130. Tamura T, Takagi Y, Okubo H, et al. Plasma concentration of osimertinib in a non-small cell lung cancer patient with chronic renal failure undergoing

hemodialysis. *Lung cancer* 2017; **112**: 225-6.

131. Vishwanathan K, Sanchez-Simon I, Keam B, et al. A multicenter, phase I, pharmacokinetic study of osimertinib in cancer patients with normal renal function or severe renal impairment. *Pharmacol Res Perspect* 2020; **8**(4): e00613.
132. Gori S, Lunardi G, Inno A, et al. Pharmacokinetics of oxaliplatin in a hemodialyzed patient: chemotherapy dose adjustment and timing of dialysis. *Clinical colorectal cancer* 2014; **13**(4): 260-3.
133. Watayo Y, Kuramochi H, Hayashi K, Nakajima G, Kamikozuru H, Yamamoto M. Drug monitoring during FOLFOX6 therapy in a rectal cancer patient on chronic hemodialysis. *Japanese journal of clinical oncology* 2010; **40**(4): 360-4.
134. Takimoto CH, Remick SC, Sharma S, et al. Dose-escalating and pharmacological study of oxaliplatin in adult cancer patients with impaired renal function: a National Cancer Institute Organ Dysfunction Working Group Study. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* 2003; **21**(14): 2664-72.
135. Synold TW, Takimoto CH, Doroshow JH, et al. Dose-escalating and pharmacologic study of oxaliplatin in adult cancer patients with impaired hepatic function: a National Cancer Institute Organ Dysfunction Working Group study. *Clinical cancer research : an official journal of the American Association for Cancer Research* 2007; **13**(12): 3660-6.
136. Biakhov MY, Kononova GV, Iglesias J, et al. nab-Paclitaxel in patients with advanced solid tumors and hepatic dysfunction: a pilot study. *Expert opinion on drug safety* 2010; **9**(4): 515-23.
137. Briasoulis E, Karavasilis V, Tzamakou E, Piperidou C, Soulti K, Pavlidis N. Feasibility study and pharmacokinetics of low-dose paclitaxel in cancer patients with severe hepatic dysfunction. *Anti-cancer drugs* 2006; **17**(10): 1219-22.
138. Tomita M, Kurata H, Aoki Y, Tanaka K, Kazama JJ. Pharmacokinetics of paclitaxel and cisplatin in a hemodialysis patient with recurrent ovarian cancer. *Anti-cancer drugs* 2001; **12**(5): 485-7.
139. Gelderblom H, Verweij J, Brouwer E, et al. Disposition of [G-(3)H]paclitaxel and cremophor EL in a patient with severely impaired renal function. *Drug metabolism and disposition: the biological fate of chemicals* 1999; **27**(11): 1300-5.
140. Joerger M, Huitema AD, Huizing MT, et al. Safety and pharmacology of paclitaxel in patients with impaired liver function: a population pharmacokinetic-pharmacodynamic study. *British journal of clinical pharmacology* 2007; **64**(5): 622-33.
141. Yu Y, Hoffman J, Plotka A, O'Gorman M, Shi H, Wang D. Palbociclib (PD-0332991) pharmacokinetics in subjects with impaired renal function. *Cancer chemotherapy and pharmacology* 2020; **86**(6): 701-10.
142. Krens LL, Baas JM, de Jong FA, Guchelaar HJ, Gelderblom H. Pharmacokinetics of panitumumab in a patient with liver dysfunction: a case report. *Cancer chemotherapy and pharmacology* 2014; **73**(2): 429-33.
143. Sharma S, Witteveen PO, Lolkema MP, et al. A phase I, open-label, multicenter study to evaluate the pharmacokinetics and safety of oral panobinostat in patients with advanced solid tumors and varying degrees of renal function. *Cancer chemotherapy and pharmacology* 2015; **75**(1): 87-95.
144. Slingerland M, Hess D, Clive S, et al. A phase I, open-label, multicenter study to evaluate the pharmacokinetics and safety of oral panobinostat in patients with advanced solid tumors and various degrees of hepatic function. *Cancer chemotherapy and pharmacology* 2014; **74**(5): 1089-98.
145. Sekiguchi Y, Takizawa H, Inano T, et al. Three cases of relapsed/refractory multiple myeloma under hemodialysis treated with panobinostat/bortezomib/dexamethasone (FVD). *International journal of hematology* 2017; **106**(4): 581-7.
146. Shibata SI, Chung V, Synold TW, et al. Phase I study of pazopanib in patients with advanced solid tumors and hepatic dysfunction: a National Cancer Institute Organ Dysfunction Working Group study. *Clinical cancer research : an official journal of the American Association for Cancer Research* 2013; **19**(13): 3631-9.
147. Mita AC, Sweeney CJ, Baker SD, et al. Phase I and pharmacokinetic study of pemetrexed administered every 3 weeks to advanced cancer patients with

normal and impaired renal function. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* 2006; **24**(4): 552-62.

148. Brandes JC, Grossman SA, Ahmad H. Alteration of pemetrexed excretion in the presence of acute renal failure and effusions: presentation of a case and review of the literature. *Cancer investigation* 2006; **24**(3): 283-7.

149. Hill J, Vargo C, Smith M, Streeter J, Carbone DP. Safety of dose-reduced pemetrexed in patients with renal insufficiency. *Journal of Oncology Pharmacy Practice* 2018; 1078155218780507.

150. Boosman RJ, Dorlo TPC, de Rouw N, et al. Toxicity of pemetrexed during renal impairment explained-Implications for safe treatment. *International journal of cancer Journal international du cancer* 2021; **149**(8): 1576-84.

151. de Rouw N, Croes S, Posthuma R, et al. Pharmacokinetically-guided dosing of pemetrexed in a patient with renal impairment and a patient requiring hemodialysis. *Lung cancer* 2019; **130**: 156-8.

152. Ji T, Rockich K, Epstein N, et al. Evaluation of the pharmacokinetics of pemigatinib in patients with impaired hepatic or renal function. *British journal of clinical pharmacology* 2022; **88**(1): 237-47.

153. Lathia C, Fleming GF, Meyer M, Ratain MJ, Whitfield L. Pentostatin pharmacokinetics and dosing recommendations in patients with mild renal impairment. *Cancer chemotherapy and pharmacology* 2002; **50**(2): 121-6.

154. Narasimhan NI, Dorer DJ, Davis J, Turner CD, Marbury TC, Sonnichsen D. Evaluation of pharmacokinetics and safety of ponatinib in subjects with chronic hepatic impairment and matched healthy subjects. *Cancer chemotherapy and pharmacology* 2014; **74**(2): 341-8.

155. Li Y, Wang X, Liu L, et al. An Open-Label, Phase 1 Study to Assess the Effects of Hepatic Impairment on Pomalidomide Pharmacokinetics. *Clin Pharmacol Drug Dev* 2019; **8**(3): 346-54.

156. Kelly KR, Gabrail N, Weitman S, et al. Phase 1 study evaluating the safety and pharmacokinetics of pralatrexate in relapsed/refractory advanced solid tumors and lymphoma patients with mild, moderate, and severe renal impairment. *Cancer chemotherapy and pharmacology* 2016; **78**(5): 929-39.

157. Judson I, Maughan T, Beale P, et al. Effects of impaired renal function on the pharmacokinetics of raltitrexed (Tomudex ZD1694). *British journal of cancer* 1998; **78**(9): 1188-93.

158. Jillella AP, Dainer PM, Kallab AM, Ustun C. Treatment of a patient with end-stage renal disease with Rituximab: pharmacokinetic evaluation suggests Rituximab is not eliminated by hemodialysis. *American journal of hematology* 2002; **71**(3): 219-22.

159. Grechko N, Skarbova V, Tomaszewska-Kiecana M, et al. Pharmacokinetics and safety of rucaparib in patients with advanced solid tumors and hepatic impairment. *Cancer chemotherapy and pharmacology* 2021; **88**(2): 259-70.

160. Chen X, Shi JG, Emm T, et al. Pharmacokinetics and pharmacodynamics of orally administered ruxolitinib (INCB018424 phosphate) in renal and hepatic impairment patients. *Clin Pharmacol Drug Dev* 2014; **3**(1): 34-42.

161. Bader JC, Abdul Razak AR, Shacham S, Xu H. Pharmacokinetics of Selinexor: The First-in-Class Selective Inhibitor of Nuclear Export. *Clinical pharmacokinetics* 2021; **60**(8): 957-69.

162. Horsmans Y, Zhou J, Liudmila M, et al. Effects of Mild to Severe Hepatic Impairment on the Pharmacokinetics of Sonidegib: A Multicenter, Open-Label, Parallel-Group Study. *Clinical pharmacokinetics* 2018; **57**(3): 345-54.

163. Miller AA, Murry DJ, Owzar K, et al. Phase I and Pharmacokinetic Study of Sorafenib in Patients With Hepatic or Renal Dysfunction: CALGB 60301. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* 2009.

164. Kennoki T, Kondo T, Kimata N, et al. Clinical results and pharmacokinetics of sorafenib in chronic hemodialysis patients with metastatic renal cell carcinoma in a single center. *Japanese journal of clinical oncology* 2011; **41**(5): 647-55.

165. Khosravan R, Toh M, Garrett M, et al. Pharmacokinetics and safety of sunitinib malate in subjects with impaired renal function. *Journal of clinical pharmacology* 2010; **50**(4): 472-81.

166. Izzedine H, Etienne-Grimaldi MC, Renee N, Vignot S, Milano G. Pharmacokinetics of sunitinib in hemodialysis. *Annals of oncology : official journal of the European Society for Medical Oncology / ESMO* 2009; **20**(1): 190-2.
167. Bello CL, Garrett M, Sherman L, Smeraglia J, Ryan B, Toh M. Pharmacokinetics of sunitinib malate in subjects with hepatic impairment. *Cancer chemotherapy and pharmacology* 2010; **66**(4): 699-707.
168. Floren LC, Hebert MF, Venook AP, Jordan VC, Cisneros A, Somberg KA. Tamoxifen in liver disease: potential exacerbation of hepatic dysfunction. *Annals of oncology : official journal of the European Society for Medical Oncology / ESMO* 1998; **9**(10): 1123-6.
169. Yu Y, Durairaj C, Shi H, Wang DD. Population Pharmacokinetics of Talazoparib in Patients With Advanced Cancer. *Journal of clinical pharmacology* 2020; **60**(2): 218-28.
170. Booka E, Imamura CK, Takeuchi H, et al. Development of an S-1 dosage formula based on renal function by a prospective pharmacokinetic study. *Gastric cancer : official journal of the International Gastric Cancer Association and the Japanese Gastric Cancer Association* 2016; **19**(3): 876-86.
171. Tomiyama N, Hidaka M, Hidaka H, et al. Safety, efficacy and pharmacokinetics of S-1 in a hemodialysis patient with advanced gastric cancer. *Cancer chemotherapy and pharmacology* 2010; **65**(4): 807-9.
172. Lunardi G, Armirotti A, Nicodemo M, et al. Comparison of temsirolimus pharmacokinetics in patients with renal cell carcinoma not receiving dialysis and those receiving hemodialysis: a case series. *Clinical therapeutics* 2009; **31**(8): 1812-9.
173. Eriksson T, Bjorkman S, Hoglund P. Clinical pharmacology of thalidomide. *European journal of clinical pharmacology* 2001; **57**(5): 365-76.
174. Ekhardt C, Kerst JM, Rodenhuis S, Beijnen JH, Huitema AD. Altered cyclophosphamide and thiotepa pharmacokinetics in a patient with moderate renal insufficiency. *Cancer chemotherapy and pharmacology* 2009; **63**(2): 375-9.
175. O'Reilly S, Rowinsky EK, Slichenmyer W, et al. Phase I and pharmacologic study of topotecan in patients with impaired renal function. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* 1996; **14**(12): 3062-73.
176. Devriese LA, Witteveen PE, Mergui-Roelvink M, et al. Pharmacodynamics and pharmacokinetics of oral topotecan in patients with advanced solid tumours and impaired renal function. *British journal of clinical pharmacology* 2015; **80**(2): 253-66.
177. O'Reilly S, Rowinsky E, Slichenmyer W, et al. Phase I and pharmacologic studies of topotecan in patients with impaired hepatic function. *Journal of the National Cancer Institute* 1996; **88**(12): 817-24.
178. Herrington JD, Figueroa JA, Kirstein MN, Zamboni WC, Stewart CF. Effect of hemodialysis on topotecan disposition in a patient with severe renal dysfunction. *Cancer chemotherapy and pharmacology* 2001; **47**(1): 89-93.
179. Anttila M, Laakso S, Nylanden P, Sotaniemi EA. Pharmacokinetics of the novel antiestrogenic agent toremifene in subjects with altered liver and kidney function. *Clinical pharmacology and therapeutics* 1995; **57**(6): 628-35.
180. Thariat J, Etienne-Grimaldi MC, Launay-Vacher V, et al. Pharmacokinetics of trabectedin on hemodialysis: an application for the management of cancer patients with end-stage renal disease. *Cancer chemotherapy and pharmacology* 2011; **68**(5): 1363-7.
181. Calvo E, Azaro A, Rodon J, et al. Hepatic safety analysis of trabectedin: results of a pharmacokinetic study with trabectedin in patients with hepatic impairment and experience from a phase 3 clinical trial. *Investigational new drugs* 2018; **36**(3): 476-86.
182. Saif MW, Becerra CR, Fakih MG, et al. A phase I, open-label study evaluating the safety and pharmacokinetics of trifluridine/tipiracil in patients with advanced solid tumors and varying degrees of renal impairment. *Cancer chemotherapy and pharmacology* 2021; **88**(3): 485-97.
183. Saif MW, Rosen L, Rudek MA, et al. Open-label study to evaluate trifluridine/tipiracil safety, tolerability and pharmacokinetics in patients with advanced solid tumours and hepatic impairment. *British journal of clinical pharmacology* 2019; **85**(6): 1239-46.
184. Weil A, Martin P, Smith R, et al. Pharmacokinetics of vandetanib in subjects with renal or hepatic impairment. *Clinical pharmacokinetics* 2010; **49**(9): 607-18.

185. Salem AH, Dave N, Marbury T, et al. Pharmacokinetics of the BCL-2 Inhibitor Venetoclax in Subjects with Hepatic Impairment. *Clinical pharmacokinetics* 2019; **58**(8): 1091-100.
186. Bedikian AY, Silverman JA, Papadopoulos NE, et al. Pharmacokinetics and safety of Marqibo (vincristine sulfate liposomes injection) in cancer patients with impaired liver function. *Journal of clinical pharmacology* 2011; **51**(8): 1205-12.
187. Isambert N, Delord JP, Tourani JM, et al. How to manage intravenous vinflunine in cancer patients with renal impairment: results of a pharmacokinetic and tolerability phase I study. *British journal of clinical pharmacology* 2014; **77**(3): 498-508.
188. Delord JP, Ravaud A, Bennouna J, et al. Phase I and pharmacokinetic study of IV vinflunine in cancer patients with liver dysfunction. *Investigational new drugs* 2013; **31**(3): 724-33.
189. Kitzen JJ, Puozzo C, de Jonge MJ, Brandely M, Verweij J. Mild to moderate liver dysfunction does not require dose reduction of oral or intravenous vinorelbine: results of a pharmacokinetic study. *European journal of cancer* 2010; **46**(2): 266-9.
190. Abou-Alfa GK, Lewis LD, LoRusso P, et al. Pharmacokinetics and safety of vismodegib in patients with advanced solid malignancies and hepatic impairment. *Cancer chemotherapy and pharmacology* 2017; **80**(1): 29-36.
191. Sbrana A, Antonuzzo A, Galli L, et al. A case of a patient with severe renal failure on hemodialysis treated with vismodegib for relapsing basal cell carcinoma. *Tumori* 2018; **104**(6): NP2-NP4.
192. Ramalingam SS, Kummar S, Sarantopoulos J, et al. Phase I study of vorinostat in patients with advanced solid tumors and hepatic dysfunction: a National Cancer Institute Organ Dysfunction Working Group study. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* 2010; **28**(29): 4507-12.
193. Ou YC, Preston RA, Marbury TC, et al. A phase 1, open-label, single-dose study of the pharmacokinetics of zanubrutinib in subjects with varying degrees of hepatic impairment. *Leukemia & lymphoma* 2020; **61**(6): 1355-63.



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COIN ID.	CID4892
Document Title.	Dose Recommendations for Anti-Cancer Drugs in Patients with Renal or Hepatic Impairment (V1)
Name of Author.	[REDACTED]
Name of Lead Pharmacist.	As above
Is the document New, Revised or a Review of a previous version.	New
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Please provide a brief description/abstract of the document.	SACT, Chemotherapy, Renal Impairment, Hepatic Impairment, idney function, liver function, drug dosing, dose reduction.
Equality Statement. (All policies and procedures need to comply with CID76 Policy for the Management of Heath Board Wide Policies, Procedures and other Written Control Documents (WCD).	N/A
Published Date.	May 2024
Last Reviewed Date.	
Next Review Due/Expiry Date.	May 2025