Medicines Management Operational Board

Minutes from the meeting held on 21st March 2024 at 14:00 via Microsoft Teams

Minutes

Present:

Dr Richard Chudleigh (RC), Consultant Physician, Diabetes (CHAIR)
Alan Clatworthy (AC), Clinical Effectiveness & Formulary Pharmacist
Amy Jayham (AJ), Head of Pharmacy Operations
Lisa Adams (LA), GP
[redacted] Medication Safety Officer
Helen Griffiths (HG), Corporate Nursing
Steve Harrowing (SH), GP, PCPAG Chair
Nimish Shah (NS), GP LMC
[redacted], Pharmacy Support Manager (notes)

Observing the meeting:
Kalyani Nagarajah, Registrar

11.24 Apologies for absence:

Dr Rajesh Peter, Rhian Newton & Stuart Evans.

12.24 Intacopan – Compassionate Use Request:

This request came via renal medicine currently unlicensed, with ongoing studies [redacted] it has come here for ratification. Clinician wishes to continue for another three months. Agreed & no concerns. MMOB support.

MMOB approved 21/03/24. *Action: Alan Clatworthy*

13.24 Minutes of previous meeting – 18th January 2024:

The minutes of the meeting held on the 23rd November 2023 accepted as a true record of the meeting.

14.24 Matters Arising:

All actions undertaken and complete. It was noted that MMSB had approved the unlicensed request for phenol injections from Dr Steve Young.

15.24 Medication Safety Report:

[redacted] agreed to circulate the Medication Safety Report with the minutes: If anyone has any questions or queries, please contact [redacted] via email.

- **Valproate alert** - An implementation group is meeting on a regular basis, last met on 28/02/24. Primary Care searches are underway to ensure capturing all patients on valproate and to be cross-referenced and included on speciality databases. Updated resources now available including healthcare booklets, patient booklets, stickers, cards, etc. [redacted] will distribute in secondary care. Also putting together a health board wide bulletin that will go out to primary care and community pharmacies to highlight how to order and obtain new resources.
- **National Patient Safety Alerts** - [redacted] highlighted numerous NPSAs, specifically one regarding salbutamol nebulizers.
- In terms of original pack dispensing, [redacted] shared a PowerPoint - the Commission on human medicines has completed a review with the MHRA, looking at valproate prescribing how we can make it safer and as part of that, the national patient safety alert has stated the need for two specialists to approve initiation of Valproate and Specialist to sign off at an annual review. Also

noted that all valproate containing medicines should be dispensed in original packaging and that's because they have the patient information leaflet in it.

- Safety warnings incorporated into the box and cards, which is another step to reduce pregnancies exposed to valproate. Part of the legislation specifies Valproate is to be dispensed in original full pack, unless there are exceptional circumstances and it allows pharmacists to supply up to 10% more, based on what they have on the prescription. For background, dispensing in original packs recommended since 2018, generally practiced to keep it in the original box.
- Initial recommendations came from the MHRA review and the valproate Pregnancy prevention program, however there is now a regulatory measure that it must be an original pack if not exceptional circumstances and processes in place to make sure patient receives the patient information leaflet.
- The MHRA initially said they were going to produce risk assessments, which has since changed and unclear guidance on risk assessments or what needs to be involved; quite vague, there is quite a lot of differentiation.

Opinion of the group on the best way forward to ensure we are satisfying new regulations:

- SJ felt a blanket form for one patient would not be sufficient for MHLD.
- LA noted in primary care it would present problems because due to the volume of scripts given out. It would be unrealistic to fill in a form each time a script issued.
- [redacted] proposed putting together a guideline that could then come back through MMOB to highlight responsibilities. The pregnancy warning is on the box and the information leaflet is in the pack, so this is the Pharmacist's responsibility rather than the prescriber's responsibility. Key that we remind all hospital Pharmacists, Community Pharmacists etc. the importance of making sure those warnings are included.

Action: MMOB supported the proposal for a guidance. [redacted] to complete

16.24 Off-label Letrozole in Oligospermia – Unlicensed Use Form:

- Off-label unlicensed use form for letrozole in oligospermia - Unlicensed use to try to improve sperm quality and number motility. Literature search to support its use, allow use as a one off unlicensed.

MMOB approved 21/03/24.

17.24 New Product requests and formulary amendments:

New product requests & formulary amendments:

a) **Nivolumab & Relatlimab (Opdualag) Melanoma Implementation Plan**

Nivolumab–relatlimab is recommended, within its marketing authorisation, as an option for untreated advanced (unresectable or metastatic) melanoma in people 12 years and over, only if: nivolumab–relatlimab is stopped after 2 years of treatment, or earlier if the cancer progresses, and the company provides it according to the commercial arrangement.
Only approved in untreated disease i.e. as an alternative first line option. People who have advanced melanoma usually have nivolumab plus ipilimumab; this will remain the preferred choice where appropriate. When this is not suitable, people can have nivolumab or pembrolizumab, but this will likely be displaced by Opdualag for some patients.

More effective than pembrolizumab monotherapy but less effective than nivolumab/ipilimumab combination. Fits middle ground, being slightly easier to tolerate than nivolumab + ipilimumab. In practice, will probably displace current pembrolizumab usage in this indication. Relatively small numbers, probably 9 patients a year. The net impact financially is [redacted] year gross of about [redacted], offsetting a lot of pembrolizumab.

Cancer new drugs group have approved the implementation plan.

MMOB Approved 21/03/24. *Action: Alan Clatworthy*

b) Targeted release Budesonide (Kinpyego) – Implementation plan (Renal)

Targeted-release budesonide is recommended as an option for treating primary immunoglobulin A nephropathy (IgAN) when there is a risk of rapid disease progression in adults with a urine protein-to-creatinine ratio of 1.5 g/g or more. Targeted-release budesonide is recommended only if: • it is an add-on to optimised standard care including the highest tolerated licensed dose of angiotensin-converting enzyme (ACE) inhibitors or angiotensin-receptor blockers (ARBs), unless these are contraindicated • the company provides it according to the commercial arrangement.
Please note local labs report PCR in mg/mmol rather than g/g, 1.5g/g=169.5mg/mmol. In addition renal clinic tend to work from albumin creatinine ratio (ACR) rather than protein creatinine ration (PCR), the equivalent ACR is approximately 118.5mg/mmol.
Place in Therapy - NICE clinical experts consider that available treatments aim to control blood pressure and reduce proteinuria to slow the rate of kidney function decline. They explained that the treatment pathway is closely aligned with the Kidney Disease Improving Global Outcomes (KDIGO) 2021 Guideline for the Management of Glomerular Diseases. Angiotensin-converting enzyme (ACE) inhibitors and angiotensin-receptor blockers (ARBs) are standard care for IgAN and can slow the rate of disease progression. The KDIGO guideline also recommends that standard care include lifestyle advice for adults with IgAN, including dietary interventions. NICE noted that while sodium-glucose cotransporter-2 (SGLT2) inhibitors and statins may be used for IgAN, these are for controlling cardiovascular risk associated with the condition.
KDIGO guideline recommends that systemic corticosteroids should only be considered when people with IgAN continue to have a high risk of disease progression despite having optimised standard care and there is no available clinical trial that could offer an alternative treatment option. The risk to benefit profile of systemic corticosteroids means that they are only suitable for people with the most severe symptoms, and that most nephrologists in the UK do not use them for treating IgAN (prednisolone is not used in local renal network)

NICE approval for primary immunoglobulin nephropathy. There are specific criteria in terms of UM patients of being, uh, increased risk and of progression with a urine protein creatinine above 1.5 grams per gram. Patients have to be optimised on other therapies. Most of the high-risk patients already on renal replacement therapy. Potentially five patients a year would be suitable. Estimated dose used, equivalent to 5 milligram of Prednisolone, whereas the treatment doses they would be receiving would be 40 milligrams of Prednisolone minimum. Numbers are small; there is a patient access scheme, which is only accessible via Hospital dispensing. It will be managed in-house within the hospital, prescribing restricted in the renal unit.

MMOB Approved 21/03/24. *Action: Alan Clatworthy*

c) Domnisol (calcifediol monohydrate) 266 micrograms
Domnisol (calcifediol monohydrate) 266 micrograms soft capsules for treatment of Vitamin D deficiency in adults. Prevention of Vitamin D deficiency in adults with identified risks. As an adjunct to specific therapy for osteoporosis in patients with Vitamin D deficiency or at risk of Vitamin D insufficiency. It is proposed Domnisol will be used as a first line treatment option.

Vitamin D guidelines and pathways developed in primary care as part of pathway development work. One difficulty would be if started using calcifediol, would have to change all of those policies again and change the treatment pathway. Current national guidelines for vitamin D deficiency say to treat anybody with a 25 hydroxy vitamin D level less than 25 nanomoles per litre. Another group between 25 and 50 depending on risk factors may need supplementation and targeting to get over 50. Some concerns in terms of efficacy and baseline levels in central study. One trial shows long-term follow up data.

LA – Issues with vitamin D prescribing in practice; patients having a high dose at incorrect interval. It is best to keep it more uncomplicated and keep existing guidelines. If you add in something else, there is more room for error.

[redacted] agreed with the safety concerns; guidelines updated initially due to patients taking high doses more frequently than prescribed/introducing another form with different intervals. Efficacy is not there because patients not taking it as frequently. For the cost savings, probably not worth it as might see poor compliance as a result.

MMOB DECLINED 21/03/24. Action: Alan Clatworthy.

d) Momelotinib (Omjjara) implementation plan

Momelotinib (Omjjara) is recommended as an option for treating myelofibrosis related splenomegaly or symptoms in adults with moderate to severe anaemia who have not had a JAK inhibitor or have had ruxolitinib, only if: • they have intermediate-2 or high-risk myelofibrosis, and • the company provides momelotinib according to the commercial arrangement. An alternative option to fedratinib or ruxolitinib. May be used sequentially to ruxolitinib (but not sequentially to fedratinib).

NICE approved. Almost all patients that require a Janus kinase are managed on ruxolitinib. 10 patients currently from old NICE guidance approval of ruxolotinib. There may be one to two a year that failed due to ADR that this might be suitable for, they can already have fedratinib. All three drugs have the same adverse effect profile, mechanism of action and the same pricing. Will be added to formulary for Haematology use only.

MMOB APPROVED 21/03/24. Action: Alan Clatworthy.

e) Daratumumab for light chain amyloidosis

Daratumumab plus bortezomib, cyclophosphamide and dexamethasone are recommended as an option for treating newly diagnosed systemic amyloid light-chain (AL) amyloidosis in adults. It is recommended only if: daratumumab is stopped after 24 cycles of treatment, or earlier if the condition progresses, and the company provides daratumumab according to the commercial arrangement.
First line in adults with newly diagnosed systemic AL amyloidosis. Daratumumab is first used with bortezomib (limited to 6 cycles), cyclophosphamide (limited to 6 cycles) and dexamethasone. Thereafter, but before disease progression, daratumumab can be offered as maintenance monotherapy for a maximum of 18 cycles, so 24 cycles in total.

NICE approved, in practice all patients go through the national amyloidosis service at UCL before they can access treatment. The patients previously referred from haematology to UCL on therapy had an associated multiple myeloma, which is a common overlap with this patient group. Although this is technically a new NICE approval, eligible patients being treated under myeloma diagnosis.

MMOB Approved 21/03/24. Action: Alan Clatworthy.

f) Durvalumab (Imfinzi)

Durvalumab plus gemcitabine and cisplatin is recommended, within its marketing authorisation, as an option for treating locally advanced, unresectable, or metastatic biliary tract cancer in adults. It is only recommended if the company provides durvalumab according to the commercial arrangement.
Limited treatments options are available for unresectable or advanced biliary tract cancer, including cancer, which reoccurs after surgery. Standard treatment includes chemotherapy with gemcitabine and cisplatin. Durvalumab would be added in to gemcitabine and cisplatin for 8 cycles, then continue as durvalumab monotherapy until disease progression.

NICE approval for unresectable biliary tract cancer, and one of our major cost pressures for the health board. The company have agreed a very high rebate on the price for this specific indication. It will be the preferred option to add in to gemcitabine and cisplatin. Noted the need to identify the relevant patients, and to claim for rebates (based on equivalent indication split with NHS England Blueteq data).

MMOB Approved 21/03/24. Action: Alan Clatworthy.

g) Ivosidenib (Tibsovo)

Ivosidenib is recommended, within its marketing authorisation, as an option for treating locally advanced or metastatic cholangiocarcinoma with an IDH1 R132 mutation in adults after 1 or more systemic treatments.
First-line treatment of cholangiocarcinoma with an IDH1 R132 mutation is cisplatin–gemcitabine chemotherapy, followed by second-line modified folinic acid plus fluorouracil and oxaliplatin (mFOLFOX) or best supportive care (BSC) to manage symptoms. The marketing authorisation for. Ivosidenib is for people who have had at least 1 previous line of treatment, so it includes use beyond second line. NICE clinical experts consider that in NHS practice, people will have only had 1 line of treatment before moving onto mFOLFOX or BSC (described by the company as active symptom control). The clinical experts advised that only approximately 40% to 45% of people will go on to have mFOLFOX after cisplatin– gemcitabine chemotherapy. The experts reiterated that this is because mFOLFOX can be poorly tolerated. Therefore, ivosidenib would become the preferred second line option and increase the number of patients that have a viable second line treatment with IDH1 R132 mutations.

MMOB Approved 21/03/24. Action: Alan Clatworthy.

h) Talazoparib (Talzenna)

Talazoparib is recommended, within its marketing authorisation, for treating HER2-negative, locally advanced or metastatic breast cancer with germline BRCA1 or BRCA2 mutations in adults who have had: an anthracycline or a taxane, or both, unless these treatments are not suitable, and endocrine therapy if they have hormone receptor (HR)-positive breast cancer, unless this is not suitable. Talazoparib is only recommended if the company provides it according to the commercial arrangement.
For HR-positive, HER2-negative advanced breast cancer with BRCA mutations: second or third line, after first-line CDK4/6 inhibitors and second-line anthracycline or taxane-based therapy (if not previously used for early breast cancer). For triple negative advanced breast cancer with BRCA mutations: first or second line, after immunotherapy, anthracycline or taxane-based therapy (if not previously used for early breast cancer). Patients should have been previously treated with an anthracycline and/or a taxane in the neo/adjuvant, locally advanced or metastatic setting unless patients were not suitable for these treatments. Patients with hormone receptor (HR)-positive breast cancer should have been treated with a prior endocrine-based therapy, or be considered unsuitable for endocrine-based therapy.

Small patient numbers, specifically looking at the germline BRCA mutation patients' second-line, [redacted]. Improvement for patients in terms of tolerability of their therapy. Approx. [redacted] a year across the [redacted] per year progression free about nine months. Would intend to manage via Homecare.

MMOB Approved 21/03/24. Action: Alan Clatworthy.

18.24 Policies for agreement & ratification:

a) Patient Group Directions – a list of current agreed protocols were noted. A copy of all PGD's can be found at: Patient Group Directions (PGDs). For noting.
Trying to limit the number of PGDs used within the Health board, working on more national PGDs, going forward.

b) **Warfarin Protocol** – Updated guideline for ratification. Protocol for administration of Warfarin in Domiciliary Care in NPTH and Swansea area. No operational changes have been made to this document. Updated Warfarin assessment form: Appendix 2. Updated flowchart: Appendix 10. Update of an existing policy for Domiciliary Administration of warfarin – changes to appendix with the risk assessment form. The main body of the policy remains unchanged.

MMOB Approved 21/03/24. *Action: AC to advise* [redacted]

c) **Updated Guideline – Protocol for Prescribing & Monitoring Valproate March 2024 (MHLD) for agreement and ratification**

VALPROIC ACID / SEMI-SODIUM VALPROATE (Depakote, Convulex, Episenta) SODIUM VALPRAOTE (Epilim). Treatment of manic episodes associated with bipolar disorder (also used in migraine prophylaxis and epilepsy – not covered in this protocol). The continuation of treatment after manic episode could be considered in patients who have responded to valproate for acute mania.

An existing protocol for prescribing monitoring which has been updated with MHRA recommendations, now looking at prescribing for females of childbearing potential. Used within mental health for mood stabilizers & on a register. [redacted] is working with primary care to ensure we capture patients across Swansea Bay, possibly around 40 patients this will affect. Specialists will do the risk assessment and send a copy to the GP, asking the GP to prescribe the contraceptive needed. Ongoing work specific to the mental health side of valproate prescribing. It is an update on an existing policy, amended with the MHRA warnings

MMOB Approved 21/03/24. *Action: Sue Jones.*

19.24 Any Other Business:

- Decision from PCPAG around tirzepatide– implementation plan approved through Medicines Management strategy board, rather than this board because of the cost impact. Approved within the implementation plan within NICE approval for use in Type 2 diabetes / patients with a high BMI. Discussion in PCPAG whether Primary Care initiation would be acceptable. PCPAG support Primary Care initiation of the drug. Prof Bain has been querying where GPs could initiate therapy; as per other GLPs under enhanced Diabetes service & clarify if MMOB would now consider GPA INITIATION acceptable; will have an impact on the cost predictions in primary care for the next 12 months to three years. Due to the global shortage of GLP1s people haven't been able to access them for the last 6-9 months. MHRA advice is to continue with existing, unless supply difficulties.
  MMOB approved primary care initiation of tirzepatide.

- AC thanked Richard Chudleigh for being an outstanding chair, MMOB very lucky to have him as chair, depending on whether we can replace the irreplaceable; profuse thanks for excellent service over many years. RC advised if a slight delay, quite happy to carry on until a suitable replacement available.

MMOB to explore replacement Chair. Action: Anjula Mehta.

20.24 Date and time of next meeting:

Thursday 23rd May 2024 at 2pm via Microsoft Teams

Medicines Management Operational Board

Agenda Item	Action Required	Person Responsible
12.24	Iptacopan compassionate use request – Approved, to inform renal team.	AC
13.24	Minutes from 18th January 2024 – Approved	-
15.24	Medication Safety Group report: - Progress Guidance option - Share presentation with the Group when minutes circulated.	[redacted]
17.24	New product requests & formulary amendments: a) Nivolumab & Relatlimab (Opdualag) Melanoma Implementation Plan - Approved b) Targeted release Budesonide (Kinpyego) – Implementation plan (Renal) - Approved c) Domnisol (calcifediol monohydrate) 266 micrograms - Declined d) Momelotinib (Omjjara) Implementation plan - Approved e) Daratumumab for light chain amyloidosis - Approved f) Durvalumab (Imfinzi) - Approved g) Ivosidenib (Tibsovo) - Approved h) Talazoparib (Talzenna) - Approved	AC AC AC AC AC AC AC
18.24	Policies for agreement & ratification: a) Patient Group Directions – agreed directions b) Warfarin Protocol - Approved c) Updated Guideline - Protocol for Prescribing & Monitoring Valproate March 2024 (MHLD) - Approved	- AC
19.24	AOB: Chair of MMOB – awaiting confirmation from Anjula Mehta on nominations.	[redacted] AM