GIG CYMRU NHS WALES

Bwrdd Iechyd Prifysgol Abertawe Bro Morgannwg University Health Board

Rapid review of tapentadol prescribing

March 2019

Rapid review of tapentadol prescribing in ABMUHB

Executive Summary

Background

Tapentadol prescribing in ABMU is significantly higher than other Health Boards in Wales and is continuing to grow.

Results

This rapid review highlighted

- 15% initiated by services not permitted to do so based on ABMU formulary recommendations
- 34% of patients prescribed tapentadol did not have a record of receiving an alternative strong opioid prior to initiation
- 71% had a recorded diagnosis of neuropathic pain, for which tapentadol has limited evidence of benefit
- 63.5% prescribed doses of tapentadol are equal to or greater than the maximum recommended oral morphine equivalent dose (OMED) of 120mg per day (68% of those, exceed 120mg OMED)

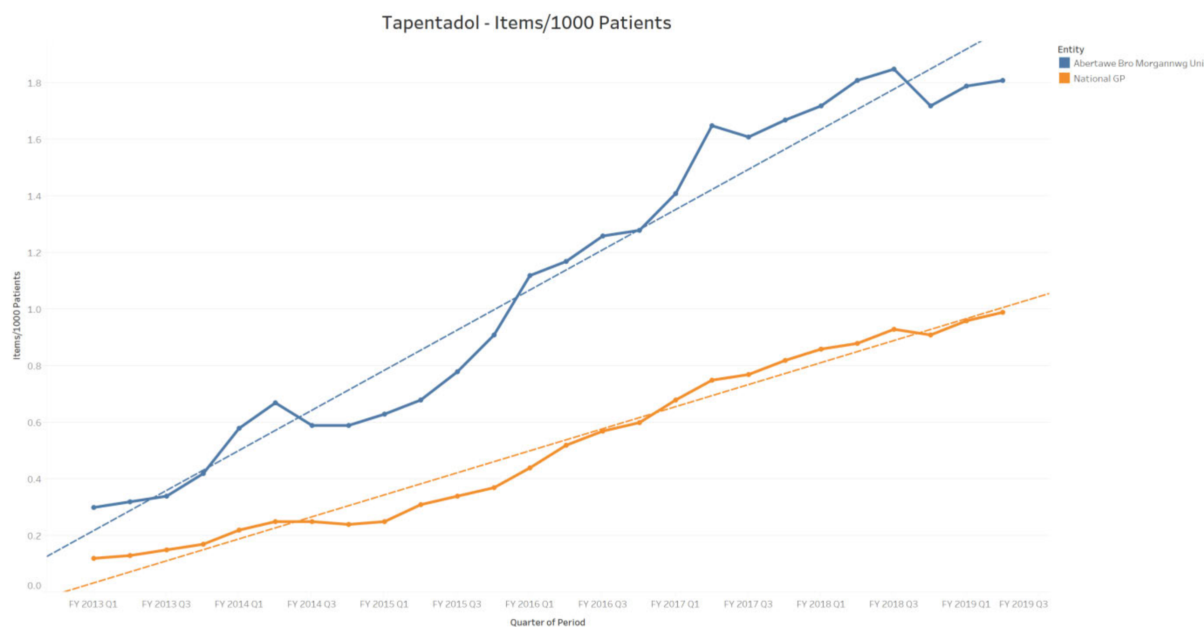
Recommendations

- Further education and audits both within primary care and specialist services
- Patients who have been prescribed tapentadol for more than 6 months should be reviewed
- Patients prescribed greater than 120mg OMED daily or higher may require specialist referral for review

Rapid review of tapentadol prescribing in ABMUHB

Background

Tapentadol is licensed for the management of severe chronic pain in adults, which can b adequately managed only with opioid analgesics. ABMUHB has the highest levels of tapentadol prescribing in Wales. Whilst this equates to relatively small numbers compared to other opioid medicines; the growth in prescribing in ABMU has been much more rapid than anywhere else since the product's launch onto the UK market mid-2011.



Medicines Management have been asked to undertake a rapid review of tapentadol prescribing on behalf of the Clinical Director for Pharmacy and Medicines Management and the Interim Medical Director for Primary Care.

Aim

- To determine if tapentadol prescribing is in line with ABMUHB formulary and AWMSG recommendations in terms of placement in therapy and specialist initiation.
- To determine influences for higher than average tapentadol prescribing in ABMUHB.

Formulary InformationControl Status:

Tapentadol

Modified release tapentadol is restricted to initiation by Chronic pain service and acute pain service/Dr Raha (for chronic pain only). Where dose is to be stabilised in Primary care the initiating consultant must provide clear advice on dose escalation and review.

Please note immediate release tapentadol is a non-formulary item in all circumstances due to All Wales Medicines Strategy Group rejection.

The Advanced Pharmacist Practitioner for Pain Management (IP&MM) also has permission from the Clinical Director for Pharmacy and Medicines Management to prescribe tapentadol, provided AWMSG/ABMUHB recommendations are followed.

Method

- Data collection form prepared by Advanced Pharmacist Practitioner in Pain Management (IP&MM) and signed-off by Head of Prescribing and Medicines Management NPT Locality.
- Data collection form to be completed by Medicines Management staff in the selected practices (randomly selected by senior technician)
- Data collated and results described by Advanced Pharmacist Practitioner in Pain Management, IP&MM at the request of the Clinical Director.

Results

- 85 patients reviewed in 15 practices in Swansea and Neath-Port Talbot localities.
- Average number of patients per practice prescribed tapentadol – 5.7 (range 3 – 15).

Table 1: Outline results for tapentadol rapid review

	Yes	No
Recorded pain diagnosis in notes	[illegible]	[illegible]
Recorded neuropathic pain diagnosis in notes	60	25
Strong opioid prescribed prior to tapentadol	56	29
Treatment outcomes recorded (pain and function)	56	29
Medication reviewed in last 12 months	57	28
Patient facing medication review	54	18
Adverse effects documented	31	54

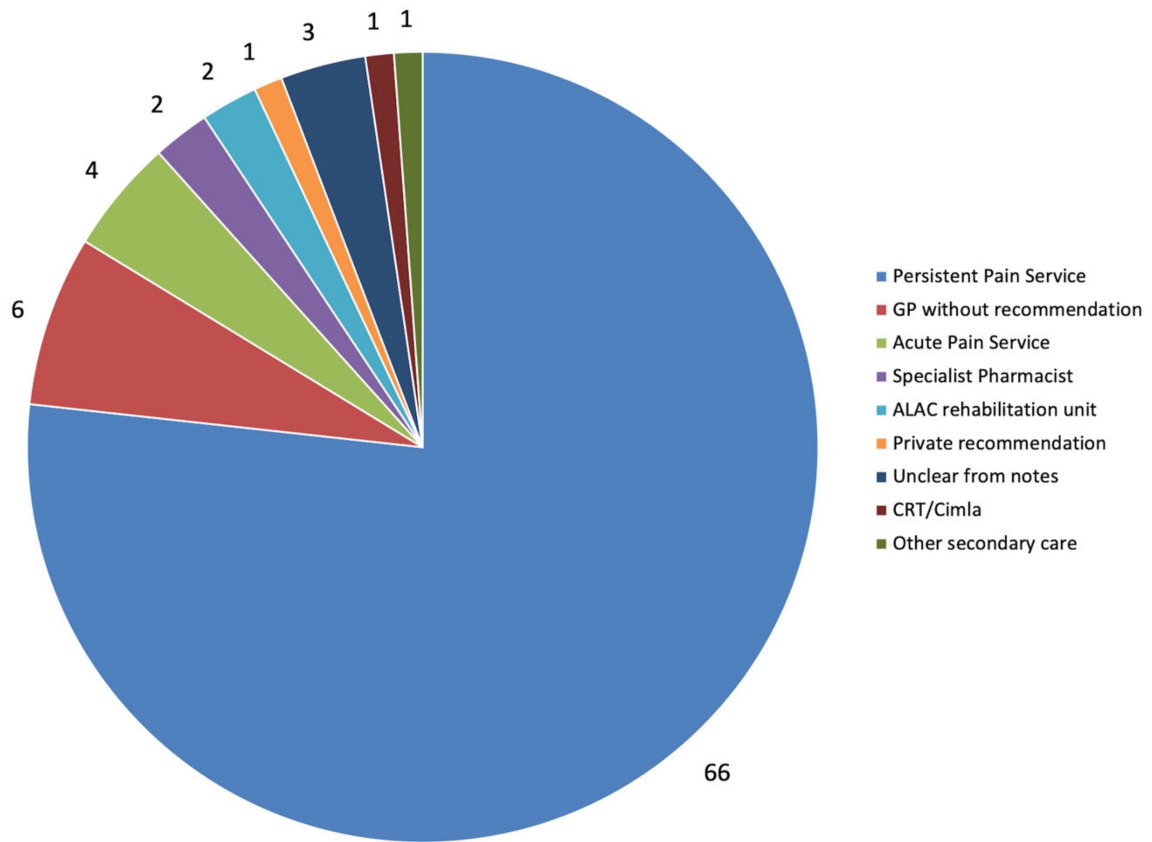
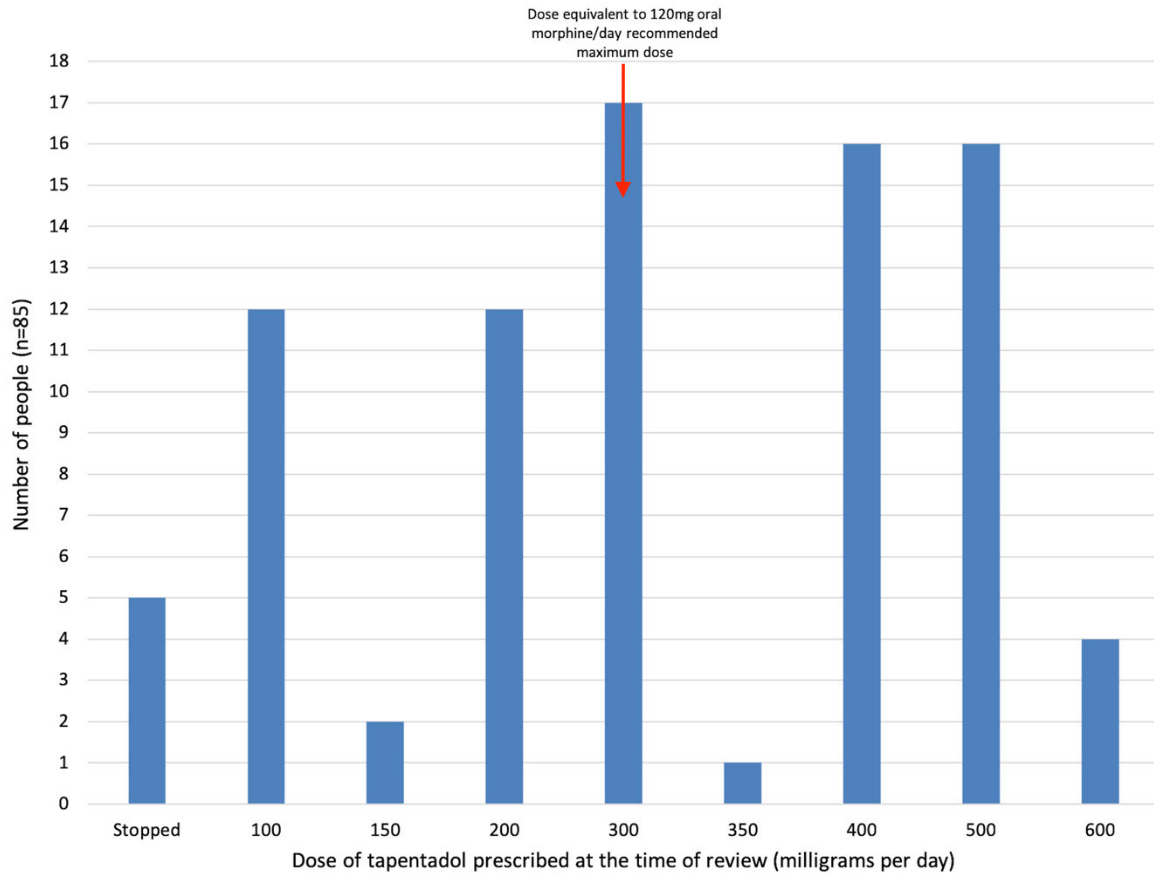


Figure 1: Diagrammatic representation of service where tapentadol SR was initiated (n=85)

- Seventy-two (85%, n=85) people currently receiving tapentadol, had it initiated by services permitted to do so based on ABMUHB formulary recommendation.
- Twenty-nine (34%, n=85) people did not have a record of previously receiving an alternative strong opioid prior to the initiation of tapentadol. Of these, [redacted]) were initiated by a GP, [redacted] by non-pain services and [redacted] by the Acute Pain Service. The rest (22 people, 76%) were initiated by the Persistent Pain Service (PPS).



- 54 (63.5%) patients currently prescribed doses of 300mg or more per day. This is equal to or greater than the maximum recommended oral morphine equivalence of 120mg per day.
- Of those 54, there were 37 (68.5%) people currently prescribed over 300mg per day. The number of people currently prescribed a dose of tapentadol that exceeds nationally agreed maximum oral morphine equivalent daily (120mg OMED) doses equated to 43.5% of the total collated, (n=85).
- Nine (24%, n=37) of the people prescribed doses above 120mg OMED dose had tapentadol initiated by services other than the Persistent Pain Service
- people are currently prescribed 600mg tapentadol per day – this exceeds the maximum licensed dose of 500mg per day. Medical records for all four indicate the dose was prescribed or recommended by the Persistent Pain Service.

Discussion

All but [redacted] patients had an easily traceable record of a pain diagnosis in their medical notes. Seventy-one percent of people receiving tapentadol also had a recorded diagnosis of neuropathic pain. The marketing company (Grunenthal) have heavily promoted the theoretical benefit of tapentadol in neuropathic pain. The theoretical benefit (in humans) is not strongly supported by the research literature.

The majority of tapentadol prescriptions were initiated by services for whom the medicine has formulary approval. However, there is still prescribing initiated by GPs (2 practices) and other non-pain specialist services. It is unknown whether other secondary care based services have taken advice from the Persistent Pain Service, in terms of initiating tapentadol (if so, it is not recorded) or whether they are simply unaware of the formulary status of the medicine.

One third of initiations were not in accordance with the precise and well defined AWMSG & ABMUHB formulary recommendations that it should only be used where a strong opioid has been effective but cannot be tolerated. The majority of formulary non-compliant initiations were made by the Persistent Pain Service, given they are the main legitimate initiators of the medicine.

It is of concern that nearly two thirds of people receiving tapentadol are prescribed doses equal to or greater than 120mg oral morphine equivalent dose (OMED) per day. The current medical and research evidence does not support the notion that there is improved analgesia at doses above 120mg OMED per day. Further, there is significant evidence of harm at doses greater than 120mg OMED, particularly in the mid to long-term, (> 6 months).

[redacted] people were receiving greater than maximum licensed doses without a clear indication. These doses all appeared to have been recommended by the Persistent Pain Service although the Primary Care Prescriber will be responsible for continuing the non-licensed dose in the longer term.

Whilst it is postulated that tapentadol carries a lower opioid load, this is only relevant in terms of certain side-effects such as constipation and sedation (based on published evidence). In terms of pain efficacy, it has only been shown to be non-inferior to other opioids, notably oxycodone. Consequently, the uses of doses higher than 120mg OMED could not be claimed to be supported by the published evidence.

There was a Medicines and Healthcare products Regulatory Agency (MHRA) warning in January 2019, on the safety of tapentadol in terms of increased risk of seizures and of serotonin syndrome when it is taken concurrently with other medicines. This demonstrates that despite the suggestion, when the medicine was launched, that is 'safer' than other opioids, post-marketing surveillance is crucial in determining potential long-term harm. Tapentadol is extremely similar to tramadol which was also launched (with similar claims of safety, tolerability and lack of 'addiction' potential, all of which have subsequently questioned, due to post marketing surveillance.

Recommendations

- The ABMUHB formulary placement and recommendations should be reinforced across all sectors, to ensure compliance.
- A more detailed review of tapentadol prescribing, in light of the MHRA warning, should be undertaken in all practices where tapentadol is being prescribed.
- All patients who have had tapentadol prescribed for more than six months should be reviewed and the opportunity for a trial of a tapering dose. This is in line with best practice guidelines for opioid prescribing and Medicines Management support to Primary Care relevant to safe and prudent prescribing of opioid medicines.
- Consideration should be given to requesting the Persistent Pain Service take responsibility for reviewing and tapering patients on tapentadol doses greater than 120mg OMED, given the safety concerns and lack of evidence to support high dose prescribing of opioids in persisting pain.
- Consideration should be given to ensuring that the Persistent Pain Service maintain tapentadol prescribing until patients have demonstrated a reduction in pain intensity AND an improvement in function, as per best practice guidance for opioid use in persisting pain. If reduced pain intensity and improved function cannot be demonstrated in the recommended time scales (normally 2-4 weeks initially), then the Persistent Pain Service should support the patient to reduce and stop tapentadol before discharging them from that service and back to Primary Care. This might assist in reducing the number of people on high dose tapentadol.
- Consideration should be given to requesting a written response from the Acute and Persistent Pain Service to this rapid review, including their rationale for using tapentadol, particularly in the absence of a trial of an alternative strong opioid and at doses greater than 120mg OMED. In addition, they should be afforded the opportunity to provide the supporting evidence and any relevant declarations of interest (as per ABMUHB policy).

Limitations

- This rapid review has not been able to examine the medical notes of every individual prescribed tapentadol in the ABMUHB area and is therefore, not a complete record. Due to the forthcoming border change, practices in Swansea and Neath Port Talbot localities were targeted as the HB will maintain influence within those practices for any required changes.
- The Acute and Persistent Pain Service have not been asked to submit their records of prescribing or recommendation of tapentadol as part of this rapid review. They should be asked to do so as this may provide more detail on their rationale for use. *(It is a condition of accepting new medicines to the ABMUHB formulary, that details of prescribing are submitted after six months but it is unclear whether those records were submitted in 2012 when due, or since.)*