NORTHERN IRELAND
MEDICINES MANAGEMENT

Health and Social Care Board

Tapentadol Supplement

February 2020

Review of NI Tapentadol Audit Data

Introduction

Tapentadol is a **Schedule 2 controlled drug**. It has a dual mode of action with both modes working in synergy to produce an analgesic effect.

- ◊ Opioid receptor (MOR) [1] agonist and
- ◊ Noradrenaline reuptake inhibitor (NRI)

The first line strong opioid in NI is oral morphine. The NI formulary[2] advises that tapentadol prolonged-release tablets may be **considered as a sole agent for mixed (neuropathic/nociceptive) pain in a specialist setting only [3].**

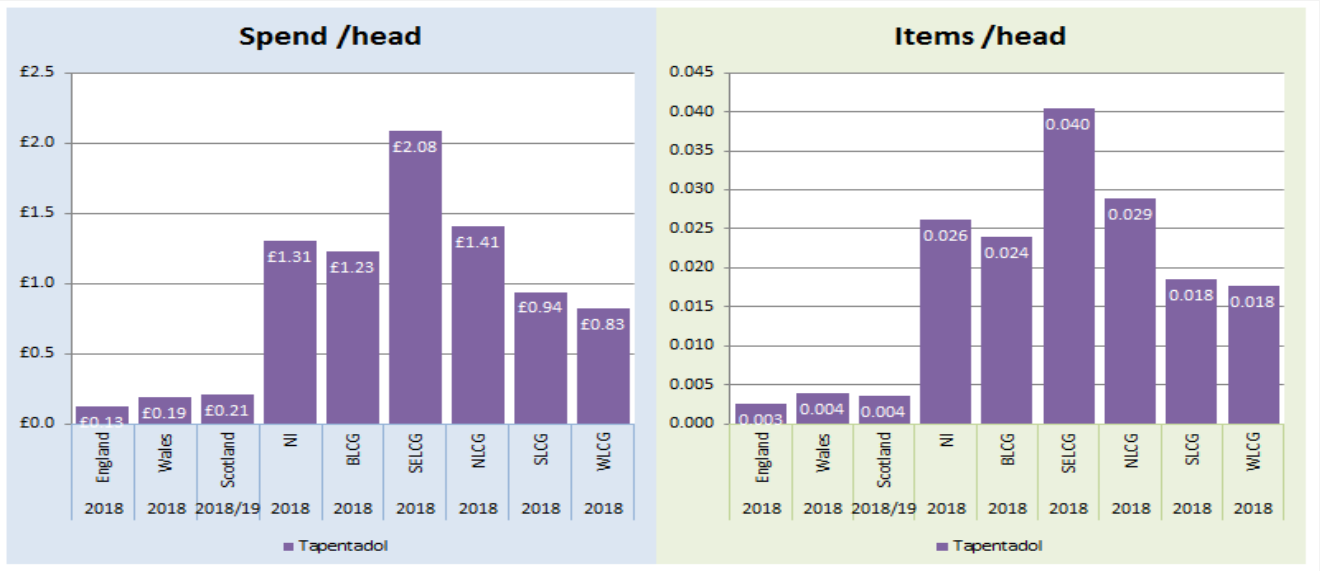
Background to audit

Despite this advice, and an overall reduction in opioid prescribing, tapentadol prescribing is increasing in NI.

DDDs /1000 STAR-PUs

	Fentanyl	Morphine	Oxycodone	Oxycodone + Naloxone	Tapentadol
2017/2018	48.25	31.72	45.59	4.99	24.02
2018/2019	44.87	30.41	44.16	4.65	28.65

NI tapentadol prescribing is significantly higher than other regional areas



Hence an audit of prescribing was undertaken in a number of GP practices across NI in July 2019.

Results of the audit

Audit criteria	Audit standard	Rationale	Result
Age	100% patients should be 18 years old or over	Tapentadol SR is indicated for the management of severe chronic pain in adults, which can be adequately managed only with opioid analgesics.(PalexiaSR SPC).	**100%**
Current strength/ form	80% patients to be on modified release products	The modified release formulation is indicated for severe chronic pain.	**84%**
Indication	100% patients to have an indication for use of tapentadol noted.	Tapentadol may be considered as a **sole** agent for **mixed** (neuropathic/nociceptive) **pain** only.[2]	**98%**
Initiation	100% patients to have been started in secondary care or on advice of a specialist	Tapentadol may be considered in a **specialist** setting only.[2] [3]	**50%**
Why tapentadol was chosen	100% patients' records should note why tapentadol was chosen	It is important that prescribers have given information on why tapentadol was chosen to assess if it is effective for their patients.	**67%**
Date initiated and most recent date of review	100% patients should have either been reviewed or started on tapentadol within the last 6 months	Current recommendations advise that patients on strong opioids should be reviewed at least every 6 months.	**49%**

A number of recommendations have been identified for action by both primary and secondary care:

Actions for primary care:

Primary care prescribers should:

- **ONLY initiate tapentadol under the advice of a specialist**. This includes patients on waiting lists to see pain specialists. In the audit 50% of patients appeared to have been started by primary care prescribers.
- **Prescribe tapentadol as a sole agent,** as per the NI formulary[2] i.e. not prescribed with other opioids or neuropathic agents.
- **Record diagnosis** and a reason for use of the drug to allow effective review. The NI formulary currently only notes tapentadol for use in mixed pain. In the audit it was prescribed for other indications e.g. headache and although 98% of patients did have an indication for use of tapentadol recorded, only 67% of records noted **why** it was chosen.
- **Clinically monitor and review patients at least every 6 months.** Some practices deferred review to secondary care. GMC[7] notes clinicians are responsible for any prescription they sign, even when prescribing at the recommendation of a professional colleague. In addition, the Controlled Drugs Regulations highlight procedures must be in place for the clinical monitoring of all patients who are

prescribed CDs in primary care. In the audit, only 49% patients had been reviewed or started on tapentadol within the last 6 months.

- **Follow regional and national guidance for persistent non-malignant and neuropathic pain[8].** NICE does not currently mention tapentadol as a possible treatment for neuropathic pain, but advises further research is needed.[10]

- **Be aware that tapentadol has the potential for opioid side-effects including dependence / addiction.** The audit revealed examples where patients, whose pain was controlled by weak opioids like tramadol, were switched to tapentadol because the prescriber thought there was less potential for side-effects like addiction. This may not have been appropriate.

Points to consider:

⇒ Tapentadol is a strong opioid and the MR formulation was proposed to the SMC by the pharmaceutical company as an alternative to oxycodone modified release or transdermal fentanyl patches in patients where morphine sulphate modified release had failed to provide adequate pain control or was not tolerated.[11]

⇒ The dual mode of action means less activation of opioid receptors may be required to achieve analgesia, possibly reducing risk of some opioid side-effects particularly GI issues like constipation. However, receptors are still activated and the SPC notes the drug has a *'potential for abuse and addiction. This should be considered when prescribing or dispensing* [tapentadol] *in situations where there is concern about an increased risk of misuse, abuse, addiction, or diversion'* [12]

⇒ The eBNF notes under tapentadol that *'Psychological dependence rarely occurs when opioids are used therapeutically (e.g. for pain relief), but tolerance can develop during long-term treatment.'*[5]

⇒ Prescribers should bear in mind that the second mode of action introduces the possibility of further side-effects with tapentadol not seen in other opioids. See BNF[5] for a list of all side effects.

⇒ Patients have presented at services in NI for treatment of tapentadol dependence.

⇒ Therefore, 'further research on tapentadol is needed to gather long-term efficacy and safety data to reach an equitable comparison between this drug and tramadol and other opioids'.[13]

Select the correct dose and formulation (MR where possible in line with the NI formulary[2].)

⇒ Remember maximum doses and indications are different for the IR and MR products. (See BNF[5] table.) In the audit overdoses were detected and there were instances where IR was used where MR may have been more appropriate for the dose regimen.

⇒ **Avoid exceeding 300mg or more of tapentadol per day** (equivalent to 120mg oral morphine equivalent– OME)[3] except on specialist advice[4]. If the maximum recommended dose of OME changes this level will also change. In the audit, 33% patients were taking 300mg or more of tapentadol per day. Of these, 42% were started on the drug by a GP / GP Practice Pharmacist.

The BNF[5] notes the following:

Indication for adult	Formulation	Initial dose	Note	Max dose per day
Moderate to severe acute pain*[6]	immediate-release	Initially 50 mg every 4–6 hours, adjusted according to response	Maximum 700mg in first 24 hours, during first 24 hours of treatment, an additional dose of 50mg may be taken 1 hour after initial dose, if pain control not achieved	**600 mg**
Severe chronic pain*	modified-release	Initially 50 mg every 12 hours, adjusted according to response		**500 mg**

***Only adequately managed with opioid analgesics**

Actions for secondary care:

- Trusts should implement policies to ensure that treatment can only be initiated by a Specialist.
- Non-specialists in secondary care should follow Trust and NI formulary.
- Improve discharge and outpatient information, including noting who is responsible for review and reason why tapentadol was chosen e.g. specific goal.
- Ensure that any guidance documents are shared with all relevant non-medical prescribers and anyone who influences prescribing e.g. non-prescribing physiotherapists.
- Scope and expedite ways to provide advice to primary care prescribers.

Conclusion

The audit demonstrated learning for both primary and secondary care, based on current evidence and good practice. GP practices are encouraged to consider the recommendations within this report and take any necessary action. The HSCB is working with Trust colleagues to address the secondary care issues.

The Pharmacy and Medicines Management team would like to take this opportunity to thank those practices and their staff who took part in the audit and contributed to its findings.

References

1. Tzschentke, T, Babette T Y. Ko¨gel Y. The Mu-Opioid Receptor Agonist/Noradrenaline Reuptake Inhibition MOR–NRI) Concept in Analgesia: The Case of Tapentadol CNS Drugs (2014) 28:319–329 DOI 10.1007/s40263-014-0151-9

2. NI formulary http://niformulary.hscni.net/Formulary/Adult/4.0/4.7/4.7c/Pages/default.aspx

3. HSCB Implementation Support Tool for Non-Malignant Neuropathic Pain Conditions in Non-Specialist Settings http://niformulary.hscni.net/Formulary/Adult/PDF/HSCB%20Neuropathic%20Pain%20Guideline%20Mar%2014.pdf

4. Pain Management West of Scotland Chronic Pain Education Group Pain Dose Calculator http://www.paindata.org/calculator.php.

5. BNF https://bnf.nice.org.uk/drug/tapentadol.html#prescribingAndDispensingInformations

6. Palexia 75 mg film-coated tablets SPC https://www.medicines.org.uk/emc/product/8046/smpc
Palexia Oral Solution 20 mg/ml SPC https://www.medicines.org.uk/emc/product/5346

7. GMC Good practice in prescribing and managing medicines and devices
https://www.gmc-uk.org/ethical-guidance/ethical-guidance-for-doctors/prescribing-and-managing-medicines-and-devices

8. NI Implementation Support Tool for Opioid Prescribing in Chronic Pain (for Non-Malignant and Non-Inflammatory Pain in Non-Specialist Settings)http://niformulary.hscni.net/Formulary/Adult/PDF/Opioids%20_in_Chronic_Pain.pdf

9. https://www.fpm.ac.uk/faculty-of-pain-medicine/opioids-aware Opioid Prescribing Frequently Asked Questions

10. NICE Neuropathic pain in adults: pharmacological management in non-specialist settings Clinical Guidance 173 (2013 with an update in April 2018) www.nice.org.uk/guidance/cg173

11. SMC Resubmission tapentadol, 50, 100, 150, 200 and 250mg prolonged-release tablets (Palexia® SR) SMC No. (654/10)
https://www.scottishmedicines.org.uk/media/2361/tapentadol_palexia_sr_resubmisison_final_may_2011_for_website.pdf
(accessed 25/7/19)

12. Palexia SR SPC https://www.medicines.org.uk/emc/product/5158/smpc

13. J. Faria , J. Barbosa, R. Moreira, O. Queir, F. Carvalho2, R.J. Dinis-Oliveira. Comparative pharmacology and toxicology of tramadol and tapentadol. Eur J Pain 22 (2018) 827--844 Accessed 18/2/20

Bibliography

DTB | ▼Tapentadol (Palexia) for moderate to severe acute pain. Vol 50 | No 3 | March 2012 | DTB | 31 BMJ group <13th October 2016>

Wolverhampton Trust. Tapentadol Information Leaflet for Primary Care. October 2014. Wolverhampton Medicines website http://medicines.wolvespct.nhs.uk/default.asp

Specialist Pharmacy Services: Tapentadol prolonged-release (Palexia SR) Published 19th July 2011, updated 24th February 2016 · North West Medicines Information Centre https://www.sps.nhs.uk/articles/tapentadol-prolonged-release-palexia-sr%c2%a8/

Vosburg SK, Severtson SG, Dart RC, Cicero TJ, Kurtz SP, Parrino MW et al. Assessment of Tapentadol API Abuse Liability With the Researched Abuse, Diversion and Addiction-Related Surveillance System. **The Journal of Pain, Vol 19, No 4 (April), 2018: pp 439-453** *Available online at www.jpain.org and www.sciencedirect.com*