PHARMACY PROFILE: Tapentadol (Palexia®)

Key Messages

- Tapentadol is a new opioid agonist for chronic pain unresponsive to non-opioid medications.
- Morphine is still considered the preferred opioid analgesic for moderate-to-severe pain because of familiarity, availability and cost, other opioids including tapentadol may be used where adverse effects of morphine are unacceptable.
- The place of tapentadol in palliative care is presently uncertain and should be used on specialist advice.
- More studies are needed to determine long term safety and tolerability of tapentadol.

Tapentadol is a novel synthetic opioid analgesic indicated in treatment of moderate-to-severe chronic disabling pain. It is a centrally acting opioid with two mechanisms of action, including agonism at the µ-opioid receptor and noradrenaline reuptake inhibition. [1] Tapentadol was marketed in two forms: immediate release, used mainly for acute pain management and sustained release (SR) for moderate-to-severe chronic pain. Only tapentadol SR has been approved by the TGA in Australia since December 2010. It is PBS listed for chronic pain not responding to non-opioid analgesics. [2]

Starting Dose and Titration

Opioid-prescribing guidelines should be adhered to when considering tapentadol SR treatment for people with chronic pain. Non-pharmacological and non-opioid measures for chronic pain should be considered and trialed before considering opioid analgesia. [3]

For opioid naïve patients, start with 50 mg controlled release tablet twice daily (12 hourly); up-titratre dose by 50 mg twice daily every 3 days, according to response. Maximum daily dose 500 mg.

For patients switching from a different opioid analgesic to tapentadol select tapentadol SR dose based on the mean daily dose of their current medicine. The accepted conversion between oxycodone and tapentadol is 1 to 5.3. [4]

Choose the nearest lower dose of tapentadol. For example, for a patient changing from oxycodone 15 mg, the converted dose of tapentadol is 79.5 mg. Use 50 mg of tapentadol rather than 100 mg of tapentadol. [4] Swallow tablets whole; do not crush or chew.

Tablets availability in Australia

- 50 mg (controlled release), 100 mg (controlled release), 150 mg (controlled release), 200 mg (controlled release), and 250 mg (controlled release). [5]

Do not mix different fentanyl products for treating breakthrough pain, use one brand only.
Evidence of efficacy

- Evidence of efficacy and safety data is limited.
- There were 3 key trials (two for osteoarthritis of the knee, one for lower back pain) with varying results, one of which did not show a significant difference in efficacy against placebo and only two achieving their primary efficacy endpoints of a significant change in baseline pain intensity compared with placebo. [4]
- A result from a meta-analysis demonstrated a small reduction (of just 0.5 on an 11-point rating scale) in average pain intensity with tapentadol compared to placebo. [4]
- The NPS [4] has concluded that the evidence supporting the use of tapentadol for chronic, severe disabling pain unresponsive to non-opioid analgesics is limited and more studies are required to evaluate long term safety of tapentadol.
- Although clinical trials have mainly compared the safety and efficacy of tapentadol SR to that of oxycodone, the double action of tapentadol SR implies it may be a potential substitute to tramadol. A 4-week phase II trial in which tapentadol SR was compared with tramadol showed neither tramadol nor tapentadol SR had greater analgesic effects than placebo. [4]
  Tramadol has relatively weak opioid activity and additional serotonin reuptake inhibition compared with tapentadol SR. Further evidence is needed to determine comparative safety and efficacy of tapentadol SR and tramadol.

Safety

- In all three main trials, patients taking tapentadol SR experienced similar adverse effects with those associated with other opioid analgesics. [4]
- Renal Impairment, CrCl ≥30 mL/minute: no dosage adjustment necessary.
- CrCl <30 mL/minute, not recommended as there is no evidence in this patient population. [6]
- Hepatic Impairment, mild impairment (Child-Pugh class A): no dosage adjustment necessary.
  Moderate impairment (Child-Pugh class B): extended release: initial: 50 mg every 24 hours or longer; maximum: 100 mg once daily. Severe impairment (Child-Pugh class C): not recommended there is no study in this patient population. [6]
- While tapentadol does not inhibit serotonin reuptake, serotonin syndrome has been reported as a severe adverse effect. The concurrent use of medications with a serotonin-reuptake inhibition mechanism or monoamine oxidase inhibitors in combination with tapentadol is not recommended, as it is thought that the increase in noradrenaline levels are associated with increased serotonin levels with development of serotonin syndrome without a known mechanism. [1]
- Tapentadol has a potential to be confused with tramadol.
Considerations for use in palliative care

- Although data from phase II/III trials showed that patients in tapentadol SR group experienced fewer adverse events than oxycodone SR, the clinical significance of this finding is unclear. The frequency of adverse events was not the primary endpoint of the trials, and the long-term safety profile is currently uncertain. Therefore, based on the available evidence, it should be presumed that tapentadol is associated with similar risks as oxycodone, and patients should be treated accordingly [4].

- The efficacy of tapentadol in the treatment of chronic severe disabling pain due to conditions other than osteoarthritis and low back pain is unclear as these are the only conditions that efficacy and safety of tapentadol SR have mainly been assessed in randomised controlled clinical trials.

- To date, there are no clinical trials evaluating the efficacy and safety of tapentadol SR in palliative care patients.

Tips for palliative care nurses

- Tapentadol SR is not intended for break-through pain. In the clinical trials patients were allowed to use paracetamol for break-through pain.

- An aperient such as docusate with senna should always be prescribed for people requiring regular opioids including tapentadol.

- Discontinuation of therapy: dose should be gradually titrated downward to prevent withdrawal signs/symptoms. Tapentadol should not be abruptly discontinued.

References


4. NPS MedicineWise. Tapentadol sustained release (Palexia SR) for chronic, severe disabling pain [Internet]. 2014 [cited 2017 Feb 10].


CareSearch is funded by the Australian Government Department of Health.
Useful resources


- Contact your local pharmacist or hospital drug information service.

- National Prescriber Service Website - 'NPS MedicineWise' is an excellent resource for consumers and health professionals.

Authors: Wassana Sorich, Deputy Director-Clinical Pharmacy, Repatriation General Hospital, South Australia.

Acknowledgement: Jenny Casanova, Clinical pharmacist RGH and Wei Terk Chang, Clinical Pharmacist, Singapore.