TAPENTADOL prolonged release tablets (Palexia® SR)

The Pan Mersey Area Prescribing Committee recommends the prescribing of TAPENTADOL prolonged release tablets (Palexia® SR) for severe chronic pain in adults only when initiated by chronic pain specialists or palliative care specialists

AMBER following specialist initiation

The Pan Mersey Area Prescribing Committee (APC) recommends the prescribing of tapentadol prolonged release tablets (Palexia® SR) for severe chronic pain only when initiated by chronic pain specialists or palliative care specialists, and within its licensed indications (the management of severe chronic pain in adults, which can be adequately managed only with opioid analgesics).

- Tapentadol should only be considered as an option, after adequate trials of modified release morphine, **and as an alternative to modified release oxycodone where oxycodone is not considered clinically appropriate.**
- **The patient should be reviewed by the chronic pain specialist and the tapentadol dose stabilised, with evidence of patient review at that dose, before asking the GP to take over prescribing of tapentadol.**
- The incidence of gastrointestinal adverse effects is less common with tapentadol than with oxycodone.
- There is some evidence from the USA that tapentadol has a lower abuse potential than other opioids, but it is not known whether there would be similar picture in the UK, and whether this would be maintained with wider use.
- Note that the comparative clinical trials assessing tapentadol in chronic pain precluded the use of supplemental/rescue analgesia, only allowing short term paracetamol or NSAIDs for unrelated pain.
- The Pan Mersey APC **does not currently recommend that immediate release tapentadol should be used in conjunction with prolonged release tapentadol** as supplemental/rescue analgesia for chronic pain.

When prescribing tapentadol, prescribers should consider NICE NG193 (07 April 2021): Chronic pain (primary and secondary) in over 16s: assessment of all chronic pain and management of chronic primary pain. Chronic primary pain is pain with no clear underlying cause, or pain (or its impact) that is out of proportion to any observable injury or disease and NICE recommends that opioids are not initiated in this type of pain.

For other chronic pain conditions, prescribers should continue to follow the appropriate NICE guidelines, including those on headaches, low back pain and sciatica, rheumatoid arthritis, osteoarthritis, spondyloarthritis, endometriosis, neuropathic pain and irritable bowel syndrome, some of which include opioids as an option.

Note: Cross-titration (transition from one strong opioid to another) has a RED RAG rating and prescribing of both opioids should be undertaken by the specialist until the first opioid has been stopped.

Note: Patients who are not eligible for treatment under this statement may be considered on an individual basis where their GP or consultant believes exceptional circumstances exist that warrant deviation from the rule of this policy. In this situation, follow locally defined processes.

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Effectiveness

Tapentadol is a dual mode analgesic that inhibits norepinephrine reuptake and has μ-opioid receptor (MOR) agonism. The efficacy of tapentadol SR has been assessed in osteoarthritis, low back and diabetic neuropathic pain in 12-week clinical trials, using dose ranges of 100 - 250 mg twice daily. It was shown to be significantly more effective than placebo in reducing average pain intensity, and was non-inferior to oxycodone modified release (MR) 20 - 50 mg twice daily.

There is a lack of long-term efficacy data, and of comparative data with opioid analgesics other than oxycodone[1] and oxycodone/naloxone[2] (the latter a 12 week open-label, non-inferiority trial).

Safety

The most common adverse effects of tapentadol (incidence >10%) are dizziness, somnolence, headache, nausea, and constipation.[3] A pooled analysis of 12-week studies showed significantly reduced incidence of constipation (16.9% vs 33%) and nausea and vomiting (23.3% vs 42.7%) compared to oxycodone. One longer term open label study showed a decreased incidence of GI adverse effects at one year (52.0% vs 64.1% for oxycodone), and an increased incidence of nervous system adverse effects (45.4% vs 39.9% for oxycodone).[1]

There is some evidence from the United States of low rate of diversion events and low street prices, indicating no substantial diversion and abuse of tapentadol in the 36 months after its introduction.[4]

Tapentadol may increase seizure risk in patients taking other medicines that lower seizure threshold, for example, antidepressants and antipsychotics. There are reports of serotonin syndrome when tapentadol is co-administered with antidepressants, such as serotonin reuptake inhibitors (SSRIs), serotonin-noradrenaline reuptake inhibitors (SNRIs), tricyclic antidepressants and antipsychotics.[5] Note: There may be other serotonergic drugs that also need to be considered. For full details of side-effects and contraindications, see the SPC.

Cost (Annual costs, NHSBSA dm+d browser, April 2021)

Equivalent to Morphine MR 20mg BD:	
Morphine MR (Zomorph®) 20mg BD caps	£ 84
Oxycodone MR (Oxycontin®) 10mg BD tabs	£326
Oxycodone MR (Oxypro®) 10mg BD tabs	£ 82
Tapentadol SR 50mg BD tabs	£325

Equivalent to Morphine MR 100mg BD:	
Morphine MR (MST Continus®) 100mg BD caps	£ 468
Oxycodone MR (Oxycontin®) 50mg BD tabs	£1,632
Oxycodone MR (Oxypro®) 50mg BD tabs	£ 408
Tapentadol SR 250mg BD tabs	£1,624

Patient factors

Contra-indications include significant respiratory depression, acute or severe bronchial asthma, hypercapnia, paralytic ileus, and acute intoxication. Tapentadol is not recommended in severe renal or hepatic impairment or in those under 18 years of age. Caution is needed in moderate hepatic impairment.

When combined with a respiratory or CNS depressant drug, the reduction of dose of one or both agents should be considered. Care should be taken when combining tapentadol with mixed mu-opioid agonist/antagonists (like pentazocine, nalbuphine) or partial mu-opioid agonists (like buprenorphine).[3]

Prescribing information

- Considering the balance of effectiveness, safety, patient factors and cost, the Pan Mersey APC recommends prescribing of tapentadol prolonged release tablets following initiation by chronic pain specialists or palliative care specialists and only after adequate trials of morphine, or as an alternative to modified release oxycodone where oxycodone is not considered clinically appropriate.
- In those not taking opioids, initiate at 50mg BD. In those currently taking opioids, initiate at an appropriate dose based on the current daily dose and equianalgesic dose ratio. The equianalgesic dose ratio of tapentadol to morphine is 2.5:1 and to oxycodone is 5:1.[1] Following initiation, the dose should be titrated on an individual basis, in increments of 50mg tapentadol (as prolonged release tablets) twice daily every 3 days, up to a maximum of 250mg twice daily.[3]
- Tapentadol is a Schedule 2 Controlled Drug. There are two different formulations of tapentadol (immediate release and prolonged release) which may cause confusion. It is important that the prescriber clearly indicates “prolonged release” in any communication or prescription. Additionally, the similarity between the names and doses of tramadol and tapentadol could cause confusion.[1]

Implementation notes

It is recommended that only chronic pain specialists or palliative care specialists initiate tapentadol. Treatment should be reviewed by the specialist and the dose stabilised before asking the GP to take over prescribing.

Cross-titration (transition from one strong opioid to another) has a RED RAG rating and prescribing of both opioids should be undertaken by the specialist until the first opioid has been stopped.

References

1. UKMi New Medicines Profile. Tapentadol prolonged release. 11/03. July 2011
2. Baron R et al. Effectiveness of Tapentadol prolonged release (PR) compared with Oxycodone/Naloxone PR for the management of severe chronic low back pain with a neuropathic component: A randomized, controlled, open-label, Phase 3b/4 Study. Pain Practice. 2015 Jun;15(5): 455-70.
3. Grunenthal Ltd. Summary of Product Characteristics: Palexia SR, last updated 23 January 2020. Accessed 26 October 2020.
4. Dart RC et al. Diversion and Illicit Sale of Extended Release Tapentadol in the United States. Pain Medicine 2016; 17: 1490–1496.
5. MHRA. Drug Safety Update: Tapentadol (Palexia): risk of seizures and reports of serotonin syndrome when co-administered with other medicines, 19 January 2020.