

New drugs

Tapentadol

Approved indication: analgesia

Palexia IR 50, 75 and 100 mg tablets (CSL)

Palexia SR 50, 100, 150, 200 and 250 mg (CSL)

Australian Medicines Handbook section 3.2

Tapentadol is a centrally-acting synthetic opioid which is structurally similar to tramadol. It is thought to bind to the mu opioid receptor and inhibit the reuptake of noradrenaline.

The immediate-release form of tapentadol is indicated for moderate to severe pain. In a trial of 603 patients, tapentadol (50, 75 or 100 mg every 4–6 hours) was compared to immediate-release oxycodone (15 mg every 4–6 hours) or placebo for acute pain after bunionectomy. Tapentadol and oxycodone were significantly better than placebo at relieving pain over the first 48 hours. The analgesic effects of tapentadol seemed to be dose-dependent with tapentadol 100 mg being comparable to oxycodone 15 mg. However, at these doses nausea and vomiting appeared to be less common with tapentadol than with oxycodone (nausea 49% vs 67%; vomiting 32% vs 42%) and somnolence seemed to be more common (21% vs 10%).¹

The efficacy of immediate-release tapentadol (50 and 75 mg) was also similar to immediate-release oxycodone (10 mg) for osteoarthritis pain due to moderate to severe joint disease (in 659 patients). Again, gastrointestinal effects were less for tapentadol than oxycodone.²

A sustained-release formulation of tapentadol has also been approved in Australia for moderate chronic pain unresponsive to non-narcotic analgesia. It has been compared to controlled-release oxycodone for chronic low back pain and osteoarthritis in several trials. In a pooled analysis of three trials (2968 patients), tapentadol (100–250 mg twice daily) was not inferior to oxycodone (20–50 mg twice daily) for pain associated with osteoarthritis of the knee and low back pain over 12 weeks of maintenance treatment.³

The adverse effects of tapentadol are similar to other opioids. The most common effects are nausea, dizziness, vomiting, somnolence, constipation and pruritus. These events seemed to be dose-related and some people discontinued treatment because of them.

After a single oral dose of tapentadol immediate-release, serum concentrations peak at 1.25 hours. It is extensively metabolised, mainly by glucuronidation,

and to a lesser extent by CYP2C9 and CYP2C19, so drug interactions mediated through cytochrome P450 are unlikely. Most of the metabolites are excreted in the urine and the terminal half-life is four hours.

The maximum serum concentrations of the sustained-release formulation are reached in 3–6 hours. Its half-life is approximately six hours.

Tapentadol is not recommended in people with severe renal or hepatic impairment. Caution is urged in those with moderately impaired liver function or a history of seizures.

As tapentadol increases noradrenaline, it should not be taken with monoamine oxidase inhibitors. Drugs that may contribute to serotonin toxicity should also be avoided with tapentadol. Additive central nervous system depression can occur if tapentadol is taken with other centrally-acting drugs, including alcohol.

Prescribers should be aware that tapentadol is not recommended for labour pain and there are inadequate data to support its use for cancer pain. Like other opioids, there is a risk of drug dependence.

The efficacy of tapentadol appears to be similar to oxycodone, but with less gastrointestinal adverse effects. It is not known how it will compare to other opioids such as tramadol.

T manufacturer provided the AusPAR and/or the product information

REFERENCES *

1. Daniels SE, Upmalis D, Okamoto A, Lange C, Häussler J. A randomized, double-blind, phase III study comparing multiple doses of tapentadol IR, oxycodone IR, and placebo for postoperative (bunionectomy) pain. *Curr Med Res Opin* 2009;25:765-6.
2. Hartrick C, Van Hove I, Stegmann JU, Oh C, Upmalis D. Efficacy and tolerability of tapentadol immediate release and oxycodone HCl immediate release in patients awaiting primary joint replacement surgery for end-stage joint disease: a 10-day, phase III, randomized, double-blind, active- and placebo-controlled study. *Clin Ther* 2009;31:260-71.
3. Lange B, Kuperwasser B, Okamoto A, Steup A, Häufel T, Ashworth J, et al. Efficacy and safety of tapentadol extended release for chronic osteoarthritis pain and low back pain. *Adv Ther* 2010;27:381-99.

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The Transparency score (**T**) is explained in 'New drugs: T-score for transparency', *Aust Prescr* 2011;34:26-7.

* At the time the comment was prepared, information about this drug was available on the website of the Food and Drug Administration in the USA (www.fda.gov).



Some of the views expressed in the following notes on newly approved products should be regarded as tentative, as there may be limited published data and little experience in Australia of their safety or efficacy. However, the Editorial Executive Committee believes that comments made in good faith at an early stage may still be of value. As a result of fuller experience, initial comments may need to be modified. The Committee is prepared to do this. Before new drugs are prescribed, the Committee believes it is important that full information is obtained from the manufacturer's approved product information, a drug information centre or some other appropriate source.