Tramadol is indicated for the relief of moderate-to-severe pain. It has opioid-like effects and serotonergic properties. The combined effect can lead to adverse effects observed with both types of agents.

Tramadol is usually considered if other 'Step 2' analgesics (from WHO pain ladder category) such as codeine are not tolerated or contraindicated. The same caution is required when prescribing tramadol as with opioid analgesics.

Although tramadol is associated with fewer of the typical opioid adverse effects (e.g., respiratory depression, constipation and addiction potential), other effects such as nausea, vomiting, and dizziness are common, and can be problematic. Some patients find that they experience fewer side effects with the slow-release tramadol preparations.

UNDERSTAND THAT TRAMADOL CAN CAUSE SEIZURES

The activity of tramadol on serotonin and noradrenaline transmission is associated with lowering of the seizure threshold. The risk of seizures increases further with:

- concurrent treatment with other medicines that lower the seizure threshold, e.g., some antidepressants and antipsychotics
- a history of seizures - tramadol is contraindicated in patients with uncontrolled epilepsy
- doses over 400 mg per day

Note: Convulsions have also been reported at recommended dose levels.

BE AWARE OF THE RISKS OF SEROTONIN SYNDROME

As with other serotonergic medicines, tramadol is associated with serotonin syndrome. Symptoms can include hyperthermia, agitation, tremor, and hyperreflexia, and fever. There is an increased risk of serotonin syndrome when higher doses of tramadol are used or when tramadol is combined with other serotonergic medicines which include some antidepressants as well as St John’s Wort and levodopa.

If serotonin syndrome is suspected, withdrawal of serotonergic medicines usually brings about rapid improvement.

Note: Some patients require analgesics and antidepressants. If tramadol is needed, advise them to report any symptoms of serotonin syndrome, and use the lowest effective dose of tramadol.

TAKE SPECIAL CARE WITH OLDER ADULTS

Most reports of adverse reactions pertaining to tramadol involve patients over 80 years of age. It is recommended that the maximum daily dose no greater than 300 mg for patients over 75 years.

Patients with renal or hepatic insufficiency may have delayed elimination of tramadol; consider increasing the dosing interval. Titrate the dose to effect, start low (50 mg) and go slow; 12 hourly dosing may be sufficient. Tramadol is not recommended for patients with severe renal or hepatic impairment.

TAKE SPECIAL CARE WITH CHILDREN

Tramadol is contraindicated in children under two years of age. Tramadol should not be given to children or adolescents for pain after surgery to remove tonsils or adenoids.
DISCUSS POTENTIAL ADVERSE EVENTS BEFORE PRESCRIBING

The most common adverse effects of tramadol are dizziness, nausea, vomiting, constipation, increased sweating and fatigue. Elevated liver enzymes and rash have been associated with tramadol, and there have been rare reports of mood alterations including mania and auditory hallucinations. Tramadol can induce delirium in some patients.

Due to the sedative effects of tramadol, patients should avoid driving or operating dangerous machinery if they are affected. There is a SafeRx® patient guide available on www.saferx.co.nz

Safety of tramadol has not been established in pregnancy, or during labour. Tramadol is not recommended during breastfeeding.

Some patients who have been previously stable on warfarin experience an increase in INR when tramadol is added. If tramadol is unavoidable, monitor the INR closely when tramadol is added or discontinued.

REMEMBER TRAMADOL IS AN OPIOID; IT HAS BEEN ASSOCIATED WITH DEPENDENCE AND WITHDRAWAL

Although tramadol appears to have a lower abuse potential compared to other opioids, there have been reports of abuse and intoxication.

There is an increased risk of fatal overdose when tramadol is taken with other central nervous system depressants such as alcohol and benzodiazepines. Tramadol is contraindicated if patients are acutely intoxicated with alcohol, hypnotics, analgesics, opioids or psychotropic medicines. The opioid component of tramadol could make some patients develop tolerance; sudden withdrawal may lead to partial withdrawal side effects which include agitation, anxiety, insomnia, tremor, pyrexia and chills.

There are no clinical studies investigating efficacy and safety of chronic tramadol use beyond six months.

Which preparation?

Tramadol is available as immediate and slow release preparations.

<table>
<thead>
<tr>
<th>Preparation</th>
<th>Doses available</th>
<th>Recommended dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate release</td>
<td>50mg capsules, Oral liquid 100mg/mL*</td>
<td>Up to every 4-6 h as required, Max 400mg in 24 h</td>
</tr>
<tr>
<td>Slow release</td>
<td>50mg*, 100mg, 150mg, 200mg, 300mg* SR tablets</td>
<td>Every 12 h</td>
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</tbody>
</table>

*Not funded in the community

Tramadol immediate release capsules may be used alone, or for breakthrough pain relief with tramadol SR tablets.

For moderate pain:

Tramadol 50-100mg twice to three times daily
OR Tramadol SR tablets 100mg twice daily

For more severe pain:

Tramadol 100mg every 4-6 hours; maximum 400mg in 24 h
OR Tramadol SR 200mg tablets twice daily

Sometimes a maximum daily dose of 600mg is used in secondary care; this dose should not be continued on discharge.

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KEY REFERENCES