

## TRAMADOL - SAFE PRESCRIBING - CONSIDER THE RISKS!

- ▶ UNDERSTAND THAT TRAMADOL CAN CAUSE SEIZURES
- ▶ BE AWARE OF THE RISKS OF SEROTONIN SYNDROME
- ▶ TAKE SPECIAL CARE WITH OLDER ADULTS
- ▶ DISCUSS POTENTIAL ADVERSE EVENTS BEFORE PRESCRIBING
- ▶ REMEMBER TRAMADOL IS AN OPIOID; IT HAS BEEN ASSOCIATED WITH DEPENDENCE AND WITHDRAWAL

Tramadol is indicated for the relief of moderate-to-severe pain. It has opioid-like effects and serotonin *and* noradrenaline reuptake-inhibitor properties. This combined effect can lead to adverse effects observed with both types of agents.

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

Although tramadol is associated with fewer of the typical opioid adverse effects (eg 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, eg some antidepressants and antipsychotics
- a history of seizures - tramadol is contraindicated in patients with uncontrolled epilepsy
- doses over 400mg 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 spontaneous clonus, 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 serotonin-enhancing medicines which include some antidepressants, 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 **300mg** 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 (50mg) and go slow; 12 hourly dosing may be sufficient. Tramadol is not recommended for patients with severe renal or hepatic impairment.

### 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<sup>®</sup> patient guide available on [www.saferx.co.nz](http://www.saferx.co.nz)  
Safety of tramadol has not been established in pregnancy, or during labour. Tramadol is not recommended during breastfeeding.

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**Note:** 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 in patients who are acutely intoxicated with alcohol, hypnotics, analgesics, opioids or psychotropic drugs. 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.

**Note:** 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.

Tramadol preparation	Doses available	Dose recommendations
Immediate release	50mg capsules Oral drops 100mg/mL*	Up to every 4-6 hours as required Max 400mg <sup>#</sup> in 24 hours
Slow release	50mg*, 100mg, 150mg, 200mg SR tablet	Every 12 hours

\*Not funded in the community

<sup>#</sup>Sometimes a maximum daily dose of 600mg is used in secondary care.

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

### For moderate pain:

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

### For more severe pain:

Tramadol 100mg capsules every 4-6 hours to a maximum of 400mg in 24 hours  
OR tramadol SR 200mg tablets twice daily.

### If patients are discharged from hospital with severe pain, they may be prescribed:

Tramadol 100mg SR tablets twice daily with tramadol capsules up to 400mg per day as required.

### ACKNOWLEDGEMENTS

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### KEY REFERENCES

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[CLICK HERE FOR FURTHER INFORMATION ON TRAMADOL AND A FULL REFERENCE LIST](#)

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