



TRAMADOL

Top tips for MURs

- Check that patient understands what tramadol has been prescribed for, the correct dosage, maximum dose and check if still indicated
- Check that patient is not using other regular opioids at the same time as tramadol (prescribed or over the counter)
- Counsel patient that treatment should be short and intermittent. If long term treatment is indicated check that a modified release twice daily preparation (maximum dose) is used as less potential for abuse
- Check that patients given modified-release form understand that the tablets/capsules should be swallowed whole with a drink of water
- Advise patient that tramadol should not be stopped abruptly after long-term treatment and the possibility of withdrawal symptoms when discontinuing treatment. On rare occasions people who have been taking tramadol for some time may feel unwell if they abruptly stop taking it. They may feel agitated, anxious, shaky or nervous.
- Counsel patient on signs / symptoms that need referral (**red flags**) or common side effects (**see overleaf**)
- Check that patient has had a tramadol treatment review after 3 months at start of therapy and then at least annually
- Counsel patient on the risk of dependency
- Counsel patient that tramadol may cause drowsiness which may affect performance of skilled tasks (e.g driving) and driving should be avoided at start of therapy and following dose changes
- Counsel patient that long- term use can lead to amenorrhoea, lowered immunity, reduced libido, infertility, depression and erectile dysfunction. Hyperalgesia (a state of abnormal pain sensitivity) has also been associated with long-term use
- Counsel patient to avoid alcohol
- Signpost patient on non-pharmacological interventions to manage pain e.g weight management, physiotherapy, exercise or TENS machines
- Signpost patient to self-help leaflets and websites or expert patient programme
- Report any medically significant adverse drug reactions to the Yellow Card Scheme

What is tramadol used for?

Tramadol is a strong opioid and is licensed for use in the treatment of moderate to severe pain but is neither more effective or better tolerated than other opioid analgesics^{1, 2}. Tramadol use should be short and intermittent for acute pain and should be used only when alternatives are not tolerated or effective in chronic pain. Repeated use may cause dependence and tolerance. Tramadol has been associated with a significant number of deaths, 175 in 2012 (this figure shows that deaths are increasing, doubled in last 4 years) and has been shown to be subject to abuse and dependence³. Pain management is often complex and the prescriber must make decisions based on the individual needs of the patient.

How does tramadol work?

Tramadol is a centrally-acting analgesic which produces analgesia by two mechanisms, an opioid effect and an enhancement of serotonergic and adrenergic pathways. It is an opioid agonist which binds to the mu opiate receptors in the CNS altering the perception and response to pain as well as inhibiting the reuptake of serotonin and noradrenaline to enhance inhibitory effects on pain transmission. It has fewer of the typical opioid side effects, e.g. less respiratory depression and constipation; however psychiatric reactions have been reported⁴. Adverse effects due to the dual mechanism of action of tramadol become more prevalent when used in high doses, however naloxone will not reverse the serotonergic effects in overdose⁴.

Tramadol and its metabolites are almost completely excreted via the kidneys, so for elderly patients and patients with renal impairment, the half-life is extended leading to reduced elimination and the dose should be adjusted according to the patient's glomerular filtration rate (GFR) and titrated as tolerated.

Lifestyle issues

- Counsel patient on reducing alcohol intake to within safe limits (up to 14 units a week, spread evenly over 3 more days, with several alcohol free days)
- Counsel patient on healthy eating, exercise & weight loss (if BMI > 25kg/m²) – advise patients to complete 30 minutes of aerobic exercise three to five times a week, reduce caffeine intake to no more than 5 cups a day and recommend 5 portions of fruit and vegetables a day
- Advise patients who smoke the benefits of stopping smoking and how to access pharmacy smoking cessation services or Stop Smoking Wales





Red flags that need referral

- Any signs of opioid toxicity (pinpoint pupils, sedation, slow respiration and blueness of lips, ears or nose, myoclonic jerks, changes in sleep pattern including snoring, vivid dreams or nightmares)
- Any symptoms of serotonin syndrome (agitation or restlessness, diarrhoea, fast heart beat and high blood pressure, hallucinations, increased body temperature, loss of coordination, nausea, overactive reflexes, rapid changes in blood pressure or vomiting)
- Any signs of increased agitation, confusion or hallucinations
- Any signs of withdrawal (anxiety, sweating and stomach pains)
- Pregnancy, as risk of teratogenicity & breastfeeding as risk of toxicity to infants
- Any loss of libido, erectile dysfunction in men or amenorrhoea in women

What are the common side effects to look out for?

Common side effects	Recommendation
Hyperalgesia (abnormal pain sensitivity where pain is more diffuse and less defined)	Refer to specialist pain team for reduction in tramadol dose or switching therapy.
Nausea and vomiting particularly at initiation of therapy, retching	Advise patient to stick to simple meals - avoid rich or spicy foods. Advise patient that symptoms normally settle after a few weeks, if persistent refer to GP for anti-emetic or drug change.
Fatigue or paraesthesia	Refer to prescriber if not tolerated.
Constipation	Refer to prescriber if persistent or troublesome.
Dry mouth	Advise patient to try chewing sugar-free gum or sucking sugar-free sweets. Refer to prescriber if not tolerated.
CNS symptoms; dizziness and drowsiness are most common but also hallucinations, vertigo, euphoria, dysphoria, mood changes, dependency, confusion, sleep disturbances, headache	Advise patient not to drive or use tools or machines, to avoid alcohol and refer to prescriber if symptoms persistent and troublesome.
Withdrawal effects (e.g anxiety, sweating and stomach pains)	Refer to GP if persistent and troublesome.

Potential drug interactions?

Tramadol interacts with many medications including:

- Alcohol – enhanced hypotensive and sedative effects when used with tramadol
- Anticoagulants – tramadol enhances the anticoagulant effect of coumarins (warfarin) which may increase INR and ecchymoses (bruising)
- Antidepressants - increased risk of convulsions and CNS toxicity including serotonin syndrome when tramadol is used with SSRIs, MAOIs, TCAs. Some manufacturers advise avoid concomitant use of MAOIs
- Antiepileptic drugs – effects of tramadol reduced by carbamazepine and it reduces the seizure threshold. Seizures have occurred at therapeutic doses but risk increases if dose greater than 400mg daily
- Antipsychotics – increased risk of convulsions when used with tramadol – avoid concomitant use
- Atomoxetine – possible increased risk of convulsions when used with tramadol

For more information on potential drug interactions – **See BNF Appendix 1: Interactions**

Where can you find more information?

- BNF Central nervous system 4.7 Analgesics : sub-section 4.7.2 : Opioid analgesics
- Pain: treatment and management distance learning packs that can be found on WCPPE website (<http://www.wcppe.org.uk>)
- NICE guidance NICE CG88: Low back pain (<http://www.nice.org.uk/cg88>)
- NICE CG96: Neuropathic pain – pharmacological management (<http://www.nice.org.uk/cg96>)
- Advisory Council on the Misuse of Drugs (ACMD) expert group review. ACMD consideration of tramadol.
- 2013. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/144116/advice-tramadol.pdf. Accessed Nov 2013

References

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2. Oxford league table of analgesics in acute pain. Bandolier 2007. Available at <http://www.medicine.ox.ac.uk/bandolier/booth/painpag/acutrev/analgesics/leagtab.html>
3. Directorate for Public Health WG. Chief Medical Officer for Wales Update 61. 2013.
4. Things to know about Tramadol, 2013. WeMeReC.