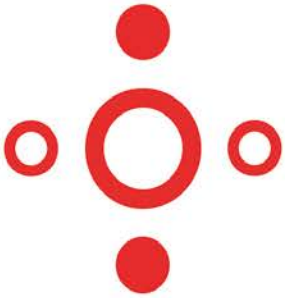
Grŵp Strategaeth Meddyginiaethau Cymru Gyfan
All Wales Medicines Strategy Group



Tramadol Educational Resources

Review 2021

September 2021

This document has been prepared by the All Wales Prescribing Advisory Group (AWPAG) with support from the All Wales Therapeutics and Toxicology Centre (AWTTC) and has subsequently been endorsed by the All Wales Medicines Strategy Group (AWMSG).

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Tramadol - Summary for prescribers

Tramadol is an analgesic that combines an opioid agonist action, with enhancement of serotonergic and noradrenergic neurotransmission[1]. Tramadol is metabolised by the cytochrome P450 enzyme system to active metabolites, which contributes to the therapeutic effect. Polymorphism in genes encoding cytochrome P450 enzymes (particularly CYP2D6), results in intra-individual variation in tramadol metabolism, and associated variation in the therapeutic effect[1].

After a number of tramadol-related deaths and other harms, safety concerns were highlighted by the UK's Advisory Council on the Misuse of Drugs (ACMD) in 2013[2], culminating in the reclassification of tramadol as a Schedule 3 controlled drug in 2014[3]. A prescription for a Controlled Drug in Schedule 3 is valid for 28 days and it is strongly recommended that the maximum quantity of Schedule 2, 3 or 4 Controlled Drugs prescribed should not exceed 30 days.

Indications
Tramadol is licensed for the treatment of moderate to severe pain. However, the National Institute for Health and Care Excellence (NICE) guideline NG193 recommends that opioids, including tramadol, are not initiated for chronic primary pain[4]. Tramadol is only indicated (for both acute and chronic pain) if it improves pain and function.

The Faculty of Pain Medicine recommends that when prescribing opioids, the patient and prescriber should identify outcomes that indicate the opioid will be of benefit, and that an initial treatment trial should be of sufficient duration to establish benefit[5]. This may be one to two weeks or longer depending upon the patient's presentation[5].

Adverse effects
Common side effects of tramadol include dizziness, constipation, drowsiness and headache. Less common and rare side effects include hallucinations, confusion, convulsions, addiction, dependence and withdrawal effects (anxiety, sweating, stomach pain).

Serotonin syndrome (or serotonin toxicity) is a predictable, drug-induced, spectrum of symptoms caused by serotonergic over-activity at synapses of the central and peripheral nervous systems. It consists of a triad of features (alteration of mental status, neuromuscular abnormalities and autonomic hyperactivity) that do not necessarily present together and can vary in severity from mild to life threatening. Serotonin syndrome can occur from:

- overdose of serotonergic agents;
- drug interactions i.e. combining drugs that result in potentiation of serotonergic neurotransmission (including tramadol);
- taking one serotonergic agent alone at normal therapeutic doses in susceptible individuals.

Advice for tapering and stopping tramadol
To reduce the risk of withdrawal effects associated with sudden cessation of opioids, taper dosage of tramadol slowly at the end of treatment. Tapering can take weeks or months, depending on individual response and the dose taken.

Healthcare professionals should advise patients not to stop taking tramadol suddenly, and not to try to self-medicate to overcome withdrawal effects. Self-medication with opioids can result in overdose and potentially death[1]. The MHRA recommended that before prescribing opioids, healthcare professionals should discuss the risk and features of tolerance, dependence and addiction with the patient. A plan for the termination of treatment should be agreed, which might include identifying a strategy to measure treatment success or failure, and a dose reduction strategy. Where physical dependence to tramadol develops, the withdrawal syndrome can be severe. Symptoms typical of opiate withdrawal may sometimes be accompanied by atypical symptoms including hallucinations, paraesthesia and severe anxiety, which may be associated with withdrawal from the serotonergic effects of tramadol[2,6].

The Faculty of Pain Medicine's Opioids Aware resource suggests tapering opioids by 10% weekly or two weekly. It is important to take into consideration that every patient and their circumstances will be different, and a prudent and individually tailored approach is required[7].

If the patient has chronic (also known as persistent) pain that has failed to respond to treatment, referral to a specialist pain service may be appropriate. If there are issues with dependence on tramadol, referral to a specialist support service where available may be appropriate.

Dosing in renal impairment

Tramadol and its metabolites are almost completely excreted through the kidneys. For elderly patients and patients with renal impairment, the half-life is extended and there is reduced elimination. If a patient has renal impairment, the dose should be adjusted according to the patient's glomerular filtration rate (GFR):

- 20–50 ml/min: dose as in normal renal function
- 10–20 ml/min: 50–100 mg every 8 hours initially, then titrate dose as tolerated
- < 10 ml/min: 50 mg every 8 hours initially, then titrate dose as tolerated.

The information above on dosage adjustments in renal impairment is taken from the Renal Drug Handbook 3rd edition (2008) which bases its dosage adjustments on creatinine clearance and not estimated GFR (eGFR)[8]. It should be noted that there are differences between absolute GFR, eGFR, and creatinine clearance (CrCl). For more detailed advice on clinical importance and management, see the British National Formulary (BNF), Renal Drug Handbook and Summary of Product Characteristics, or refer to local Medicines Information Service.

Prescribing key points

- Pain management should assist the patient to achieve goals that have been identified in partnership with the prescriber, adopting patient-centred care principles[9].
- Before prescribing tramadol, discuss the risks and features of tolerance, dependence and addiction with the patient, and agree a treatment strategy for the end of treatment[10].
- Help patients to develop their understanding of the value of self-management and non-pharmaceutical approaches, and support

them to access the tools, resources and support available to put these approaches into practice.

- Only prescribe tramadol where it is clearly indicated (for both acute and chronic pain) if it improves pain and function.
- Provide clinical advice to patients regarding the likely risks of their medicines causing side effects which may impair driving. It is a driver's responsibility to decide whether they consider their driving is, or they believe might be, impaired. Patients should be advised not to drive if any symptoms or signs develop suggesting that their driving may be impaired, such as experiencing sleepiness, poor co-ordination, impaired or slowed thinking, dizziness, or visual problems; and not to drive at the start of therapy, and when doses are increased. (See Department for Transport Guidance for healthcare professionals on drug driving).
- Explain the risks of unintentional overdose, and counsel patients and caregivers on signs and symptoms of opioid overdose (see the Medicines and Healthcare products Regulatory Agency (MHRA) opioids safety information leaflet).
- Provide regular monitoring and support especially to individuals at increased risk, such as those with current or past history of substance use disorder (including alcohol misuse) or mental health disorder.
- At the end of treatment, taper dosage slowly to reduce the risk of withdrawal effects; tapering from a high dose may take weeks or months.
- Consider the possibility of hyperalgesia if a patient on long-term tramadol therapy presents with increased sensitivity to pain.
- If there are issues with chronic (also known as persistent) pain or dependence on tramadol, referral to a specialist service may be appropriate.
- Report suspected dependence or addiction to any medicine, including tramadol, through the Yellow Card scheme.

1.0 Introduction

These resource materials aim to support the appropriate prescribing of tramadol in NHS Wales by providing key healthcare professionals with audit materials to review the prescribing of tramadol within the often complex context of pain management.

The resources are intended to raise awareness amongst prescribers and patients of the potential harms associated with the misuse and diversion of tramadol, as well as the risks of dependence and addiction associated with prolonged use, even at therapeutic doses[10].

Concerns about the risks associated with tramadol were first highlighted by the Advisory Council on the Misuse of Drugs (ACMD) in February 2013[2]. All Wales educational resource materials were developed by the All Wales Prescribing Advisory Group (AWPAG) and the All Wales Therapeutics and Toxicology Centre (AWTTC) and were endorsed for national use by AWMSG in November 2013. Tramadol was included as a National Prescribing Indicator (NPI) in April 2014 and prescribing has been monitored and reported since[11]. In June 2014 tramadol was reclassified as a Class C drug and placed in Schedule 3 of the Misuse of Drugs Regulations 2001[12].

In September 2020, the Medicines and Healthcare products Regulatory Agency (MHRA) reviewed the risk of dependence and addiction associated with prolonged use of opioid medicines such as tramadol. The MHRA recommended that before prescribing opioids, healthcare professionals should discuss the risk and features of tolerance, dependence and addiction with the patient[10]. A plan for the termination of treatment should be agreed, which might include identifying a strategy to measure treatment success or failure, and a dose reduction strategy[10]. An MHRA Drug Safety Update also advises healthcare professionals to report suspected dependence or addiction to any medicine, including to an opioid, through the Yellow Card scheme.

These resources have been developed with consideration of the often complex nature of pain management and it is acknowledged that the prescriber must make decisions based on the individual needs of the patient. Tramadol is an opioid analgesic, licensed for moderate to severe pain, and is a useful treatment for patients for whom other options are not tolerated or effective. NICE guideline NG193 recommends that opioids, including tramadol, are not initiated for chronic primary pain[4]. However, it is recognised that there may be a place for tramadol in pain management for some patients. The audits included in this resource aim to provide prescribers with the information and support to make evidence-based decisions, taking into account the risks and benefits of tramadol, and to encourage a holistic approach to prescribing in pain management.

2.0 Background

Tramadol is an opioid analgesic licensed for the treatment of moderate to severe pain. Tramadol produces analgesia by two mechanisms: an opioid receptor agonist effect and enhancement of serotonergic and noradrenergic neurotransmission[13]. Tramadol is perceived to have fewer opioid-related side effects, including respiratory depression and constipation, than other medicines in this group[14]. However, the dual pharmacological action of tramadol increases the risk of adverse effects in overdose[2].

Deaths involving tramadol in England and Wales have increased over time, with 175 deaths in 2012 and 201 deaths in 2019. In Wales, the number of deaths more than doubled, from 6 in 2017 to 14 in 2018, although this figure then fell to 7 in 2019[15]. Whilst the interpretation of data relating to drug-related deaths can be challenging, the data highlight the need for appropriate use and continued review of tramadol within the wider context of prescribing for pain.

Dizziness and nausea are the most commonly reported adverse effects of tramadol, with headache, drowsiness, vomiting, constipation, dry mouth, fatigue and sweating also frequently reported[16]. Rare adverse effects include hallucinations, confusion, sleep disturbance, anxiety and nightmares, as well as cases of dependence and withdrawal effects[16]. To minimise the risk of convulsions, patients with a history of epilepsy or those susceptible to seizures should only be treated with tramadol if there are compelling reasons to do so[16]. In addition, tramadol should be used with caution in patients taking concomitant medicines that can lower the seizure threshold, such as tricyclic antidepressants or selective serotonin reuptake inhibitors (SSRIs)[16]. The use of tramadol is contraindicated in uncontrolled epilepsy and in patients receiving, or who have recently discontinued (within the previous two weeks) monoamine oxidase inhibitors[16].

Caution is recommended in elderly patients, because opioids have been associated with an increased risk of falls and fractures in this patient group. Particular caution is required in those patients aged over 75 years, because elimination may be prolonged, leading to an increased risk of adverse effects. Where necessary the dosage should be adjusted according to the patient's requirements[16,17].

2.1 Advice for tapering and stopping tramadol

To reduce the risk of withdrawal effects associated with sudden cessation of opioids, taper the dosage of tramadol slowly at the end of treatment. This can take weeks or months, depending on individual response and the dose taken. Healthcare professionals should advise patients not to stop taking tramadol suddenly, and not to try to self-medicate to overcome withdrawal effects. Self-medication with opioids can result in overdose and potentially death[1]. The MHRA recommended that before prescribing opioids, healthcare professionals should discuss the risk and features of tolerance, dependence and addiction with the patient[10]. A plan for the termination of treatment should be agreed, which might include identifying a strategy to measure treatment success or failure, and a dose reduction strategy[10]. Where physical dependence to tramadol develops, the withdrawal syndrome can be severe, with symptoms

typical of opiate withdrawal sometimes accompanied by atypical symptoms including seizures, hallucinations and anxiety[2,6].

The Faculty of Pain Medicine's Opioids Aware resource suggests tapering opioids by 10% weekly or two weekly[18]. It is important to take into consideration that every patient and their circumstances will be different, and a prudent and individually tailored approach is required.

If the patient has chronic (also known as persistent) pain that has failed to respond to treatment, referral to a specialist pain service may be appropriate. If there are issues with dependence on tramadol, referral to a specialist support service where available may be appropriate.

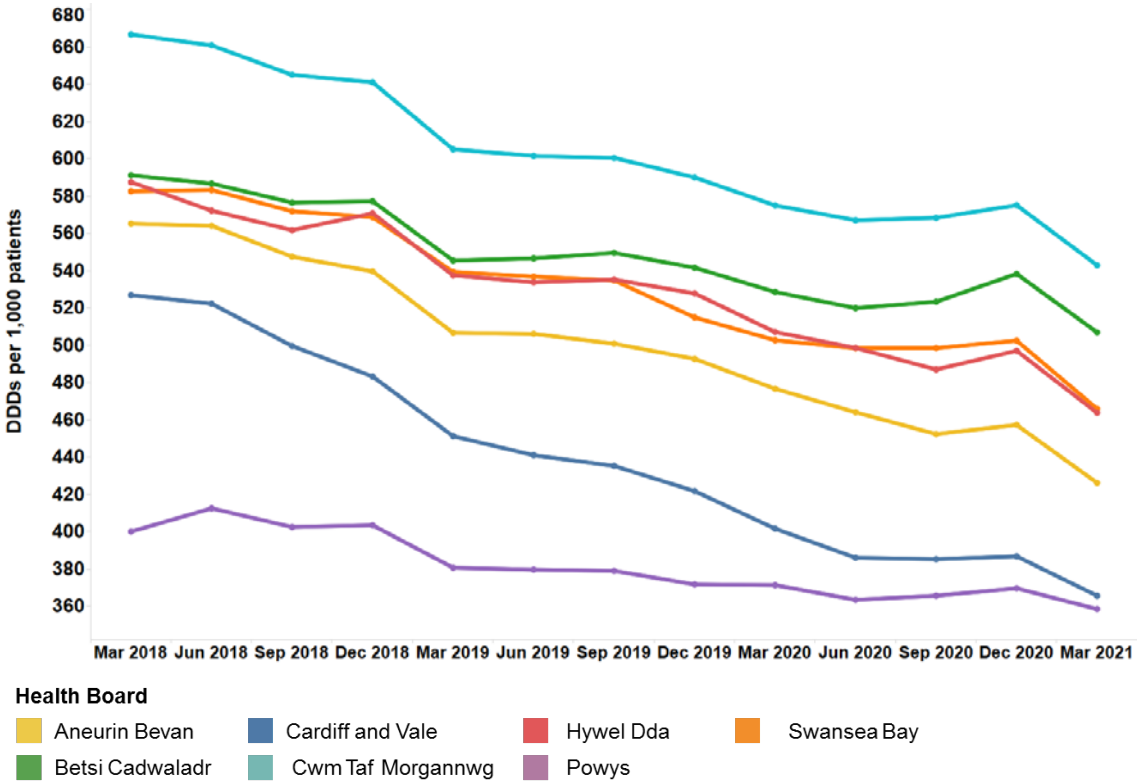
The Prescribed Medication Support Service (PMSS) in Betsi Cadwaladr University Health Board provides an example of a service that aims to:

- reduce the number of people dependent on prescribed medication e.g. (hypnotics and anxiolytics)
- provide professionals and members of the public with information, empowering them to hold a more informed perspective. This, in turn, will enable them to help this patient group.
- enable people to understand their dependence and help them make appropriate life changes.

3.0 Prescribing data

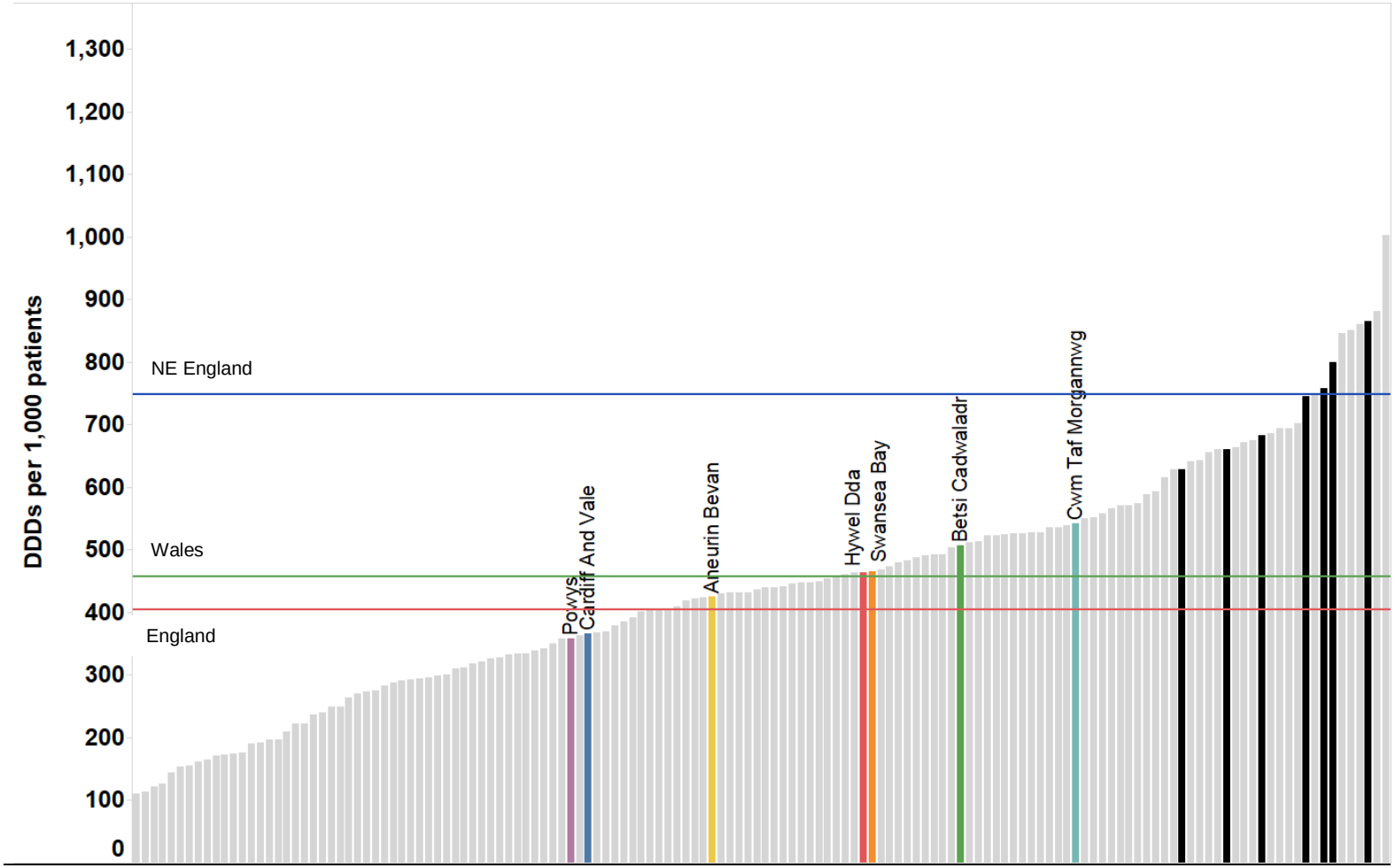
Tramadol has been monitored as a National Prescribing Indicator since June 2014 and up to date prescribing data can be found on the prescribing data dashboard SPIRA. National Prescribing Indicators provide consistency of metrics for health boards[11].

Figure 1. Trend in tramadol DDDs per 1,000 patients* to quarter ending March 2021



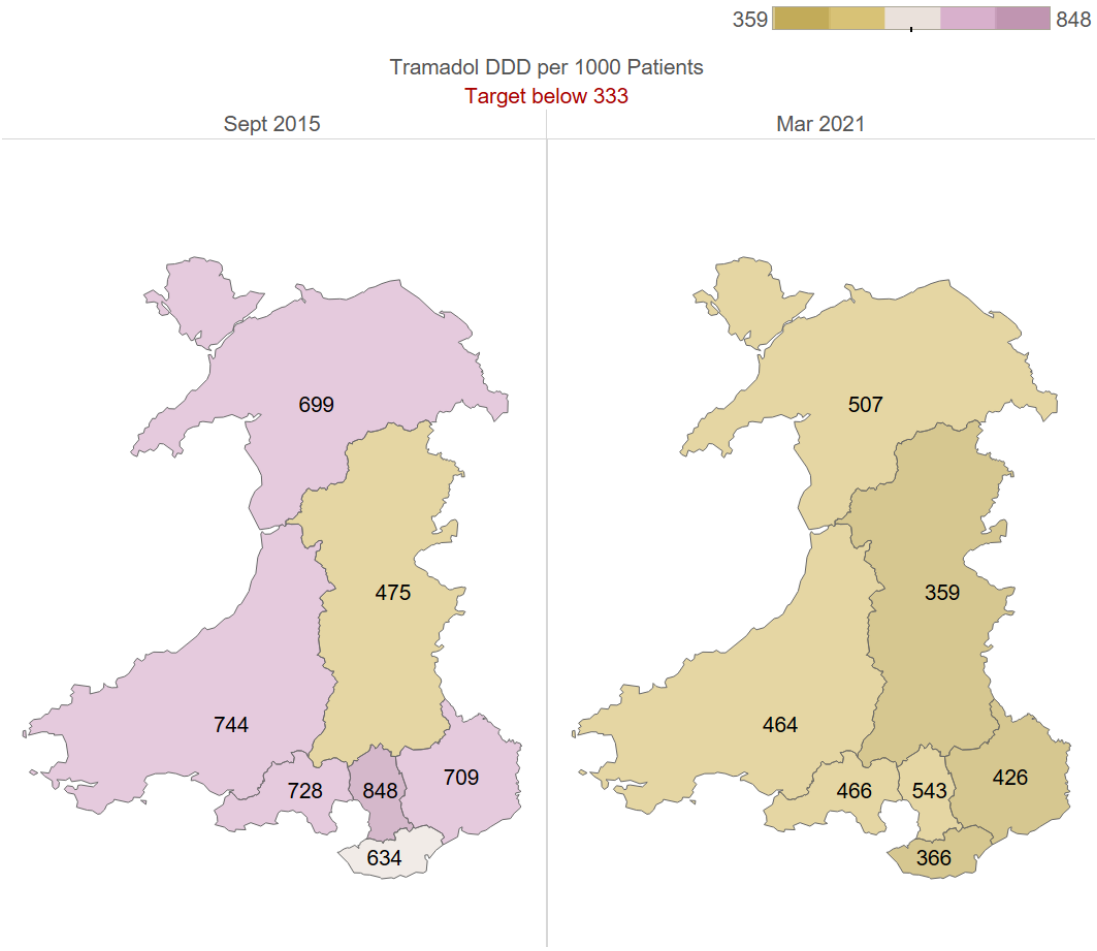
*DDDs per 1,000 patients - the defined daily dose (DDD) developed by the World Health Organization is a unit of measurement whereby each medicine is assigned a value within its recognised dosage range. The value is the assumed average maintenance dose per day for a medicine when used for its main indication in adults. A medicine can have different DDDs depending on the route of administration.

Figure 2. Tramadol DDDs per 1,000 patients in Welsh health boards and English CCGs - quarter ending March 2021



The highlighted coloured columns represent the health boards in Wales (as labelled), and the highlighted black columns represent CCGs in North East England, an area that has a population with similar demographic characteristics to Wales.

Figure 3. Map of tramadol prescribing DDDs per 1,000 patients – comparing quarter ending September 2015 to quarter ending March 2021



4.0 Useful resources

- NICE guideline (NG59) Low back pain and sciatica in over 16s: assessment and management (https://www.nice.org.uk/guidance/NG59)
- NICE clinical guideline (CG96) Neuropathic pain in adults: pharmacological management in non-specialist settings (https://www.nice.org.uk/guidance/cg96)
- NICE guideline (NG193) Chronic pain (primary and secondary) in over 16s: assessment of all chronic pain and management of chronic primary pain. (https://www.nice.org.uk/guidance/NG193)
- Live well with Pain (https://my.livewellwithpain.co.uk/)
- Faculty of Pain Medicine of the Royal College of Anaesthetists: Opioids aware (https://www.fpm.ac.uk/opioids-aware)
- AWMSG National Prescribing Indicators (https://awmsg.nhs.wales/medicines-appraisals-and-guidance/medicines-optimisation/national-prescribing-indicators/)
- AWMSG persistent pain resources (https://awmsg.nhs.wales/medicines-appraisals-and-guidance/medicines-optimisation/prescribing-guidance/persistent-pain-resources/)
- AWMSG Polypharmacy: Guidance for prescribing (https://awmsg.nhs.wales/medicines-appraisals-and-guidance/medicines-optimisation/prescribing-guidance/polypharmacy-guidance-for-prescribing/)
- MHRA Opioids: risk of dependence and addiction (https://www.gov.uk/drug-safety-update/opioids-risk-of-dependence-and-addiction). September 2020.
- MHRA Benzodiazepines and opioids: reminder of risk of potentially fatal respiratory depression (https://www.gov.uk/drug-safety-update/benzodiazepines-and-opioids-reminder-of-risk-of-potentially-fatal-respiratory-depression) March 2020.
- Yellow Card Centre Wales – offers education and training sessions on suspected adverse drug reactions to all healthcare professionals and patient groups (https://www.awttc.org/taxonomy/term/5)
- Health Education and Improvement Wales (HEIW) virtual learning. NPIs Priority Areas - Analgesics: Tramadol (https://gpcpd.heiw.wales/clinical/all-wales-national-prescribing-indicators-20-21/safety-analgesics-tramadol/)
- Welsh Government - Living with Persistent Pain in Wales: (https://gov.wales/sites/default/files/publications/2019-05/living-with-persistent-pain-in-wales.pdf)

5.0 Information for patients

- NHS medicines A–Z: information about tramadol (https://www.nhs.uk/medicines/tramadol/)
- MHRA Opioid medicines and the risk of addiction - Safety leaflet on opioid medicines to help patients and their families reduce the risks of harm (https://www.gov.uk/guidance/opioid-medicines-and-the-risk-of-addiction)
- Faculty of Pain Medicine of the Royal College of Anaesthetists: Opioids Aware - a resource for patients and healthcare professionals to support

prescribing of opioid medicines for pain (https://www.fpm.ac.uk/opioids-aware)

- NHS Chronic Pain A–Z health (https://www.nhs.uk/live-well/healthy-body/ways-to-manage-chronic-pain/)
- Action on Pain (http://www.action-on-pain.co.uk/)
- Pain concern (https://painconcern.org.uk/)
- Pain toolkit (https://www.paintoolkit.org/)
- Live well with Pain: resources for patients (https://my.livewellwithpain.co.uk/)

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Appendix 1 – Primary care tramadol audit

Purpose of the audit

- To promote the safe and appropriate prescribing of tramadol in primary care in NHS Wales.
- To benchmark tramadol prescribing in primary care and identify areas of good practice, enabling yearly review.

Objectives

- To aid the appropriate prescribing of tramadol by encouraging practices to examine their tramadol prescribing in line with the current evidence base and current guidelines.
- To reduce the risk of patients having adverse drug reactions and encountering interactions.
- To ensure that, before starting treatment with opioids, a treatment strategy is in place and a plan for end of treatment has been agreed with the patient.
- To ensure patients initiated on tramadol are reviewed at 2–4 weeks to encourage appropriate prescribing and to reduce the number of patients put onto long-term repeat prescriptions.
- To ensure that patients prescribed tramadol for chronic pain are reviewed regularly as part of their chronic pain management plan with a view to stopping treatment where appropriate and safe.

Good practice points

- Refer to local pain guidelines where appropriate.
- Treatment should be short and intermittent.
- NICE's guideline NG193 on chronic pain (primary and secondary) in over 16s (April 2021) recommends that opioids, including tramadol, are not initiated for chronic primary pain.
- Maximum dose should not exceed 400 mg in 24 hours.
- Initiation of tramadol should be a trial and reviewed within 2–4 weeks, whether for an acute or chronic pain diagnosis.
- Before starting treatment with tramadol, agree with the patient a treatment strategy and plan for end of treatment.
- Discuss with patients that prolonged use of opioids, such as tramadol, may lead to drug dependence and addiction, even at therapeutic doses.
- After 3 months, there is evidence to suggest that the pain is no longer acute and has become a chronic condition. If tramadol is judged to be appropriate by the prescriber as part of a pain management plan and there are no other contraindications then tramadol should be reviewed every 12 months or as per practice guidance. Review should consider:
    - How and when is it taken?
    - Have alternatives been tried, both medication and non-medication approaches?
    - Can it be stepped down or stopped gradually?
- Only prescribe if first-line opioids (e.g. codeine, co-codamol) are not appropriate or tolerated.
- Tramadol should not be co-prescribed with other opioids.

- Consider the possibility of hyperalgesia if a patient on long-term opioid therapy presents with increased sensitivity to pain.
- Consult the latest advice and warnings for opioids during pregnancy in the product information and in clinical resources.
- Explain the risks of tolerance and potentially fatal unintentional overdose, and counsel patients and caregivers on signs and symptoms of opioid overdose to be aware of (see MHRA opioids safety information leaflet).
- Use with caution in:
    - patients taking other interacting medicines
    - patients taking medication that can lower the seizure threshold or cause central nervous system (CNS) toxicity (particularly SSRIs and TCAs)
    - concomitant therapeutic use of tramadol and serotonergic drugs, such as selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), MAO inhibitors, tricyclic antidepressants and mirtazapine may cause serotonin toxicity (see Summary of Product Characteristics for tramadol)
    - patients with a history of addiction or dependence
    - patients with a history of epilepsy or those susceptible to seizures; should only be prescribed in these patients if there are compelling reasons to do so
    - patients with renal impairment.
- Any medically significant adverse drug reactions to tramadol should be reported via the Yellow Card Scheme. Yellow Cards can be found at the back of the British National Formulary (BNF) or online at www.mhra.gov.uk. Also report suspected dependence or addiction to any medicine, including to an opioid, through the Yellow Card scheme.
- Be aware of patients asking for extra or interim prescriptions of tramadol as this may indicate that the patient's pain is not being managed appropriately, or that the patient is stockpiling or diverting supplies. There will be cases where a patient will need extra pain relief during worsening symptoms, but any emerging patterns should be flagged by prescriptions staff.
- Patients discharged on tramadol for acute pain from secondary care should be reviewed after discharge, and treatment discontinued where appropriate to ensure that they are not continued on treatment in primary care for longer than is necessary. Discharge medication reviews conducted by community pharmacists could identify patients discharged on tramadol from secondary care and facilitate review where appropriate.
- Benzodiazepines (and benzodiazepine-like drugs) and opioids can both cause respiratory depression; when used together, additive effects on the central nervous system increase the risks of sedation, respiratory depression, coma, and death. Only prescribe benzodiazepines (or benzodiazepine-like drugs) and opioids together if there is no alternative.

Notes on safety

Dosing in renal impairment

Tramadol and its metabolites are almost completely excreted through the kidneys. For elderly patients and patients with renal impairment, the half-life is extended and there is reduced elimination. If a patient has renal impairment, the

dose should be adjusted according to the patient's glomerular filtration rate (GFR):

- 20–50 ml/min: dose as in normal renal function
- 10–20 ml/min: 50–100 mg every 8 hours initially, then titrate dose as tolerated
- < 10 ml/min: 50 mg every 8 hours initially, then titrate dose as tolerated.

The information above on dosage adjustments in renal impairment is taken from the Renal Drug Handbook 3rd edition (2008) which bases its dosage adjustments on creatinine clearance and not estimated GFR (eGFR). It should be noted that there are differences between absolute GFR, eGFR, and creatinine clearance (CrCl). For more detailed advice on clinical importance and management, see BNF, Renal Drug Handbook and Summary of Product Characteristics, or refer to local Medicines Information Service.

Please note that the information in the Renal Drug Handbook is compiled from a wide range of sources and from the clinical experience of the editorial board of the UK Renal Pharmacy Group, all of whom are involved in the pharmaceutical care of renally impaired patients. As such, some of the information in the Renal Drug Handbook may not be in accordance with the licensed indications or use of the drug.

Advice for tapering and stopping tramadol

To reduce the risk of withdrawal effects associated with sudden cessation of opioids, taper dosage of tramadol slowly at the end of treatment. This can take weeks or months, depending on individual response and the dose taken. Healthcare professionals should advise patients not to stop taking tramadol suddenly, and not to try to self-medicate to overcome withdrawal effects. Self-medication with opioids can result in overdose and potentially death. The MHRA recommended that before prescribing opioids, healthcare professionals should discuss the risk and features of tolerance, dependence and addiction with the patient. A plan for the termination of treatment should be agreed, which might include identifying a strategy to measure treatment success or failure, and a dose reduction strategy. Where physical dependence to tramadol develops, the withdrawal syndrome can be severe, with symptoms typical of opiate withdrawal sometimes accompanied by atypical symptoms including seizures, hallucinations and anxiety.

The Faculty of Pain Medicine's Opioids Aware resource suggests tapering opioids by 10% weekly or two weekly. It is important to take into consideration that every patient and their circumstances will be different, and a prudent and individually tailored approach is required.

If the patient has chronic (also known as persistent) pain that has failed to respond to treatment, referral to a specialist pain service may be appropriate. If there are issues with dependence on tramadol, referral to a specialist support service where available may be appropriate.

Audit criteria
The target is not an absolute value and can be achieved if there is movement towards the suggested audit standard in subsequent audits.

Standard	Exceptions
1. All patients prescribed tramadol have a clear indication for which it is prescribed in their patient medication record	None
2. Dosage instructions for tramadol clearly indicate the maximum dose in 24 hours	None
3. All patients were prescribed previous analgesia such as weaker opioids or NSAIDs if not contraindicated before being prescribed tramadol*	Unless contraindicated
4. No other opioids are co-prescribed with tramadol	None
5. Interacting drugs are not prescribed alongside tramadol	Unless the clinical reasons for doing so outweigh the risks and the patient is monitored accordingly
6. No patients are initiated on tramadol if there is a history of substance misuse	Unless the clinical reasons for doing so outweigh the risks and the patient is monitored accordingly with involvement from specialist services where appropriate
7. No patients are initiated on tramadol where there are relevant co-morbidities, such as depression, epilepsy, or renal impairment	Unless the clinical reasons for doing so outweigh the risks and the patient is monitored accordingly
8. A pain management plan is in place for all patients prescribed tramadol	None
For acute pain/short-term tramadol patients	
9. All patients initiated on tramadol are initially put onto acute prescriptions and are reviewed at 2–4 weeks	None
For long-term tramadol patients	
10. All patients on regular tramadol prescriptions are reviewed at least every 12 months	None
11. No patients receive interim prescriptions or acute prescriptions more frequently than the normal duration of the prescription	None

***** NICE's clinical knowledge summary for tramadol recommends tramadol for people with neuropathic pain (except trigeminal neuralgia), only if acute rescue therapy is needed.

Method

For the purposes of the audit, the data collection has been split into two sections:

1. Patients who have been taking tramadol for a relatively short period of time (less than 12 months). These patients may fall into an acute pain group or may be patients for whom pain has recently become chronic.
2. Patients who have been taking tramadol regularly for a long period of time (more than 12 months). For these patients, pain is a chronic condition and the nature of the chronic pain condition requires regular review and careful management.

Opioid medicines provide relief from moderate to severe short-term pain; however, there is little evidence of their benefit in chronic pain or non-cancer pain and long-term use of opioids in non-cancer pain (longer than 3 months) carries an increased risk of dependence and addiction (see MHRA's Opioids: risk of dependence and addiction) . As a practice you may want to focus on both groups of patients or just on one, depending on the priorities of the individual practice.

Data collection

- Run a search to identify patients for sample selection for acute pain and/or chronic pain as detailed in Methods 1 and 2. Include combination products containing tramadol and paracetamol such as Tramacet®, and those containing tramadol and dexketoprofen (Skudexa®) in your search. Tramadol is the generic term; please see below for a list of brand names.

Tramadol brand names	
Brimisol® PR	Tramquel® SR
Invodol® SR	Tramulief® SR
Larapam® SR	Ultram
Mabron®	Zamadol®
Marol®	Zamadol® 24hr
Maxitram® SR	Zamadol® SR
Skudexa®	Zeridame® SR
Tilodol® SR	Zydol®
Tradorec® XL	Zydol® SR
Tramacet®	Zydol® XL

- Select the sample. The table below is a guide on the number of patients that would need to be selected to ensure a representative sample. However, for the purposes of using this document as an audit tool for improving the appropriateness of tramadol prescribing by GP practices, a smaller number decided locally would suffice.

Total number of patients prescribed tramadol	Sample size: 95% confidence; +/-5%
50	44
100	79
150	108
200	132
500	217
1000	278
2000	322

- Collect data using Patient Data Collection Sheets for acute pain patients and/or chronic pain patients.
- Collate data in Data Summary Sheets for acute pain patients and/or chronic pain patients.
- Return Data Summary Sheet *[localities to insert contact].*
- Fill out practice review sheet.

1. Method – Acute or short-term tramadol patients
Use the patient's medical records to complete Patient Data Collection Sheet.

(A) Find the total number of patients in the practice started on a <u>new</u> repeat or acute tramadol prescription in the past 12 months
Search the practice computer system for all patients prescribed tramadol as an acute or repeat prescription in the past 12 months (remember to search for branded products as well).

You will need to **<u>EXCLUDE</u>**:

- Patients who have received tramadol prescriptions for longer than 12 months;
- Newly registered patients already taking tramadol at time of registration.

Enter the figure for the total number of patients on Patient Data Collection Sheet and Data Summary Sheet.

(B) Select the sample
Randomly select a sample from **(A)**. If **(A)** is a small number it may be appropriate to audit all patients; however, the sample size will depend on the number of patients in your list.

(C) Patient prescribed the initial supply of tramadol as an acute prescription
The first prescription of tramadol should be given as an acute prescription.

(D) Indication
Tramadol is licensed for moderate to severe pain; the reason (indication) for tramadol initiation should be clearly documented.

(E) Initiated in primary care
Whether tramadol was initiated (prescribed or recommended) in primary or secondary care will inform the practice of where the majority of tramadol prescriptions are being initiated.

(F) i) and (F) ii) Tramadol review
Patients initiated on tramadol should be reviewed at 3 months. After 3 months, there is evidence to suggest that the pain is no longer acute and has become a chronic condition. For patients with chronic pain conditions, the pain management (of which medication is a part of an overall management strategy) should be reviewed every 12 months or as per practice guidance. For patients with chronic pain where the prescriber feels it necessary for the patient to take tramadol on a regular basis, it may be more appropriate for the medication to be added to the patient's repeat and reviewed regularly as a repeat medication.

(G) Dosage instructions
The dosage instructions should clearly indicate the maximum daily dose. The maximum daily dose of tramadol should not exceed 400 mg in 24 hours and the dosage instructions and maximum daily dose should be clear and non-ambiguous. For example 'Take two when required' would not be appropriate as this does not give the patient a clear indication of the maximum daily dose they can take.

(H) Previous analgesia tried
Tramadol should only be prescribed if first-line opioids (e.g. codeine, co-codamol) are not effective or are not appropriate and/or tolerated.

(I) Other opioids
Other regular opioids should not be co-prescribed with tramadol as this may increase the risk of patients experiencing adverse effects.

(J) Interacting medication
Other medication that interacts with tramadol, includes warfarin, SSRIs, TCAs, MAOIs, mirtazapine, venlafaxine, anti-psychotics, epilepsy medication and medication that lowers the seizure threshold. See Stockley's Drug Interactions or the BNF for further detail on clinical importance and management.

(K) History of substance misuse
Indicate whether the patient has a history of substance misuse, including over-the-counter and prescription medication, as well as alcohol and illicit substances.

(L) and (M) Relevant co-morbidities
For the purposes of this audit, other relevant co-morbidities include epilepsy, seizures and renal impairment. Other relevant co-morbidities may be of importance and the person conducting the audit may wish to make note of these, even though they are not specifically mentioned in the Patient Data Collection Sheet.

Patient data collection sheet – Tramadol for acute pain in primary care

Number of patients in the practice who have received a new repeat or acute prescription for tramadol in the past 12 months _____ **(A)**

Number of patients in the sample _____ **(B)**

Patient ID					
Age					
Patient prescribed the initial supply of tramadol on an acute prescription (Y/N)? (C)					
Indication for tramadol clearly recorded (Y/N)? (D)					
Was the tramadol initiated in primary care (Y/N)? (E)					
Has the patient been taking tramadol for longer than 3 months (Y/N)? (F) – *answer two questions below only if response is yes*					
• ***Review at 3 months (Y/N)? (F) i)***					
• ***Was the most recent prescription on repeat (Y/N)? (F) ii)***					
Dosage instructions clearly indicate the maximum daily dose (Y/N)? (G)					
Before prescribing tramadol, have other analgesics been tried (Y/N)? (H)					
Patient co-prescribed other regular opioid (Y/N)? (I)					
Patient co-prescribed interacting medication (Y/N)? (If yes, please specify) **(J)**					
History of substance misuse (Y/N)? (K)					
History of epilepsy/seizures (Y/N)? (L)					
Is the patient's GFR <20 ml/min (Y/N)? (M)					
Comments and notes					

Data summary sheet – Acute pain

The target is not an absolute value and can be achieved if there is movement towards the suggested audit standard in subsequent runs of the audit.

	Number	Percentage of practice population
Practice list size		100%
(A) Number of patients in the practice started on a new repeat or acute tramadol prescription in the past 12 months		

	Number	Percentage of the audit sample	Suggested audit standard
(B) Sample size i.e. number of patients with a tramadol prescription included in the audit		100%	N/A
(C) Number of patients prescribed the initial supply of tramadol on an acute prescription			100%
(D) Number of patients with a clear indication for tramadol documented in their records			100%
(E) Number of tramadol prescriptions initiated in primary care			N/A
(F) Number of patients taking tramadol for longer than 3 months			N/A
• ***(F) i) Number reviewed at 3 months***			100%
• ***(F) ii) Number with most recent prescription on repeat***			N/A
(G) Number of patients whose dosage instructions clearly indicate the maximum daily dose			100%
(H) Number of patients prescribed other analgesia before prescribing tramadol			100%
(I) Number of patients co-prescribed another regular opioid			0%
(J) Number of patients on interacting medication			0%
(K) Number of patients with a history of substance misuse			0%
(L) Number of patients with history of epilepsy/seizures			0%
(M) Number of patients where the dose is appropriate according to GFR			100%

2. Method – Chronic pain or long–term tramadol patients
Use the patient's medical records to complete the Patient Data Collection Sheet.

(A) Find the total number of patients in the practice prescribed tramadol on repeat or acute prescriptions for over 12 months:
Search the practice computer system for all patients prescribed tramadol as an acute or repeat prescription for longer than 12 months.

You will need to **EXCLUDE**:

- Patients who have been prescribed tramadol for fewer than 12 months;
- Patients who have not received a prescription within the last 3 months (to eliminate one-off acute prescriptions from previous history).

Enter the figure for the total number of patients on the Patient Data Collection Sheet and Data Summary Sheet.

(B) Select the sample
Randomly select a sample of patients from the total number of patients prescribed tramadol **(A)**; the sample size will depend on the number of patients in your list.

(C) and (C) i) Number of patients prescribed tramadol on an acute prescription
The patient's initial supply of tramadol should be on an acute prescription, as ideally treatment should be short and intermittent. However, for patients who have been reviewed and are being prescribed long-term tramadol, where a prescription is being collected every month it **may** be more appropriate to put this onto repeat prescription. All patients on long-term tramadol should be reviewed at least every 12 months.

(D) Indication
Tramadol is licensed for moderate to severe pain; the reason (indication) for tramadol initiation should be clearly documented.

(E) Extra or interim prescriptions
It should be clear from the patient record if a patient is asking for extra or interim prescriptions (for patients on repeat prescriptions) or requesting acute prescriptions more frequently than the normal duration of the prescription. This may indicate that the patient's pain is not being managed appropriately, or that the patient is stockpiling or diverting supplies.

(F) Number of patients with a review of tramadol prescribing within the last 12 months
Patients should be reviewed annually or more frequently in accordance with practice guidelines.

(G) Dosage instructions
The dosage instructions should clearly indicate the maximum daily dose. The maximum daily dose of tramadol should not exceed 400 mg in 24 hours and the dosage instructions and maximum daily dose should be clear and non-ambiguous. For example, 'Take two when required' would not be appropriate as this does not give the patient a clear indication of the maximum daily dose they can take.

(H) Number of patients where dose has been stepped down or stopped
Patients prescribed long-term tramadol should be reviewed regularly. Questions to consider are:

- Have alternatives been prescribed?
- Can tramadol be stepped down or stopped?

Please note: Avoid abrupt withdrawal after long-term treatment. Where physical dependence to tramadol develops, the withdrawal syndrome can be severe, with symptoms typical of opiate withdrawal sometimes accompanied by atypical symptoms including seizures, hallucinations and anxiety.

To minimise the risk of withdrawal reactions, the CHM recommends the dose of opioid should be tapered slowly at the end of treatment. This can take weeks or months, depending on individual response and the dose taken. See notes on safety and refer to specialist advice where appropriate.

(I) Previous analgesia tried
Tramadol should only be prescribed if first-line opioids (e.g. codeine, co-codamol) are not effective or are not appropriate or tolerated.

(J) Other opioids
Other regular opioids should not be co-prescribed with tramadol as this may increase the risk of patients experiencing adverse effects.

(K) Interacting medication
Other medication prescribed that interacts with tramadol includes warfarin, SSRIs, TCAs, MAOIs, mirtazapine, venlafaxine, anti-psychotics, epilepsy medication and medication that lowers the seizure threshold. See Stockley's Drug Interactions or the BNF for further details on clinical importance and management.

(L) History of substance misuse
Indicate whether the patient has a history of substance misuse, including over-the-counter and prescription medication, as well as alcohol and illicit substances.

(M) and (N) Relevant co-morbidities
For the purposes of this audit, other relevant co-morbidities include epilepsy or history of seizures, and renal impairment. Other relevant co-morbidities may be of importance and the person conducting the audit may wish to make note of these, even though they are not specifically mentioned in the Patient Data Collection Sheet.

(O) Pain management plan
Please indicate whether there is a pain management plan in place and recorded in the notes.

(P) Modified-release preparations
Please indicate whether modified-release preparations of tramadol are prescribed.

Patient data collection sheet – Tramadol for chronic pain in primary care

Number of patients in the practice on repeat or acute tramadol prescriptions for longer than 12 months _____ **(A)**

Number of patients in the sample _____ **(B)**

Patient ID and age				
Patient prescribed tramadol on acute prescription (Y/N)? (C)				
• ***For acute prescriptions – is the patient having a prescription every month (Y/N)? (C) i)***				
Indication for tramadol clearly recorded (Y/N)? (D)				
Have any interim prescriptions been issued? (Y/N)? (E)				
Has there been a review in the last 12 months (Y/N)? (F)				
Dosage instructions clearly indicate the maximum daily dose (Y/N)? (G)				
Since starting tramadol, has the dose ever been stepped down or stopped (Y/N)? (H)				
Before prescribing tramadol, have other analgesics been tried (Y/N)? (I)				
Patient co-prescribed other regular opioid with tramadol (Y/N)? (J)				
Patient co-prescribed interacting medication (Y/N)? (If yes, please specify) **(K)**				
History of substance misuse (Y/N)? (L)				
History of epilepsy/seizures (Y/N)? (M)				
Is the patient's GFR <20 ml/min (Y/N)? (N)				
Is there a pain management plan in place (Y/N)? (O)				
Is a modified-release tramadol preparation prescribed (Y/N) (P)				
Comments and notes				

Data summary sheet – Chronic pain

The target is not an absolute value and can be achieved if there is movement towards the suggested audit standard in subsequent runs of the audit.

	Number	Percentage of practice population
Practice list size		100%
(A) Number of patients in the practice on repeat or acute tramadol prescriptions for longer than 12 months		

	Number	Percentage of the audit sample	Suggested audit standard
(B) Sample size i.e. number of patients on tramadol longer than 12 months included in the audit		100%	N/A
(C) Number of patients prescribed tramadol on an acute prescription			N/A
• ***(C) i) Number of patients collecting an acute prescription every month***			0%
(D) Number of patients with a clear indication for tramadol documented in their records			100%
(E) Number of patients receiving extra or interim prescriptions			0%
(F) Number of patients with a review within the last 12 months			100%
(G) Number of patients whose dosage instructions clearly indicate the maximum daily dose			100%
(H) Number of patients where the dose has ever been stepped down or stopped			N/A
(I) Number of patients prescribed other analgesia before prescribing tramadol			100%
(J) Number of patients co-prescribed another regular opioid			0%
(K) Number of patients on interacting medication			0%
(L) Number of patients with a history of substance misuse			0%
(M) Number of patients with history of epilepsy/seizures			0%
(N) Number of patients where the dose is appropriate according to GFR			100%
(O) Is there a pain management plan in place (Y/N)?			100%
(P) Is a modified-release tramadol preparation prescribed (Y/N)			N/A

Practice review sheet

A. What lessons did the practice learn from carrying out this audit?

B. What discussion/activities did the practice undertake as a result of the audit?

C. What changes has the practice agreed to implement as a result of this audit?

This audit was completed by:

Name(s)

_____

Signature(s)

_____

Appendix 2 – Secondary care tramadol audit

Purpose

- To promote the safe and appropriate prescribing of tramadol in secondary care in NHS Wales.
- To aid the appropriate prescribing of tramadol for patients discharged from a secondary care setting.
- To prevent patients being prescribed tramadol long term as a result of being discharged from secondary care with tramadol for acute pain.

Objectives

- To assess the appropriateness of tramadol prescribing for acute pain in secondary care.
- To assess whether tramadol is being co-prescribed with other opioids in secondary care.
- To determine the appropriateness of tramadol prescribing on discharge prescriptions in secondary care.
- To assess whether tramadol is being prescribed with a clear discontinuation or review date on discharge prescriptions.
- To quantify the amount of tramadol dispensed on discharge prescriptions.

Good practice points

- Refer to local pain guidelines where appropriate.
- Treatment should be short and intermittent.
- Use only for moderate and severe pain.
- Tramadol should only be prescribed if first-line opioids (e.g. codeine, co-codamol) are not appropriate or tolerated.
- Tramadol should not be co-prescribed with other regular opioids.
- Patients should also be prescribed regular paracetamol and/or NSAID if appropriate.
- Before starting treatment with tramadol, agree with the patient a treatment strategy and plan for end of treatment. Counsel patients on the nature of an acute prescription from a hospital discharge.
- Consult the latest advice and warnings for opioids during pregnancy in the product information and in clinical resources.
- Discuss with patients that prolonged use of opioids, such as tramadol, may lead to drug dependence and addiction, even at therapeutic doses.
- Explain the risks of tolerance and potentially fatal unintentional overdose, and counsel patients and caregivers on signs and symptoms of opioid overdose to be aware of (see MHRA opioids safety information leaflet).
- Patients discharged on tramadol should only be given a short supply, and a discontinuation or review date should be clearly indicated on the discharge prescription to ensure that they are not continued on treatment in primary care for longer than is necessary. Communication with community pharmacists via discharge medication reviews could identify patients discharged on tramadol from secondary care and facilitate review and patient counselling on tramadol treatment where appropriate.

- Use with caution in:
  - patients with a history of substance misuse
  - patients with a history of epilepsy or those susceptible to seizures; tramadol should only be prescribed in these patients if there are compelling reasons to do so
  - patients taking medication that can lower the seizure threshold or cause CNS toxicity (particularly SSRIs and TCAs)
  - patients taking other interacting medicines
  - patients with renal impairment
  - patients taking benzodiazepines and opioids; when used together, these have additive effects on the central nervous system, increasing the risk of sedation, respiratory depression, coma, and death. Only prescribe benzodiazepines (or benzodiazepine-like drugs) and opioids together if there is no alternative.
- Any medically significant adverse drug reactions that may be associated with tramadol should be reported through the Yellow Card Scheme. Yellow Cards can be found at the back of the British National Formulary (BNF) or on-line at www.mhra.gov.uk.

Notes on safety

Dosing in renal impairment

Tramadol and its metabolites are almost completely excreted through the kidneys. For elderly patients and patients with renal impairment, the half-life is extended and there is reduced elimination. If a patient has renal impairment, the dose should be adjusted according to the patient's glomerular filtration rate (GFR):

- 20–50 ml/min: dose as in normal renal function
- 10–20 ml/min: 50–100 mg every 8 hours initially, then titrate dose as tolerated
- < 10 ml/min: 50 mg every 8 hours initially, then titrate dose as tolerated.

The information above on dosage adjustments in renal impairment is taken from the Renal Drug Handbook 3rd edition (2008) which bases its dosage adjustments on creatinine clearance and not estimated GFR (eGFR). It should be noted that there are differences between absolute GFR, eGFR, and creatinine clearance (CrCl). For more detailed advice on clinical importance and management, see BNF, Renal Drug Handbook and Summary of Product Characteristics, or refer to local Medicines Information Service.

Please note that the information in the Renal Drug Handbook is compiled from a wide range of sources and from the clinical experience of the editorial board of the UK Renal Pharmacy Group, all of whom are involved in the pharmaceutical care of renally impaired patients. As such, some of the information in the Renal Drug Handbook may not be in accordance with the licensed indications or use of the drug.

Advice for tapering and stopping tramadol

To reduce the risk of withdrawal effects associated with sudden cessation of opioids, taper dosage of tramadol slowly at the end of treatment. This can take weeks or months, depending on individual response and the dose taken. Healthcare professionals should advise patients not to stop taking tramadol suddenly, and not to try to self-medicate to overcome withdrawal effects. Self-medication with opioids can result in overdose and potentially death. The MHRA recommended that before prescribing opioids, healthcare professionals should discuss the risk and features of tolerance, dependence and addiction with the patient. A plan for the termination of treatment should be agreed, which might include identifying a strategy to measure treatment success or failure, and a dose reduction strategy. Where physical dependence to tramadol develops, the withdrawal syndrome can be severe, with symptoms typical of opiate withdrawal sometimes accompanied by atypical symptoms including seizures, hallucinations and anxiety.

The Faculty of Pain Medicine's Opioids Aware resource suggests tapering opioids by 10% weekly or two weekly. It is important to take into consideration that every patient and their circumstances will be different, and a prudent and individually tailored approach is required.

If the patient has chronic (also known as persistent) pain that has failed to respond to treatment, referral to a specialist pain service may be appropriate. If there are issues with dependence on tramadol, referral to a specialist support service where available may be appropriate.

Audit criteria
The target is not an absolute value and can be achieved if there is movement towards the suggested audit standard in subsequent runs of the audit.

Standard	Exception
1. All patients prescribed tramadol have a clear and appropriate indication for prescribing	None
2. No patients are co-prescribed other regular opioids with tramadol	None
3. All patients admitted on tramadol have a review during admission to assess if it is appropriate to continue with treatment	None
4. All patients are initiated on tramadol only if first-line weak opioids are not suitable	Contraindications to other first-line opioids
5. The daily dose of tramadol does not exceed 400 mg in 24 hours	None
6. Patients are not co-prescribed interacting medicines	Unless the clinical benefits outweigh the risks and patients are monitored accordingly
7. Tramadol is not initiated where there is a history of substance misuse	Unless the clinical benefits outweigh the risks and patients are monitored accordingly
8. Tramadol is not initiated where there is a history of epilepsy	Unless the clinical benefits outweigh the risks and patients are monitored accordingly
9. All patients are dosed appropriately according to their renal function	None
Discharge prescriptions	
10. All patients prescribed tramadol for acute pain are discharged with no more than one week's supply unless judged to be appropriate by the prescriber	Unless a longer course of treatment is judged to be appropriate in the individual circumstances of the patient
11. All discharge prescriptions for tramadol for acute pain have a clear review or discontinuation date	None

Method
Data collection should take place over a specified one-day period or as decided locally depending on the amount of data expected to be captured. Collect data on all patients prescribed tramadol on drug chart and/or discharge prescriptions using Patient Data Collection Sheet.

Patient data collection sheet – Tramadol in secondary care

Audit number …… Date of data collection ...../...../…...

Speciality that patient was under care of/discharged from……

Diagnosis for treatment……

Total number of patients on ward……

Total number of patients prescribed tramadol……..

		Yes	No	Comments
1	Is the indication for tramadol is clearly recorded?			
2	Is the patient co-prescribed another regular opioid? If yes, state which.			
3	Was the patient taking tramadol prior to admission?			
4	Was tramadol prescribed first line? If yes, were there any contraindications to other first-line opioids such as codeine?			
5	Does the daily dose of tramadol exceed 400 mg in 24 hours or is the maximum dose ambiguous?			
6	Is the patient co-prescribed an interacting medicine?			
7	Does the patient have a history of substance misuse?			
8	Does the patient have a history of epilepsy or seizures?			
9a	Is the patient's GFR < 20 ml/min?			
9b	If the patient's GFR is < 20 ml/min, has the dose been adjusted?			
10	**Questions relating to discharge prescriptions only**			
10a	Is there a discontinuation date or review date for tramadol clearly indicated on discharge prescription?			
10b	Does the duration of tramadol prescribed exceed one week?			

Appendix 3 – Emergency Department tramadol audit

Purpose

- To review overdose admissions through emergency departments in Wales and to identify the frequency of tramadol overdose and misuse incidents in Wales.
- To promote the safe and appropriate prescribing of tramadol for moderate to severe pain in secondary care in NHS Wales and to raise awareness of the concerns regarding the diversion and misuse of tramadol.
- The results of the audit can be used to benchmark the admissions through emergency departments in Wales due to tramadol, and to assess the main risk areas and contributing factors for tramadol overdose cases, in order to review tramadol prescribing in primary and secondary care. Subsequent re-runs of the audit would determine whether work done to review tramadol prescribing within primary and secondary care had been effective.

Objectives

- To determine the frequency of overdose cases involving tramadol presenting through emergency departments in Wales.
- To determine other factors which are associated with tramadol overdose and/or misuse.

Good practice points

- Any medically significant adverse drug reactions to tramadol should be reported through the Yellow Card Scheme. Yellow Cards can be found at the back of the British National Formulary (BNF) or online at www.mhra.gov.uk.

General notes on safety with regard to tramadol prescribing

Dosing in renal impairment

Tramadol and its metabolites are almost completely excreted through the kidneys. For elderly patients and patients with renal impairment, the half-life is extended and there is reduced elimination. If a patient has renal impairment, the dose should be adjusted according to the patient's glomerular filtration rate (GFR):

- 20–50 ml/min: dose as in normal renal function
- 10–20 ml/min: 50–100 mg every 8 hours initially, then titrate dose as tolerated
- < 10 ml/min: 50 mg every 8 hours initially, then titrate dose as tolerated.

The information above on dosage adjustments in renal impairment is taken from the Renal Drug Handbook 3rd edition (2008) which bases its dosage adjustments on creatinine clearance and not estimated GFR (eGFR). It should be noted that there are differences between absolute GFR, eGFR, and creatinine clearance (CrCl). For more detailed advice on clinical importance and management, see BNF, Renal Drug Handbook and Summary of Product Characteristics, or refer to local Medicines Information Service.

Please note that the information in the Renal Drug Handbook is compiled from a wide range of sources and from the clinical experience of the editorial board of the UK Renal Pharmacy Group, all of whom are involved in the pharmaceutical care of renally impaired patients. As such, some of the information in the Renal Drug Handbook may not be in accordance with the licensed indications or use of the drug.

Advice for tapering and stopping tramadol

To reduce the risk of withdrawal effects associated with sudden cessation of opioids, taper dosage of tramadol slowly at the end of treatment. This can take weeks or months, depending on individual response and the dose taken. Healthcare professionals should advise patients not to stop taking tramadol suddenly, and not to try to self-medicate to overcome withdrawal effects. Self-medication with opioids can result in overdose and potentially death[1].

The MHRA recommended that before prescribing opioids, healthcare professionals should discuss the risk and features of tolerance, dependence and addiction with the patient. A plan for the termination of treatment should be agreed, which might include identifying a strategy to measure treatment success or failure, and a dose reduction strategy. Where physical dependence to tramadol develops, the withdrawal syndrome can be severe, with symptoms typical of opiate withdrawal sometimes accompanied by atypical symptoms including seizures, hallucinations and anxiety.

The Faculty of Pain Medicine's Opioids Aware resource suggests tapering opioids by 10% weekly or two weekly. It is important to take into consideration that every patient and their circumstances will be different, and a prudent and individually tailored approach is required.

If the patient has chronic (also known as persistent) pain that has failed to respond to treatment, referral to a specialist pain service may be appropriate. If there are issues with dependence on tramadol, referral to a specialist support service where available may be appropriate.

Audit criteria

The target is not an absolute value and can be achieved if there is movement towards the suggested audit standard in subsequent runs of the audit.

Standard	Exception
1. No overdose admissions involved tramadol	None
2. No overdose admissions involving tramadol resulted in death	None

Method

For the specified one-month period, identify all cases of overdose admissions through the emergency department and fill out the Patient Data Collection Sheet.

Collate data and insert into Data Summary Sheet.

- Total number of patients admitted with overdose (both accidental and deliberate) **(A)**
- Total number of patients admitted with overdose resulting in death **(B)**
- Number of overdose admissions where tramadol was involved **(C)**
- Number of overdose deaths where tramadol was involved **(D)**

Patient data collection sheet – Overdose admissions involving tramadol in emergency departments

Data collection over one month ____ / _____ / _____ to ___ / _____ / ____

Age and sex of patient	Did overdose involve tramadol? (Y/N)	Did overdose result in death? (Y/N)	Was the overdose directly linked to tramadol? (Y/N or N/A)	Was the patient prescribed tramadol as part of their medication history? (Y/N)	Was the patient on interacting medication*? (Y/N)	Did the patient have a history of drug or alcohol dependency? (Y/N)	Did the patient have a history of depression? (Y/N)	Did the patient have a history of epilepsy? (Y/N)	Did the patient have a history of renal impairment? (Y/N)	Other comments

*Interacting medications include SSRIs, TCAs, MAOIs, mirtazapine, venlafaxine, anti-psychotics, warfarin, epilepsy medication and other medication that lowers the seizure threshold. See BNF or Stockley's Drug Interactions for complete list and information on clinical significance and management.

Data summary sheet – Overdose admissions involving tramadol in emergency departments

Data collection over one month ____ / _____ / _____ to ___ / _____ / ____

Total number of overdose admissions (A)	Total number of overdose admissions resulting in death (B)	Number of overdose admissions involving tramadol (C)	Number of overdose admissions involving tramadol resulting in death (D)	Number of overdose admissions involving tramadol where:						
				overdose was directly linked to tramadol	tramadol was prescribed as part of medication history	interacting medication was implicated	patients had history of drug or alcohol dependency	patients had history of depression	patients had history of epilepsy	patients had renal impairment