All Wales Medicines Strategy Group

Grŵp Strategaeth Meddyginiaethau Cymru Gyfan

Tramadol Educational Resource Materials

Audit Materials

November 2013

(Updated August 2014)

These educational resource materials have been prepared by a multiprofessional collaborative group, with support from the All Wales Prescribing Advisory Group (AWPAG) and 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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1.0 INTRODUCTION

The purpose of these audits is to promote the appropriate prescribing of tramadol in NHS Wales. The audits form part of an educational resource pack, which also includes WeMeReC bulletins, an educational slide set, a patient information leaflet and a shared decision-making toolkit. These educational resource materials are intended to raise awareness amongst prescribers and patients of the potential harms associated with the misuse and diversion of tramadol, and to provide healthcare professionals with information and training to aid in the appropriate prescribing of tramadol as part of an overall pain management strategy. The audit tools are to be used by prescribers and other healthcare professionals as a template to review the prescribing of tramadol within the often complex context of pain management.

Concerns regarding the risks associated with tramadol were highlighted by the Advisory Council on the Misuse of Drugs (ACMD) in February 2013[1], and have also been the subject of media attention[2–4]. Although the recent concerns have prompted a review of tramadol prescribing in NHS Wales, it must be noted that pain management is often complex and that the prescriber must make decisions based on the individual needs of the patient. Tramadol is a strong opioid, licensed for moderate to severe pain, and is a useful treatment for patients for whom other options are not tolerated or effective. There is a recognised place for tramadol in pain management, and the purpose of the audits is 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.

Advice for stepping down or stopping tramadol

Avoid abrupt withdrawal after long-term treatment[5]. 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[1,6]. For patients taking regular tramadol, or those who may be dependent on tramadol, a careful approach is required. If it is appropriate for a patient's tramadol to be stepped down or stopped, it is important to note that the dose must be reduced slowly to ensure the patient's safety and to minimise the risk of withdrawal symptoms and/or adverse reactions.

To encourage patient engagement and concordance, a suggested approach would be to reduce the dose at each reduction step, e.g. by one 50 mg dose, and to titrate by how the patient manages, rather than by setting time limits for the next reduction. Every patient and their circumstances will be different, and a prudent and individually tailored approach is required.

If there are issues with chronic pain or dependence on tramadol, referral to a specialist service may be appropriate.

2.0 BACKGROUND

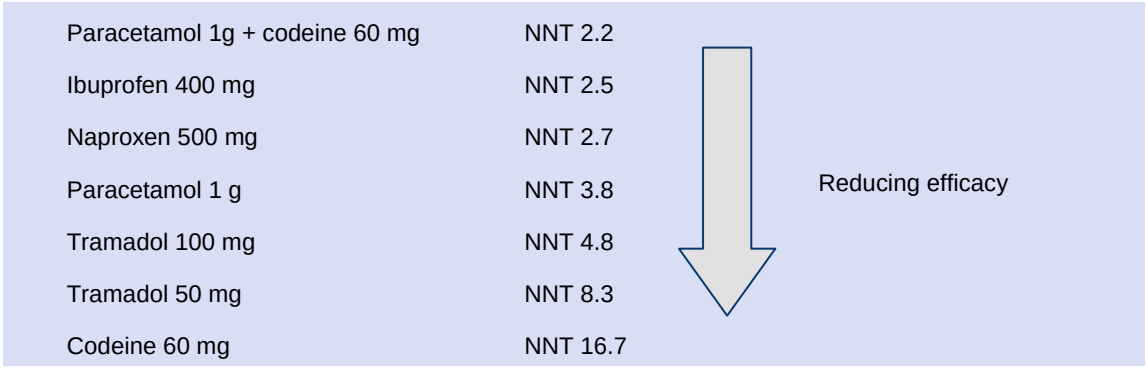
Tramadol is licensed for the treatment of moderate to severe pain and is classed as a strong opioid. Tramadol produces analgesia by two mechanisms: an opioid effect and an enhancement of the serotonergic and adrenergic pathways[5]. It has fewer of the typical opioid side effects, e.g. less respiratory depression and constipation, but psychiatric reactions have been reported.

Tramadol is subject to abuse and dependence and there are concerns with regard to interactions[7]. Office for National Statistics data show a steady increase in the number of deaths in England and Wales involving tramadol. Between 2008 and 2012, such deaths increased from 83 to 175[8]. Tramadol also accounts for an increasing number of reports to the National Poisons Information Service (NPIS)[7,9]. Tramadol appears seventh on the list of the top ten telephone enquiries for pharmaceutical agents in 2012–2013 with 691 enquiries. Fifty-one of these enquiries originated in Wales[9].

The ACMD recommended that the UK Government should reclassify tramadol as a class C substance, and place it within Schedule III to the Misuse of Drugs Regulations[1]. A consultation was launched by Crime Prevention Minister Jeremy Browne, which closed on the 11 October 2013[10]. The conclusion of the consultation was to place tramadol within Schedule III to the Misuse of Drugs Regulations but with exemptions from safe custody. The changes came into force on the 10 June 2014.

Figure 1 shows the number needed to treat (NNT) figures for some commonly prescribed analgesics[11]. The NNT is calculated for the proportion of patients with at least 50% pain relief over 4–6 hours compared with placebo in randomised, double-blind, single dose studies in patients with moderate to severe pain[11]. The figure shows that tramadol is not as effective, in terms of NNT, as paracetamol, paracetamol combined with codeine, naproxen or ibuprofen. This review did not include dihydrocodeine; however, the NNT for a single dose of dihydrocodeine 30 mg in moderate to severe postoperative pain was assessed in another review as 8.1 for at least 50% pain relief when compared to placebo over a period of four to six hours[12].

Figure 1. NNT figures for commonly prescribed analgesics



Dizziness and constipation are common side effects of tramadol. Hallucinations, confusion and convulsions, as well as rare cases of drug dependence and withdrawal, have been reported with tramadol at therapeutic doses[13].

To minimise the risk of convulsions, the Committee on Safety of Medicines recommends that patients with a history of epilepsy take tramadol only if there are compelling reasons to do so[13]. In addition, tramadol should be used with caution in patients taking concomitant drugs that can lower the seizure threshold, such as tricyclic antidepressants (TCAs) or selective serotonin reuptake inhibitors (SSRIs)[13]. The use of tramadol is contra-indicated in uncontrolled epilepsy and in patients receiving, or who have recently discontinued (within the previous two weeks), monoamine oxidase inhibitors (MAOIs).

3.0 PRESCRIBING DATA

Prescribing data are taken from Comparative Analysis System for Prescribing Audit (CASPA) and Electronic Prescribing Analysis and Cost (ePACT)[14,15], applications which are tools for analysis of prescribing trends in primary care for NHS Wales and England respectively.

3.1 Wales

Tramadol prescribing rates for primary care in NHS Wales increased by 25% (defined daily doses [DDDs] per 1,000 patients) from the year ending March 2009 to the year ending March 2013 and prescribing of tramadol accounts for 42% of the total opioids prescribed (quarter ending June 2013). The 42% refers to tramadol within the category of opioids and does not include combination products such as co-codamol and co-dydramol. However, Figure 2 below shows tramadol as a percentage of total opioids prescribed including other commonly prescribed combination products, such as co-codamol and co-dydramol, to give a more complete picture within the context of prescribing in pain.

The data show that tramadol accounts for a large proportion of opioid prescribing in all health boards and also show that there is some variation between health boards.

Figure 2. Opioid analgesic breakdown by health board as a percentage of total opioid prescribing. Quarter ending June 2013

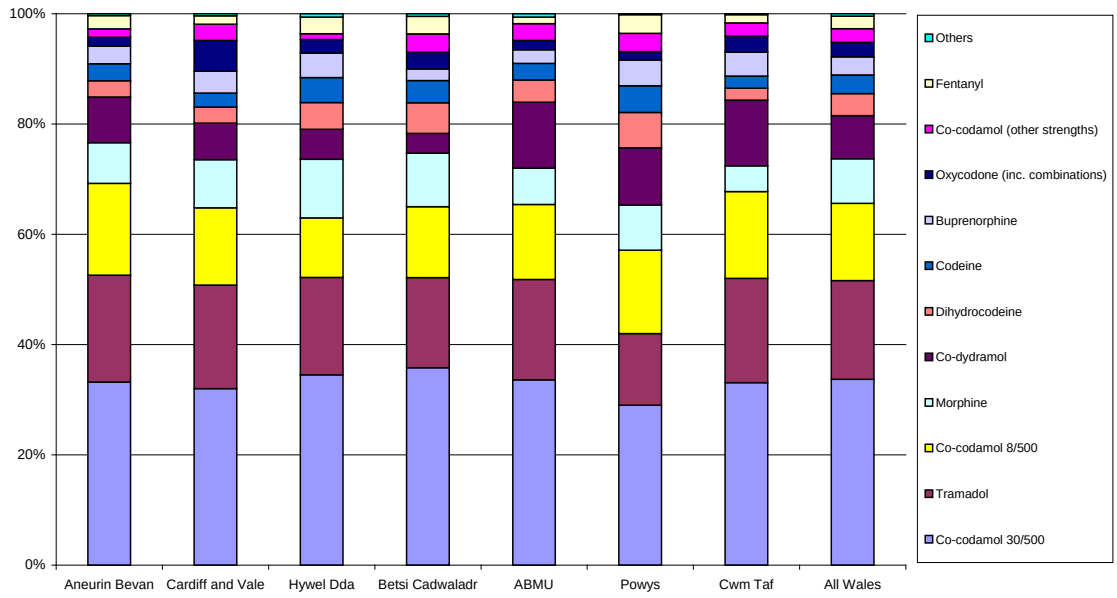


Figure 3 shows a map of Wales comparing the prescribing of tramadol as DDDs per 1,000 patients across the different localities for the quarter ending June 2013. The data show the variation between the geographical regions of Wales with higher prescribing rates in areas of Aneurin Bevan Health Board, Cwm Taf Health Board and Abertawe Bro Morgannwg University Health Board, and the lowest prescribing rates seen in Powys Teaching Health Board and areas of Betsi Cadwaladr University Health Board.

Figure 3. Tramadol prescribing in Wales by locality (DDDs per 1,000 patients). Quarter ending June 2013

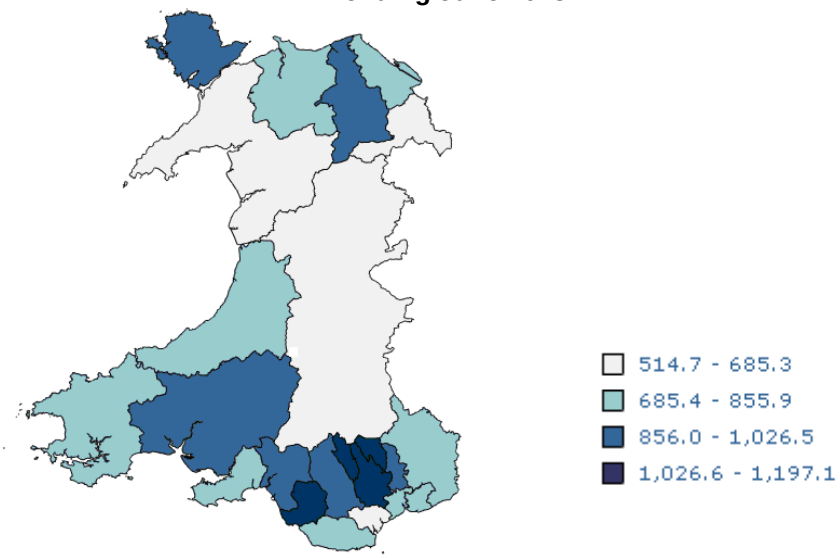
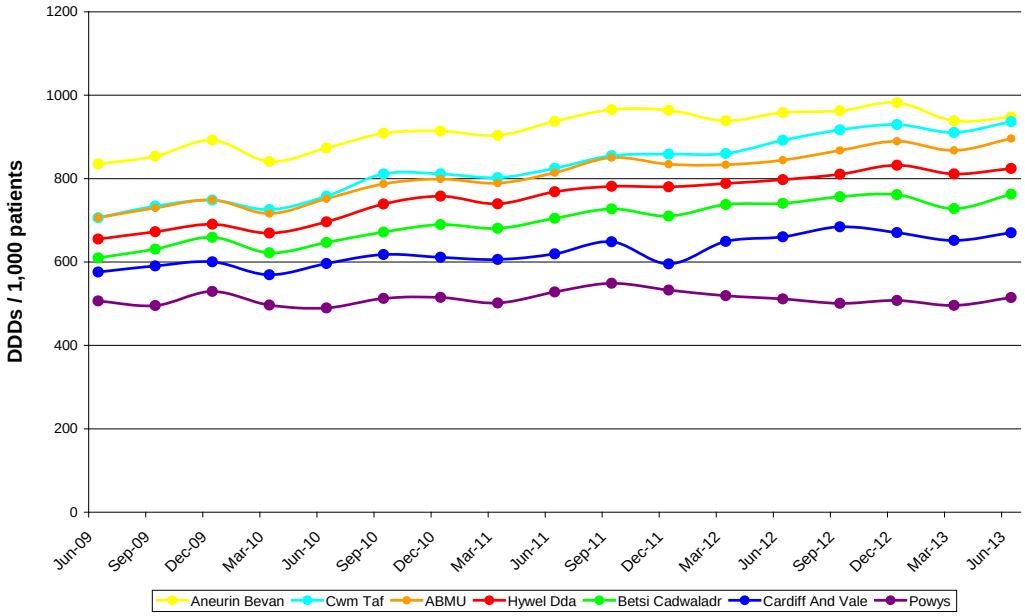


Figure 4 shows the prescribing trends for each of the health boards in Wales. The data show that prescribing rates continue to increase in Wales and that in some health boards this rate is increasing more than in others.

The prescribing rates in Powys Teaching Health Board have only slightly increased (1.6% increase from June 2009–June 2013), whereas the prescribing rates for the other health boards have seen large rises from June 2009 to June 2013, with four health boards seeing a rise of more than 20%. Aneurin Bevan Health Board, although the highest prescriber in the quarter ending June 2009, has not increased prescribing at the same rate as some other health boards (an 11% increase for the same time period).

Figure 4. Tramadol prescribing trends of Welsh health boards (DDDs per 1,000 patients). June 2009–June 2013



3.2 Comparison of Wales with England

Figure 5 shows the prescribing trend for primary care prescribing in Wales compared to England and North East (NE) England (the area of England most similar to Wales demographically). Primary care prescribing of tramadol in Wales is higher per 1,000 patients than in England, but lower than in NE England. Please note that due to the transition from Primary Care Trusts (PCTs) to Clinical Commissioning Groups (CCGs) in April 2013, prescribing data for NE England was not readily available for the purposes of comparison beyond March 2013.

Figure 5. Tramadol prescribing trends for Wales, England and NE England (DDDs per 1,000 patients). June 2009–June 2013

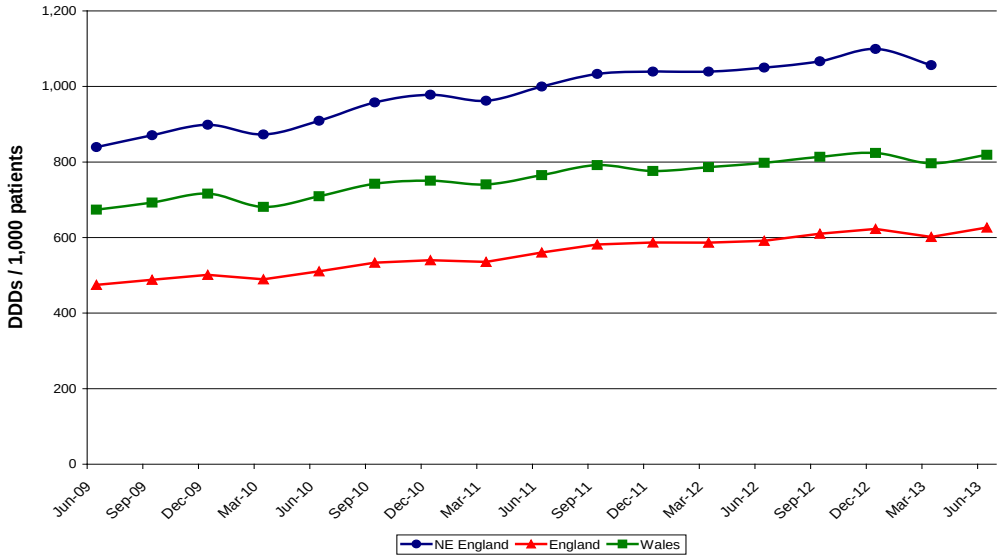
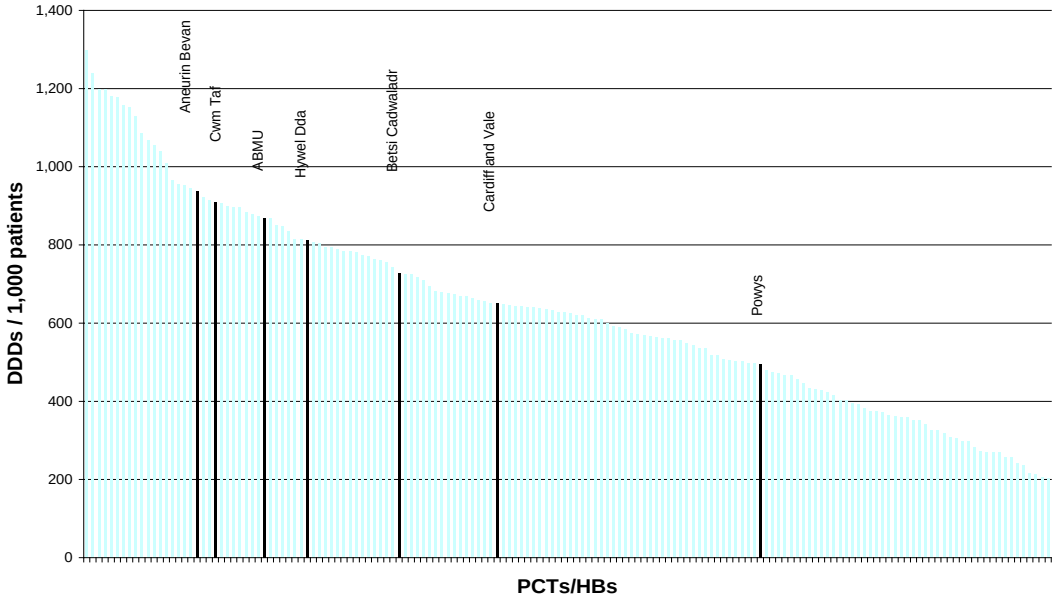


Figure 6 shows tramadol prescribing in Welsh health boards compared with English PCTs for the quarter ending March 2013. The data show that most health boards in Wales sit within the higher end of this chart, and therefore indicate that most Welsh health boards prescribe more tramadol (DDDs per 1,000 patients) than most PCTs in England.

Figure 6. Tramadol prescribing of Welsh health boards compared with English PCTs (DDDs per 1,000 patients). Quarter ending March 2013



4.0 SURVEY RESULTS

Two surveys were designed and conducted to help inform the work to review tramadol prescribing in Wales. The first survey was sent out to all GP practices in Wales and the second was sent to specialist prescribers with an interest in pain management and substance misuse within secondary care in Wales. Both surveys included the questions:

- Do you think tramadol is overprescribed within your practice locality/hospital?
- Are you aware of any work that has been undertaken to review tramadol prescribing in your locality?

These two opening questions were sent to both primary and secondary care prescribers to gain some understanding into how the prescribing of tramadol is perceived by prescribers, and to assess if work had been undertaken anywhere in Wales to review tramadol prescribing. The other questions were tailored to either primary or secondary care and the responses to these questions are detailed below.

4.1 Primary care survey

The primary care survey was sent to all GP practices in Wales, asking practice managers to forward to GPs. There are 483 GP practices in Wales (with around 2,022 GPs in Wales)[16,17] and from these 262 GPs responded and the results are detailed below.

- 62% of GPs felt that tramadol was overprescribed in their locality.
- 85% of GPs were not aware of any work that had been undertaken to review tramadol prescribing in their practice area.
- 53% of GPs perceived there to be a problem with tramadol dependence in their practice locality.
- 50% of GPs had experienced patients obtaining tramadol from sources other than on prescription.
- 61% of GPs were concerned about some of their patients taking more than the prescribed dose of tramadol.
- 89% of GPs had prescribed tramadol for patients as a result of them being discharged from hospital on the medication.
- 81% of GPs had had patients who had experienced an adverse reaction to tramadol.
- 86% of GPs find tramadol a useful analgesic and feel that it has a place in therapy.
- Encouragingly, only 3% of GPs would use tramadol first line for severe pain.

4.2 Secondary care survey

The secondary care survey was sent out to the Chief Pharmacists in each health board, asking for the survey to be forwarded to prescribers in their health board with an interest in pain management or substance misuse. Of these, there were 51 responses and the results are detailed below.

- 33% of prescribers felt that tramadol was overprescribed in their hospital(s).
- 87% of prescribers were not aware of work that had been undertaken to review tramadol prescribing.
- 41% of prescribers had seen cases of patients being dependent on tramadol.
- 79% of prescribers said that tramadol featured in their local pain guidelines.
- 23% of prescribers said that their hospital(s) used pre-packed tramadol.
- Prescribers thought that the use of a national audit, educational slide sets, information bulletins and patient information leaflets would be useful to support the appropriate prescribing of tramadol within their hospitals.

Survey results informed the development of audits for primary and secondary care, information bulletins, educational slide sets and patient information leaflets.

5.0 USEFUL RESOURCES

- NHS Wales Clinical Effectiveness Prescribing Programme Local Comparators 2013–2014 (a copy can be requested from Health Board Medicines Management teams)
- NICE CG88: Low back pain (http://www.nice.org.uk/cg88)
- NICE CG96: Neuropathic pain – pharmacological management (http://www.nice.org.uk/cg96)
- The British Pain Society – Opioids in persistent pain – Good practice (http://www.britishpainsociety.org/book_opioid_main.pdf)
- Management of acute low back pain (http://www.wemerec.org/Documents/Bulletins/BacksBulletinOnlineOPT.pdf)
- Welsh Backs website (http://www.welshbacks.com/)
- Brief Pain Inventory (http://www.npcrc.org/usr_doc/adhoc/painsymptom/briefpain_short.pdf)
- Yellow Card Centre Wales – offers education and training sessions on suspected adverse drug reactions to all healthcare professionals and patient groups (http://www.yellowcardwales.org/)

SECTION 1 – PRIMARY CARE TRAMADOL AUDIT

Purpose of the audit

- To promote the safe and appropriate prescribing of tramadol for moderate to severe pain in both acute pain and chronic pain management 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 patients initiated on tramadol are reviewed at 3 months 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.

Good practice points

- Refer to local pain guidelines where appropriate.
- Treatment should be short and intermittent.
- Use only for moderate and severe pain.
- Maximum dose should not exceed 400 mg in 24 hours.
- Patients initiated on tramadol should be put onto an acute prescription and reviewed at 3 months to discourage long-term use for patients with acute pain. After 3 months, there is evidence to suggest that the pain is no longer acute and has become a chronic condition[18]. If tramadol is judged to be appropriate by the prescriber as part of a pain management plan and there are no other contra-indications 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.
- 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)
  - patients with a history of addiction or dependence
  - patients with a history of depression
  - 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.
- 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.

NOTES ON SAFETY

Dosing in renal impairment

Tramadol and its metabolites are almost completely excreted via the kidneys. For elderly patients and patients with renal impairment, the half-life is extended and there is reduced elimination. Where 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[19]

It should also be noted that there are differences between absolute GFR, estimated GFR (eGFR), and creatinine clearance (CrCl). eGFR is not validated for use in acute illness, the very elderly, extremes of body mass index, amputees and pregnancy. For more detailed advice on clinical importance and management, see BNF[5], Renal Drug Handbook[19] 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 stepping down or stopping tramadol

Avoid abrupt withdrawal after long-term treatment[5]. 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[1,6]. For patients taking regular tramadol, or those who may be dependent on tramadol, a careful approach is required. If it is appropriate for a patient's tramadol to be stepped down or stopped, it is important to note that the dose must be reduced slowly to ensure the patient's safety and to minimise the risk of withdrawal symptoms and/or adverse reactions.

To encourage patient engagement and concordance, a suggested approach would be to reduce the dose at each reduction step, e.g. by one 50 mg dose, and to titrate by how the patient manages, rather than by setting time limits for the next reduction. Every patient and their circumstances will be different, and a prudent and individually tailored approach is required.

If there are issues with chronic pain or dependence on tramadol, referral to a specialist service 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 as per WHO pain ladder before being prescribed tramadol	Unless contraindicated
4. Other regular opioids are not prescribed alongside tramadol	None
5. Interacting drugs are not prescribed alongside tramadol unless there are compelling reasons to do so	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 drug dependence or addiction, unless there are compelling reasons to do so	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
For acute pain/short-term tramadol patients	
8. All patients initiated on tramadol are initially put onto acute prescriptions and are reviewed at 3 months	None
For chronic pain/long-term tramadol patients	
9. All patients on regular tramadol prescriptions are reviewed at least every 12 months	None
10. No patients request or receive interim prescriptions or acute prescriptions more frequently than the normal duration of the prescription	Dependent on prescriber's assessment of patient and their condition
11. No patients prescribed tramadol on acute prescriptions for chronic pain collect a prescription every month. (For most chronic pain patients collecting an acute tramadol prescription every month, a repeat prescription may be more appropriate)	Dependent on prescriber's assessment of patient and their condition

Method

For the purposes of the audit, the data collection has been split into two sections. The first deals with patients who have been taking tramadol for a relatively short amount of time (less than 12 months), and these patients may fall into an acute pain group or may be patients for whom pain has recently become chronic. The second focuses on 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. 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® in your search. Tramadol is the generic term; please see below for a list of brand names.

Tramadol brand names	
Larapam® SR	Zamadol®
Mabron®	Zamadol® 24hr
Marol®	Zamadol® SR
Maxitram SR®	Zeridame® SR
Tradorec XL®	Zydol®
Tramacet®	Zydol® SR
Tramquel® SR	Zydol XL®
Ultram	

- 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 new 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 **EXCLUDE**:

- Patients who have received tramadol prescriptions for longer than 12 months
- Patients who have been newly started on tramadol within the last 3 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
Patients prescribed the first prescription of tramadol should be given as an acute prescription.

(D) Indication
Tramadol is licensed for moderate to severe pain; a clear indication for which tramadol was initiated should be clearly documented in the patient's record.

(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 the purposes of data collection it may be easier to see whether the patient was seen by a GP or had a phone call from a GP at this point. Although it may not be documented in the notes that this was specifically for the review of tramadol, it could be assumed that the tramadol was reviewed in relation to the reason for which it had been initially prescribed. 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 then be added to the patient's repeat and that the medication is 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, e.g. '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 according to the pain ladder
Tramadol should only be prescribed if first-line opioids (e.g. codeine, co-codamol) are not appropriate and/or not tolerated.

Patients at all stages of the WHO ladder should be prescribed paracetamol and/or an NSAID unless contraindicated.

(I) Other opioids
Other regular opioids should not be prescribed alongside tramadol as this may increase the risk of patients experiencing side effects.

(J) Interacting medication
Other medication prescribed that interacts with tramadol, e.g. warfarin, SSRIs, TCAs, MAOIs, mirtazapine, venlafaxine, anti-psychotics, epilepsy medication and other 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 addiction or dependence
Please indicate whether the patient had a history of drug dependence or addiction, including over the counter and prescription medication, as well as alcohol and illicit substances.

(L), (M) and (N) Relevant co-morbidities
For the purposes of this audit, other relevant co-morbidities include epilepsy or history of depression, fits 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 according to the pain ladder (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 addiction or dependence (Y/N)? (K)					
History of depression (Y/N)? (L)					
History of epilepsy/seizures (Y/N)? (M)					
Is the dose appropriate according to the patient's renal function as per GFR (Y/N)? (N)					
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 (Y/N)?			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 previous analgesia as per pain ladder 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 addiction or dependence			0%
(L) Number of patients with history of depression			0%
(M) Number of patients with history of epilepsy/seizures			0%
(N) 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 less 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 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 patients initial supply of tramadol should be as an acute prescription, as ideally treatment should be short and intermittent. However, for patients who have been reviewed and are being prescribed tramadol for chronic pain, where a prescription is being collected every month it **may** be more appropriate to put this onto repeat prescription. All patients on tramadol for chronic pain should be reviewed at least every 12 months.

(D) Indication
Tramadol is licensed for moderate to severe pain; a clear indication for which tramadol was initiated should be clearly documented in the patient's record.

(E) Extra or interim prescriptions
It should be clear from the patient record history 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 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, e.g. '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 tramadol for chronic pain should be reviewed regularly. Questions to consider are:

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

Please note: withdrawal from tramadol may be dangerous. See notes on safety and refer to specialist advice where appropriate.

(I) Previous analgesia prescribed according to the pain ladder
Tramadol should only be prescribed if first-line opioids (e.g. codeine, co-codamol) are not appropriate or tolerated. Patients at all stages of the WHO ladder should be prescribed paracetamol and/or an NSAID unless contraindicated.

(J) Other opioids
Other regular opioids should not be prescribed alongside tramadol as this may increase the risk of patients experiencing adverse effects or side effects.

(K) Interacting medication
Other medication prescribed that interacts with tramadol, e.g. warfarin, SSRIs, TCAs, MAOIs, mirtazapine, venlafaxine, anti-psychotics, epilepsy medication and other 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 addiction or dependence
Please indicate whether the patient had a history of drug dependence or addiction, including over the counter and prescription medication, as well as alcohol and illicit substances.

(M), (N) and (O) Relevant co-morbidities
For the purposes of this audit, other relevant co-morbidities include epilepsy or history of fits, depression 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 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					
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 there been any requests for extra or interim prescriptions (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 according to the pain ladder (Y/N)? (I)					
Patient prescribed other regular opioid alongside tramadol (Y/N)? (J)					
Patient co-prescribed interacting medication (Y/N)? (If yes, please specify) **(K)**					
History of addiction or dependence (Y/N)? (L)					
History of depression (Y/N)? (M)					
History of epilepsy/seizures (Y/N)? (N)					
Is the dose appropriate according to the patient's renal function as per GFR (Y/N)? (O)					
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 requesting 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 previous analgesia as per pain ladder 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 addiction or dependence			0%
(M) Number of patients with history of depression			0%
(N) Number of patients with history of epilepsy/seizures			0%
(O) Number of patients where the dose is appropriate according to GFR			100%

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)

SECTION 2 – SECONDARY CARE TRAMADOL AUDIT

Purpose

- To promote the safe and appropriate prescribing of tramadol for moderate to severe pain 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 determine the appropriateness of tramadol prescribing on discharge prescriptions in secondary care.
- 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 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, as per WHO analgesic ladder.
- Patients discharged on tramadol are given only a short supply, and a discontinuation or review date is 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 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 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
- 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 on-line at www.mhra.gov.uk.

NOTES ON SAFETY

Dosing in renal impairment

Tramadol and its metabolites are almost completely excreted via the kidneys. For elderly patients and patients with renal impairment, the half-life is extended and there is reduced elimination. Where 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[19]

It should also be noted that there are differences between absolute GFR, estimated GFR (eGFR), and creatinine clearance (CrCl). eGFR is not validated for use in acute illness, the very elderly, extremes of body mass index, amputees and pregnancy. For more detailed advice on clinical importance and management, see BNF[5], Renal Drug Handbook[19] 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 stepping down or stopping tramadol

Avoid abrupt withdrawal after long-term treatment[5]. 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[1,6]. For patients taking regular tramadol, or those who may be dependent on tramadol, a careful approach is required. If it is appropriate for a patient's tramadol to be stepped down or stopped, it is important to note that the dose must be reduced slowly to ensure the patient's safety and to minimise the risk of withdrawal symptoms and/or adverse reactions.

To encourage patient engagement and concordance, a suggested approach would be to reduce the dose at each reduction step, e.g. by one 50 mg dose, and to titrate by how the patient manages, rather than by setting time limits for the next reduction. Every patient and their circumstances will be different, and a prudent and individually tailored approach is required.

If there are issues with chronic pain or dependence on tramadol, referral to a specialist service 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 prescribed other regular opioids alongside tramadol	None
3. All patients are also prescribed regular paracetamol as per WHO analgesic ladder	Paracetamol is contraindicated for the patient
4. All patients are also prescribed regular NSAID if appropriate as per WHO analgesic ladder	NSAIDs are contraindicated for the patient
5. All patients admitted on tramadol have a review during admission to assess if it is appropriate to continue with treatment	None
6. All patients are initiated on tramadol only if first-line weak opioids are not suitable	Contraindications to other first-line opioids
7. The daily dose of tramadol does not exceed 400 mg in 24 hours	None
8. Patients are not co-prescribed interacting medicines	Unless the clinical benefits outweigh the risks and patients are monitored accordingly
9. Tramadol is not initiated where there is a history of addiction or dependence	Unless the clinical benefits outweigh the risks and patients are monitored accordingly
10. Tramadol is not initiated where there is a history of depression	Unless the clinical benefits outweigh the risks and patients are monitored accordingly
11. Tramadol is not initiated where there is a history of epilepsy	Unless the clinical benefits outweigh the risks and patients are monitored accordingly
12. All patients are dosed appropriately according to their renal function	None
Discharge prescriptions	
13. 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
14. 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 appropriate and clearly recorded?			
2	Is the patient co-prescribed another regular opioid? If yes, state which.			
3	Is the patient co-prescribed paracetamol as per WHO analgesic ladder?			
4	Is the patient co-prescribed an NSAID if appropriate as per WHO analgesic ladder?			
5	Was the patient taking tramadol prior to admission?			
6	Was tramadol prescribed first line? If yes, were there any contraindications to other first-line opioids such as codeine?			
7	Does the daily dose of tramadol exceed 400 mg in 24 hours or is the maximum dose ambiguous?			
8	Is the patient co-prescribed an interacting medicine?			
9	Does the patient have a history of addiction or dependence?			
10	Does the patient have a history of depression?			
11	Does the patient have a history of epilepsy or seizures?			
12	Is the dose appropriate according to the patient's renal function as per GFR?			
13	**Questions relating to discharge prescriptions only**			
13a	Is there a discontinuation date or review date for tramadol clearly indicated on discharge prescription?			
13b	Does the duration of tramadol prescribed exceed one week?			

SECTION 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 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.

GENERAL NOTES ON SAFETY WITH REGARD TO TRAMADOL PRESCRIBING

Dosing in renal impairment

Tramadol and its metabolites are almost completely excreted via the kidneys. For elderly patients and patients with renal impairment, the half-life is extended and there is reduced elimination. Where 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[19]

It should also be noted that there are differences between absolute GFR, estimated GFR (eGFR), and creatinine clearance (CrCl). eGFR is not validated for use in acute illness, the very elderly, extremes of body mass index, amputees and pregnancy. For more detailed advice on clinical importance and management, see BNF[5], Renal Drug Handbook[19] 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 stepping down or stopping tramadol

Avoid abrupt withdrawal after long-term treatment[5]. 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[1,6]. For patients taking regular tramadol, or those who may be

dependent on tramadol, a careful approach is required. If it is appropriate for a patient's tramadol to be stepped down or stopped, it is important to note that the dose must be reduced slowly to ensure the patient's safety and to minimise the risk of withdrawal symptoms and/or adverse reactions.

To encourage patient engagement and concordance, a suggested approach would be to reduce the dose at each reduction step, e.g. by one 50 mg dose, and to titrate by how the patient manages, rather than by setting time limits for the next reduction. Every patient and their circumstances will be different, and a prudent and individually tailored approach is required.

If there are issues with chronic pain or dependence on tramadol, referral to a specialist service 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

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