All Wales Medicines Strategy Group

Grŵp Strategaeth Meddyginiaethau Cymru Gyfan

National Prescribing Indicators 2020–2021

Supporting Safe and Optimised Prescribing

February 2020

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This document has 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).

Please direct any queries to AWTTC:

All Wales Therapeutics and Toxicology Centre
University Hospital Llandough
Penlan Road
Llandough
Vale of Glamorgan
CF64 2XX

awttc@wales.nhs.uk
029 2182 6900

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INTRODUCTION

Prescribing indicators are used to highlight therapeutic priorities for NHS Wales and compare the ways in which different prescribers and organisations use particular medicines or groups of medicines. Prescribing indicators should be evidence-based, clear, easily understood and allow health boards, primary care clusters, GP practices and prescribers to compare current practice against an agreed standard of quality. Ideally they should be validated by a group of experts, and should recommend the direction that prescribing should move, even if it is not possible to specify an exact value that represents 'good practice'. They should usually be standardised to allow comparison between health boards, primary care clusters, or practices serving different sized populations. Weighting can also consider the age and demographics of the population.

In October 2003, the All Wales Medicines Strategy Group (AWMSG) agreed that National Prescribing Indicators (NPIs) were useful tools to promote rational prescribing across NHS Wales, and since then, NPIs have evolved to include secondary care in addition to primary care. It was agreed that NPIs should address efficiency as well as quality and that targets should be challenging but achievable, and applicable at practice level. In order to undertake monitoring, the NPIs for 2020–2021 draw on a variety of data sources such as CASPACluster, Medusa, Audit+ and the Medicines and Healthcare products Regulatory Agency (MHRA).

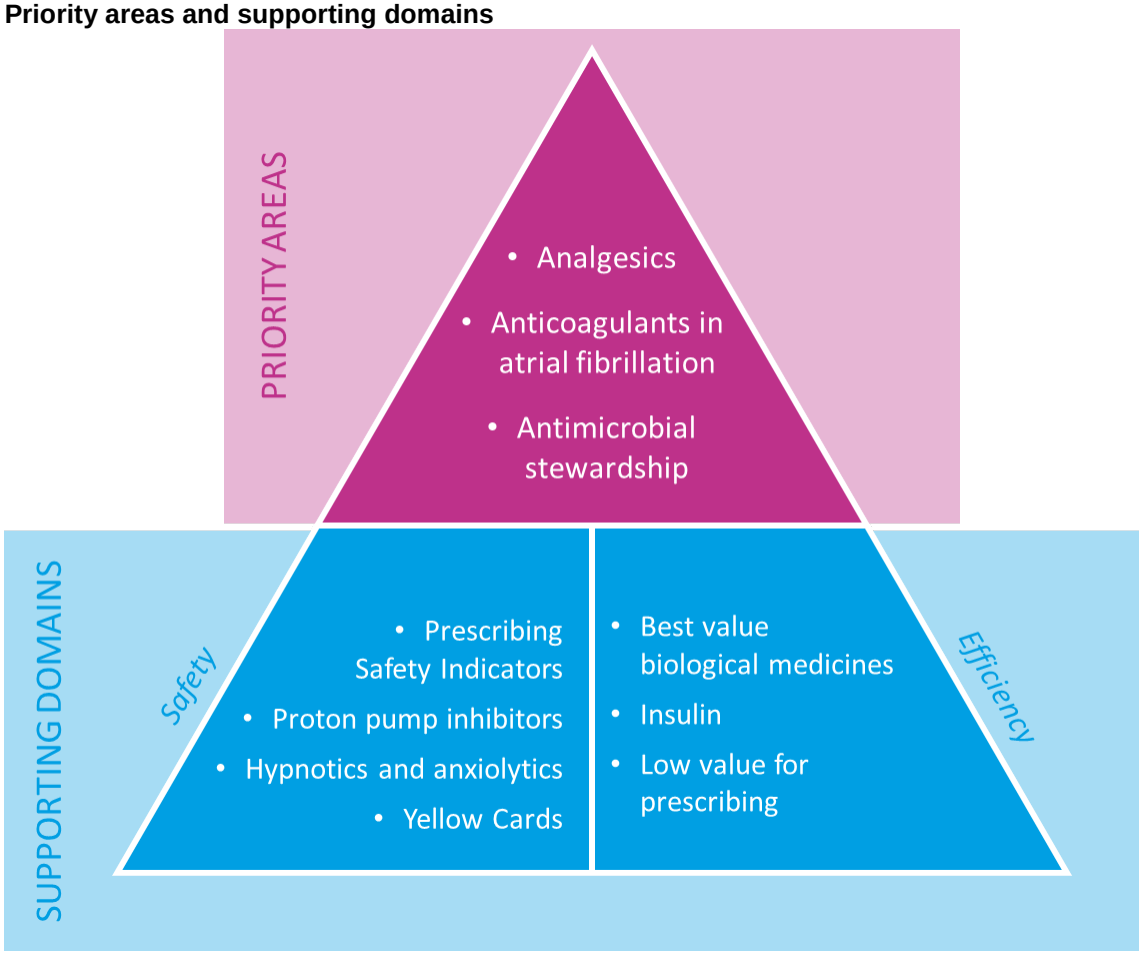
Key changes for 2020-2021

For 2020-2021 the National Prescribing Indicators: Supporting Safe and Optimised Prescribing, have been refreshed with a focus on three priority areas, supported by safety and efficiency domains as shown in Figure 1. The refresh continues with the philosophy of Prudent Healthcare, enabling higher quality and value through reducing variation, waste and harm, in addition to contributing to two themes in the Quadruple Aim of *A Healthier Wales*, Welsh Government's plan for health and social care[1], namely:

- Population health and wellbeing – better prevention and self-management
- Higher value health and social care – rapid improvement and innovation, enabled by data, focussed on outcomes.

This signifies a move towards a more patient-focussed approach, with measures considering whether the right patients are getting the right medicines and whether these medicines are making a difference to their outcomes, as recommended in the 2016 Wales Audit Office report[2].

Figure 1. National Prescribing Indicators: Supporting Safe and Optimised Prescribing – Priority areas and supporting domains



There are a number of measures within each of the priority and supporting areas, the background and evidence for which are included within this document, together with reporting methods and data source.

Method used to review and update NPIs

An NPI Task and Finish Group of the All Wales Prescribing Advisory Group (AWPAG) was established to review the 2019–2020 NPIs and discuss potential changes for 2020–2021.

Prior to the NPI Task and Finish Group meeting, a questionnaire was sent to health board medicines management teams, prescribing leads, GPs, cluster pharmacists, secondary care prescribers and pharmacists, and Medicines and Therapeutics Committees. This asked for comment on the continued relevance of the 2019–2020 NPIs and additional priority areas that may be appropriate to monitor and provide feedback on the NPI document, *Supporting Information for Prescribers and Healthcare Professionals* resource, and NPI slide set. This information then fed into the discussions of the NPI Task and Finish Group.

Measures

ADQ: The average daily quantity (ADQ) is a measure of prescribing volume based upon prescribing behaviour in England. It represents the assumed average maintenance dose per day for a medicine used for its main indication in adults. ADQ is not a recommended dose but an analytical unit to compare prescribing activity.

DDD: 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.

PU: Prescribing units (PUs) were adopted to take account of the greater need of elderly patients for medication in reporting prescribing performance in primary care. Patients aged 65 years and over are counted as three prescribing units; patients under 65 years and temporary residents are counted as one.

STAR-PU: Specific therapeutic group age–sex related prescribing units (STAR-PUs) are designed to measure prescribing weighted for age and sex of patients. There are differences in the age and sex of patients for whom medicines in specific therapeutic groups are usually prescribed. To make such comparisons, STAR-PUs have been developed based on costs of prescribing or items within therapeutic groups.

- Where possible, measures used should be accessible to all medicines management teams through CASPACluster, SPIRA, Audit+ or Medusa.
- The ADQ and STAR-PU measurements are used for certain indicators instead of the DDD measurement and PU weighting in order to benchmark with the 'Medicines optimisation: key therapeutic topics' (MO KTT) comparators in England. ADQ measurements are available on CASPACluster and STAR-PU measurements are updated on a quarterly basis by the NHS Wales Shared Services Partnership (NWSSP): Primary Care Services.
- The NHS Wales Informatics Service (NWIS) will provide Audit+ data on the Prescribing Safety Indicators, which will be accessed by the Welsh Analytical Prescribing Support Unit (WAPSU) at a health board and cluster level.
- The MHRA will provide data on Yellow Card reporting which will be analysed by WAPSU.
- Secondary care medicines data will be supplied by NWIS through the Medusa data warehouse.
- Where data are provided by external sources, WAPSU cannot be held accountable for errors in data provided or delay in provision of data.
- An NPI specification document detailing drug baskets used will be available on the awttc.org website.

Targets

- Details of NPI targets are listed in Tables 1 and 2.
- NPI targets should be challenging but achievable and, unless otherwise stated, based on the principle of encouraging all health boards, local cluster groups and practices to achieve prescribing rates in the best quartile. In these instances, the target is therefore not an absolute value and can be achieved if there is movement towards the threshold set.
  - For primary care NPIs with a threshold, this will normally be set at the 75th percentile (i.e. the prescribing rate of the best performing 25% of practices), for the quarter ending 31st December 2019.
  - Unless otherwise stated, the primary care thresholds are based on prescribing data for all general practices in Wales.

Tables 1 and 2 detail the 'priority area' and 'supporting domain' NPIs for 2020–2021 respectively, with units of measure and targets where applicable.

Evidence

The evidence, prescribing data (where available), and supporting prescribing messages are outlined in the body of the document.

Table 1 Priority area NPIs for 2020–2021

National Prescribing Indicator	Applicable to:	Unit of measure	Target for 2020–2021	Data source
Priority areas				
Analgesics	Primary care	Opioid burden user defined group (UDG) ADQs per 1,000 patients	Maintain performance levels within the lower quartile, or show a reduction towards the quartile below.	NWSSP
		Tramadol DDDs per 1,000 patients	Maintain performance levels within the lower quartile, or show a reduction towards the quartile below.	NWSSP
		Gabapentin and pregabalin DDDs per 1,000 patients	Maintain performance levels within the lower quartile, or show a reduction towards the quartile below.	NWSSP
Anticoagulants in atrial fibrillation	Primary care	The number of patients with AF and a CHA_2DS_2-VAS_C score of 2 or more who are currently prescribed an anticoagulant, as a percentage of all patients with AF.	To increase the number of patients with AF and a CHA_2DS_2-VAS_C score of 2 or more prescribed an anticoagulant.	NWIS
		The number of patients diagnosed with AF who are prescribed an anticoagulant and have received an anticoagulant review within the last 12 months, as a percentage of all patients diagnosed with AF who are prescribed an anticoagulant.	To increase the number of patients who are prescribed an anticoagulant and have received an anticoagulant review within the last 12 months.	
		The number of patients diagnosed with AF who are prescribed antiplatelet monotherapy, as a percentage of all patients diagnosed with AF.	To reduce the number of patients with AF prescribed antiplatelet monotherapy.	
Antimicrobial stewardship	Primary care	Total antibacterial items per 1,000 STAR-PUs	Health board target: a quarterly reduction of 5% against a baseline of April 2018–March 2019. GP Practice target: Maintain performance levels within the lower quartile, or show a reduction towards the quartile below.	NWSSP
		Number of 4C antimicrobial (co-amoxiclav, cephalosporins, fluoroquinolones and clindamycin) items per 1,000 patients	Health board target: A quarterly reduction of 10% against a baseline of April 2018–March 2019. GP Practice target: Maintain performance levels within the lower quartile, or show a reduction towards the quartile below.	NWSSP

Table 2. Supporting domain NPIs 2020–2021

National Prescribing Indicator	Applicable to:	Unit of measure	Target for 2020–2021	Data source
Supporting Domain: Safety				
Prescribing Safety Indicators	Primary care	Number of patients identified	No target set	NWIS
Proton pump inhibitors	Primary care	PPI DDDs per 1,000 PUs	Maintain performance levels within the lower quartile, or show a reduction towards the quartile below	NWSSP
Hypnotics and anxiolytics	Primary care	Hypnotic and anxiolytic UDG ADQs per 1,000 STAR-PUs	Maintain performance levels within the lower quartile, or show a reduction towards the quartile below	NWSSP
Yellow Cards	Primary care	Number of Yellow Cards submitted	One Yellow Card per 2,000 GP practice population	MHRA
	Health board		One Yellow Card per 2,000 health board population 20% or greater increase from baseline (2019–2020) for Yellow Cards submitted by secondary care 50% or greater increase from baseline (2019–2020) for Yellow Cards submitted by members of the public	
	Community pharmacy		No target set. Reported as the number of Yellow Cards submitted by health board	
Supporting Domain: Efficiency				
Best value biological medicines	Primary + secondary care	Quantity of best value biological medicines prescribed as a percentage of total 'biosimilar' plus 'reference' product.	Increase the appropriate use of cost-efficient biological medicines, including biosimilar medicines	NWSSP NWIS
Insulin	Primary + secondary care	Items/number of long-acting insulin analogues as a percentage of total long- and intermediate-acting insulin prescribed	Reduce prescribing of long-acting insulin analogues and achieve prescribing levels below the Welsh average	NWSSP NWIS
Low value for prescribing	Primary care	Low value for prescribing UDG spend per 1,000 patients	Maintain performance levels within the lower quartile or show a reduction towards the quartile below	NWSSP

Please note:
Implementation of the recommended NPIs does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer. This is supported by the prudent healthcare agenda, which encourages the creation of a prescribing partnership where the process of prescribing, dispensing and administering medicines puts the patient at its centre and encourages shared decision making[3].

1.0 PRIORITY AREAS

1.1 ANALGESICS

Analgesics are medicines used in the treatment of pain, which can be defined as acute or persistent, depending on the length of time the person has experienced pain. Persistent, also known as chronic, pain is usually defined as occurring when pain has been present for three months or more[4]. Analgesic medicines have been the mainstay of pain treatment for decades; however, for persistent pain, individual response rates to analgesics vary greatly and failure rates are high[5]. A number of analgesic medicines with different mechanisms of action and licensed indications are available; however, these NPIs focus on total opioid use, tramadol, and gabapentin and pregabalin, as concerns have been raised regarding the appropriate use and review of these medicines, in addition to the potential for dependence, diversion and misuse.

There is increasing evidence that many analgesics, including opioids, gabapentin and pregabalin, have the potential for harm and abuse. Cases of dependency have been described and there are reports of an increasing street value and risk of drug misuse[6]. Patients should be given information on the potential benefits of their medicine, and its risks and reported side effects, including the potential for such medicines to lead to abuse or dependence[6]. In September 2019, due to the growing problem of dependence and addiction to prescription medicines, Public Health England published a review of the evidence for dependence on and withdrawal from prescribed medicines, which included opioids and gabapentinoids. The review made a number of recommendations, including: increasing the availability and use of data on the prescribing of medicines that can cause dependence or withdrawal to support greater transparency and accountability and help ensure practice is consistent and in line with guidance; and improving information for patients on prescribed medicines and other treatments, and increasing informed choice and shared decision making between clinicians and patients[7]. It is anticipated that this priority area will support these recommendations.

1.1.1 Opioid burden

***Purpose*:**
To encourage the appropriate use and review of opioids in primary care, minimising the potential for dependence, diversion, misuse and ADRs.
Unit of measure:
Opioid burden UDG ADQs per 1,000 patients.
Target for 2020–2021:
Maintain performance levels within lower quartile, or show a reduction towards the quartile below.

Note
Monitoring of trends in total analgesic prescribing and other analgesics should be undertaken alongside these NPIs in order to assess the overall picture of analgesia prescribing in Wales.

Figure 2. Trend in opioid burden ADQs per 1,000 patients to quarter ending September 2019

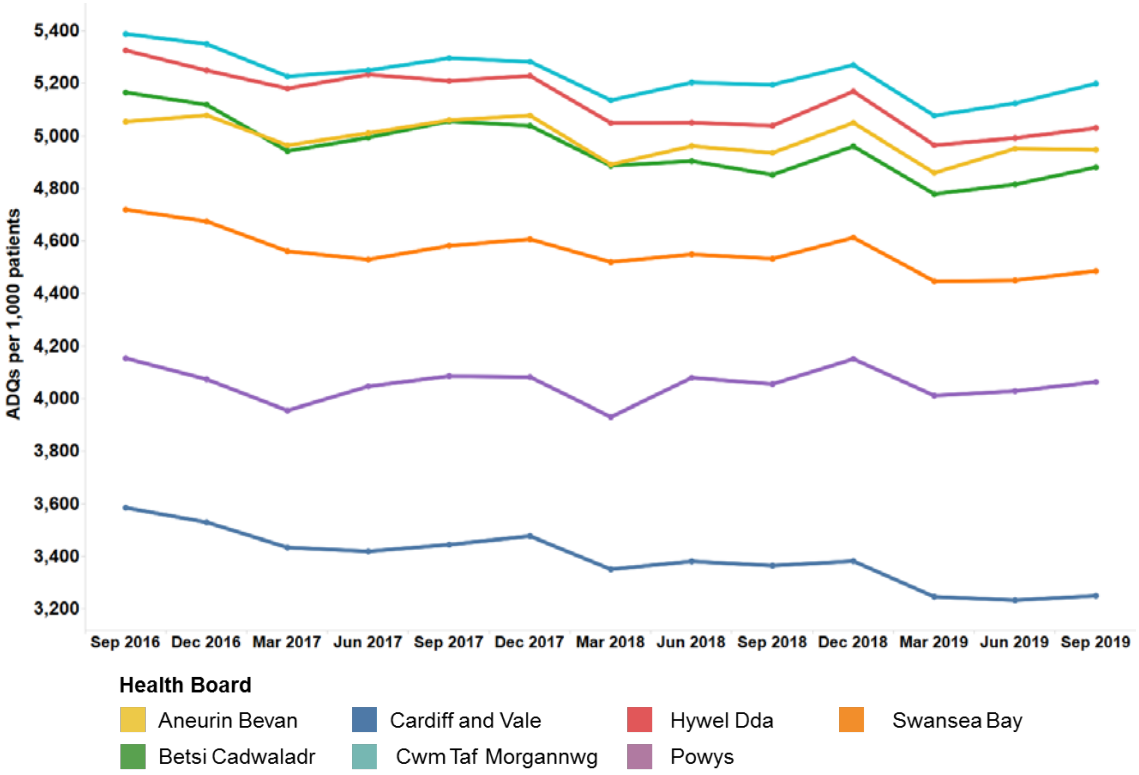
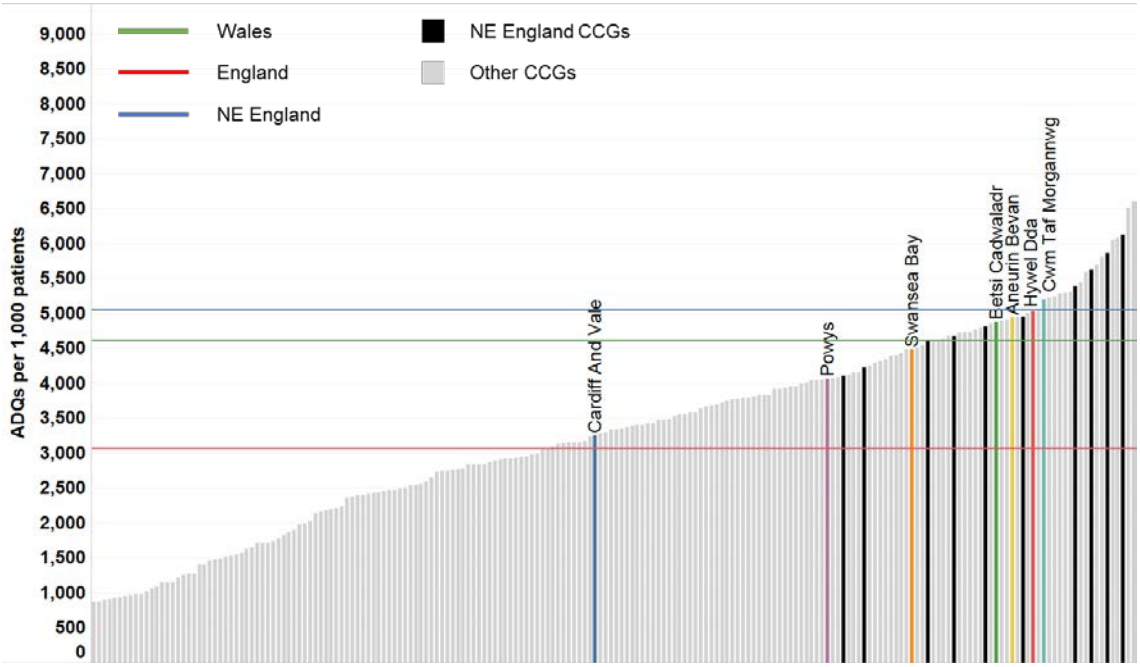


Figure 3. Opioid burden ADQs per 1,000 patients Welsh health boards and English CCGs – Quarter ending September 2019



Background and evidence

Opioid analgesics have long been used as the gold standard to treat severe pain, most notably for acute pain and in palliative care[8]. The WHO analgesic ladder, which advocates a stepwise approach from non-opioid analgesics to opioids for mild to moderate pain, followed by opioids for moderate to severe pain, was developed with the aim of helping patients with cancer achieve freedom from pain[9].

There is a lack of consistent good-quality evidence to support strong clinical recommendation for the long-term use of opioids for patients with chronic pain[10]. Often, the WHO's analgesic ladder is used as a guide to the treatment of chronic pain, resulting in patients receiving increasing doses of strong opioids; however, it has never been validated in this setting[10], and this simple approach is not appropriate for chronic pain, which is highly complex[11].

An estimated 49% of patients in the UK suffering from chronic pain also suffer from depression[10], and there is variable interplay between biological, psychological and social factors[12]. With so many issues affecting the patient's experience and reporting of chronic pain, it is not surprising that pain scores do not respond in any predictable fashion to opioids. Attempts to lower pain scores using opioids have led to overuse and adverse outcomes without any appreciable lowering of the chronic pain burden at the population level[11].

Opioid analgesics have well established side effects including constipation, nausea and vomiting, and respiratory depression, and repeated administration may cause tolerance and dependence[13]. Whilst concerns regarding tolerance and dependence should be no deterrent in the control of pain in terminal illness[13], consideration should be given to this when prescribing for other causes of pain. A systematic review in 2015 suggested that rates of misuse of opioids in patients treated for chronic pain ranged from 21% to 29% and that addiction resulted in between 8% and 12% of patients taking opioids[14].

The Royal College of Anaesthetists Faculty of Pain Medicine highlights that patients who do not achieve useful pain relief from opioids within two to four weeks are unlikely to gain benefit in the long term[15]. A briefing paper by the BMA, *Chronic Pain: supporting safer prescribing of analgesics,* notes that too many people with chronic pain are prescribed opioids at high doses. The dose above which harms outweigh benefits is 120mg oral morphine equivalent in 24 hours. Increasing opioid load above this dose is unlikely to yield further benefits but exposes the patient to increased harm[16]. There is no evidence of efficacy of high-dose opioids in long-term pain[15]. A table providing approximate equivalence values for opioids can be found in Appendix 2.

Despite the lack of evidence for use in chronic non-cancer pain, research in the UK has found an escalation of strong opioid prescribing in primary care, predominantly for non-cancer patients[8]. Across Wales, 1,010,579 prescriptions for opioid analgesics were dispensed during 2007–2008[17]. This increased by 50% over ten years, with more than 1.5 million prescriptions dispensed in 2017–2018[18]. During the same period, opioid related deaths in Wales increased from 96 in 2007 to 164 in 2018, an increase of 71%[19]. Concerns about the harms caused by extensive prescribing of opioids have become particularly pertinent as a result of their extensive misuse in the USA[10], with subsequent increases in prescription opioid deaths and admissions for misuse[11]. A November 2018 briefing statement to health professionals on the management of opioid medications, issued by the Faculty of Pain Medicine of the Royal College of Anaesthetists, highlights that there is professional and governmental concern regarding misuse of prescription medicines and the number of prescriptions of opioid analgesics. Key messages from the briefing statement include the urgent need to screen and assess people on opioids, and to make clinical decisions about opioid reduction and optimal pain management[20].

If benefit in pain reduction and improved function is not achieved at low dose, opioids should be discontinued, even if no other treatment is readily available[10]. In addition, opioids should be tapered or stopped if the underlying painful condition resolves; the patient receives a definite pain relieving intervention (e.g. joint replacement); the patient develops intolerable side effects, or there is strong evidence that the patient is diverting their medication to others[16]. The decision to taper and stop an established opioid regimen needs to be discussed carefully with the patient, and should include an

explanation of the rationale for stopping opioids including the potential benefits of opioid reduction (avoidance of long-term harms and the ability to engage in self-management strategies); agreeing outcomes of opioid tapering; arrangements for monitoring and support during opioid taper; and documented agreement of the tapering schedule. The dose of drug can be tapered by 10% weekly or fortnightly[16].

NICE guidance on *Controlled drugs: safe use and management* highlights that when making decisions about prescribing controlled drugs, consideration should be given to: the benefits of treatment; the risks of prescribing, including dependency, overdose and diversion; all prescribed and non-prescribed medicines the person is taking, and whether the person may be opioid naïve[21]. The Royal College of Anaesthetists Faculty of Pain Medicine has produced a checklist to aid prescribers when discussing opioid treatment with patients[22].

Chronic pain is a complex condition, which has a substantial impact on the lives of those affected. The relief of pain should be seen as a clinical priority, yet the prescribing of opioids is often not the most appropriate or effective treatment option for many patients with chronic pain, and can risk exposing patients to unnecessary harm[10]. If it is thought opioid therapy may play a role in a patient's pain management, a trial should be initiated to establish whether a patient achieves a reduction in pain with the use of opioids – if not they should be stopped. Patients should be fully informed of potential benefits and harms from this trial[10]. Dose escalation should be limited as risk of harm rises as dose increases, especially if there is inadequate relief of pain[10].

This NPI promotes a prudent approach to prescribing opioid analgesics, taking into account the indication, risks and benefits, and encouraging timely review of patients prescribed opioids for chronic pain.

Useful resources

- MHRA Opioids e-learning module
- RCoA Faculty of Pain Medicine (2019) Opioids Aware: Tapering and stopping opioids
- AWMSG (2016) Persistent pain resources
- RCoA Faculty of Pain Medicine (2019) Opioids Aware
- RCoA Faculty of Pain Medicine (2019) Checklist for Prescribers
- WeMeReC (2010) Stopping compound medications containing codeine

1.1.2 Tramadol

***Purpose*:**
To encourage the appropriate use and review of tramadol in primary care, minimising the potential for dependence, diversion, misuse and ADRs.
Unit of measure:
Tramadol DDDs per 1,000 patients.
Target for 2020–2021:
Maintain performance levels within lower quartile, or show a reduction towards the quartile below.

Note
Monitoring of trends in total analgesic prescribing and other analgesics should be undertaken alongside these NPIs in order to assess the overall picture of analgesia prescribing in Wales.

Figure 4. Trend in tramadol DDDs per 1,000 patients to quarter ending September 2019

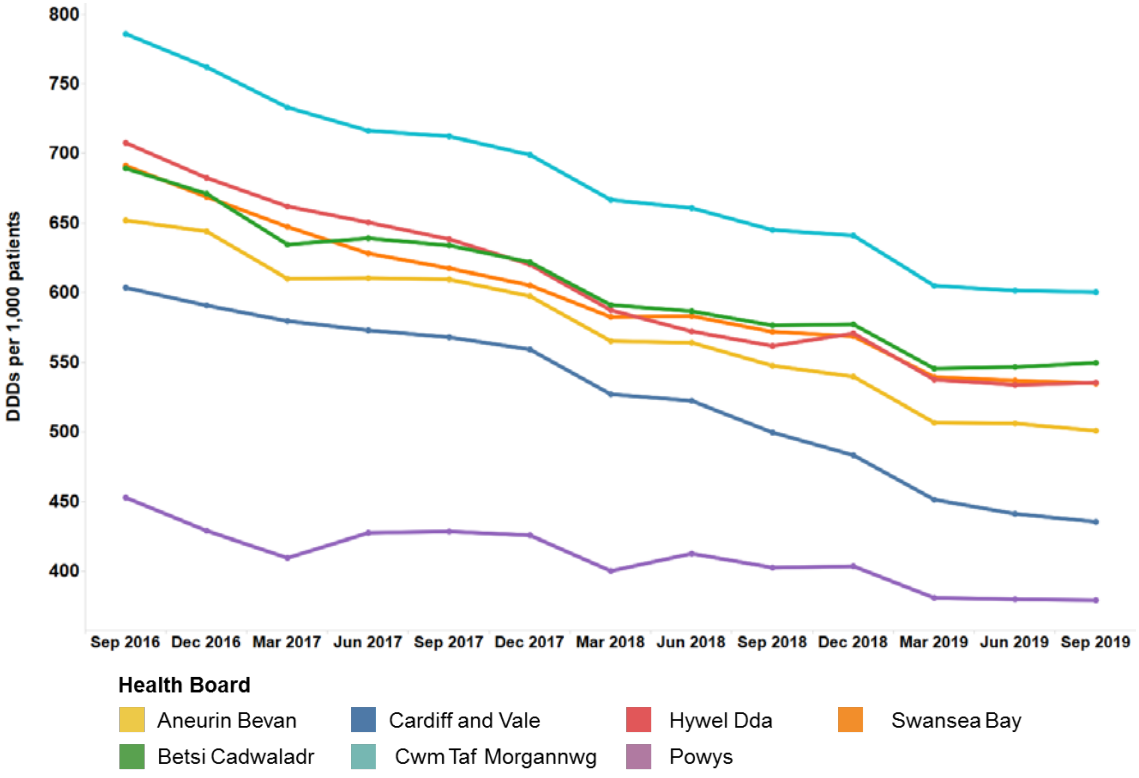
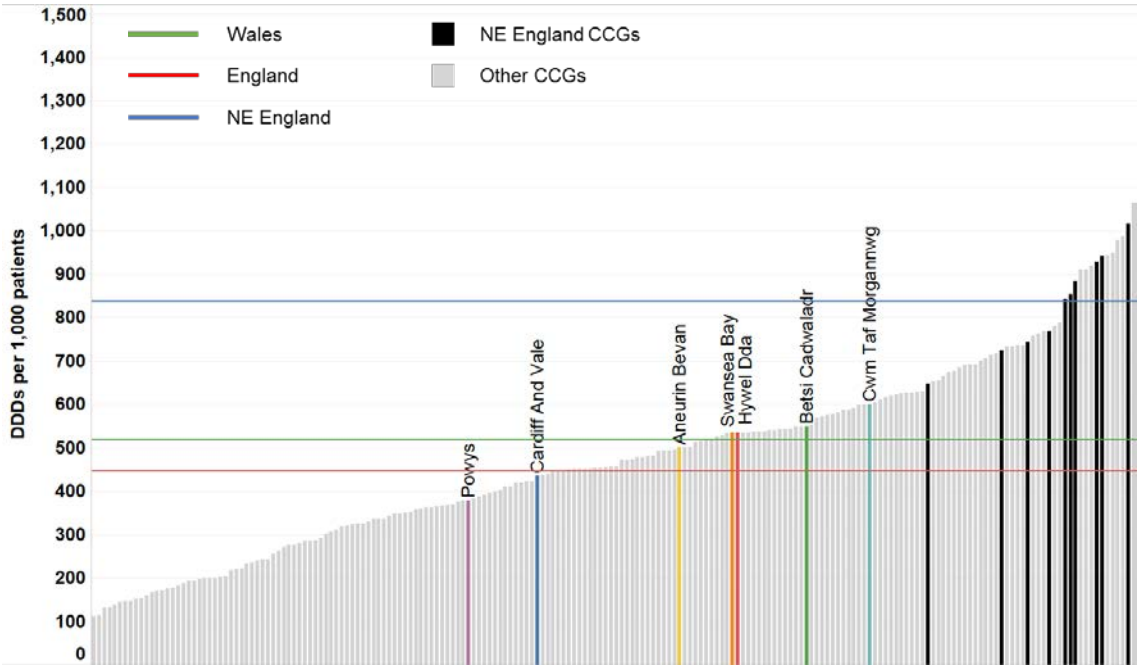


Figure 5. Tramadol DDDs per 1,000 patients Welsh health boards and English CCGs Quarter ending September 2019



Background and evidence

Tramadol is an opioid analgesic licensed for the treatment of moderate to severe pain. Tramadol produces analgesia by two mechanisms: an opioid effect and an enhancement of the serotonergic and adrenergic pathways[13]. It has fewer of the typical opioid side effects (notably, less respiratory depression, less constipation and less addiction potential); psychiatric reactions have been reported[13]. The unique dual-action pharmacological profile of tramadol increases the risk of adverse effects seen in overdose[23].

In 2013, the Advisory Council on the Misuse of Drugs recommended that the UK Government should reclassify tramadol as a class C substance, and place it within Schedule III of the Misuse of Drugs Regulations 2001, due to concerns regarding abuse, dependence and an increasing number of deaths involving tramadol[23]. The changes came into force in June 2014. Despite a fall in deaths involving tramadol in England and Wales over recent years, 2018 saw an increase of 19% compared with the number of deaths in 2017. In Wales, the number of deaths more than doubled, from 6 deaths in 2017 to 14 deaths in 2018[19]. This is a concerning increase and highlights the need for appropriate use and review of tramadol.

Dizziness and nausea are the most commonly reported adverse effects, with headache, drowsiness, vomiting, constipation, dry mouth, fatigue and sweating also frequently reported[24]. Rare adverse effects include hallucinations, confusion, sleep disturbance, anxiety and nightmares, as well as cases of dependence and withdrawal[24]. 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[24]. 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)[24]. 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[24].

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. 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[23,25]. 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 according to 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[26].

This NPI does not measure the prescribing of tramadol and paracetamol combination products as there are no DDDs available; however, these products are included in the *Medicines Identified as Low Priority for Funding in NHS Wales – Paper 2*, due to a lack of advantage over the individual preparations, with prescribing data made available on SPIRA.

While there is a recognised place in pain management for tramadol, concerns regarding the risks associated with misuse and diversion have prompted a review of tramadol prescribing in NHS Wales. It must be noted that pain management is often complex and prescribers need to make evidence-based, informed decisions based on the individual needs of the patient. This NPI promotes a prudent approach to prescribing tramadol, taking into account the risks and benefits of tramadol and encouraging timely review.

Useful resources

- AWMSG (2013) Tramadol Educational Resource Materials
- AWMSG (2013) Tramadol Audit Materials
- AWMSG (2013) Tramadol Shared Decision Making Toolkit
- AWMSG (2013) Tramadol Patient Information Leaflet
- AWMSG (2016) Persistent pain resources

1.1.3 Gabapentin and pregabalin

***Purpose*:**
To encourage the appropriate use and review of gabapentin and pregabalin in primary care, minimising the potential for dependence, diversion, misuse and ADRs.
Unit of measure:
Gabapentin and pregabalin DDDs per 1,000 patients.
Target for 2020–2021:
Maintain performance levels within lower quartile, or show a reduction towards the quartile below.

Note
Monitoring of trends in total analgesic prescribing and other analgesics should be undertaken alongside these NPIs in order to assess the overall picture of analgesia prescribing in Wales.

Figure 6. Trend in gabapentin and pregabalin DDDs per 1,000 patients to quarter ending September 2019

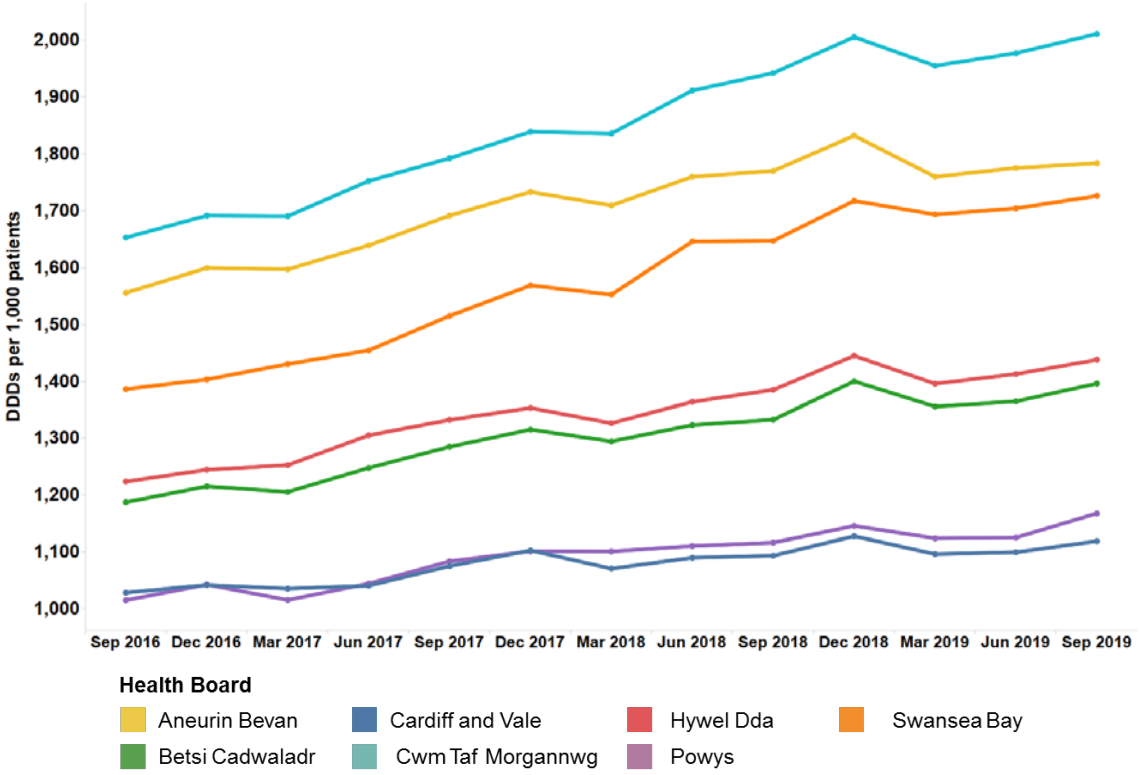
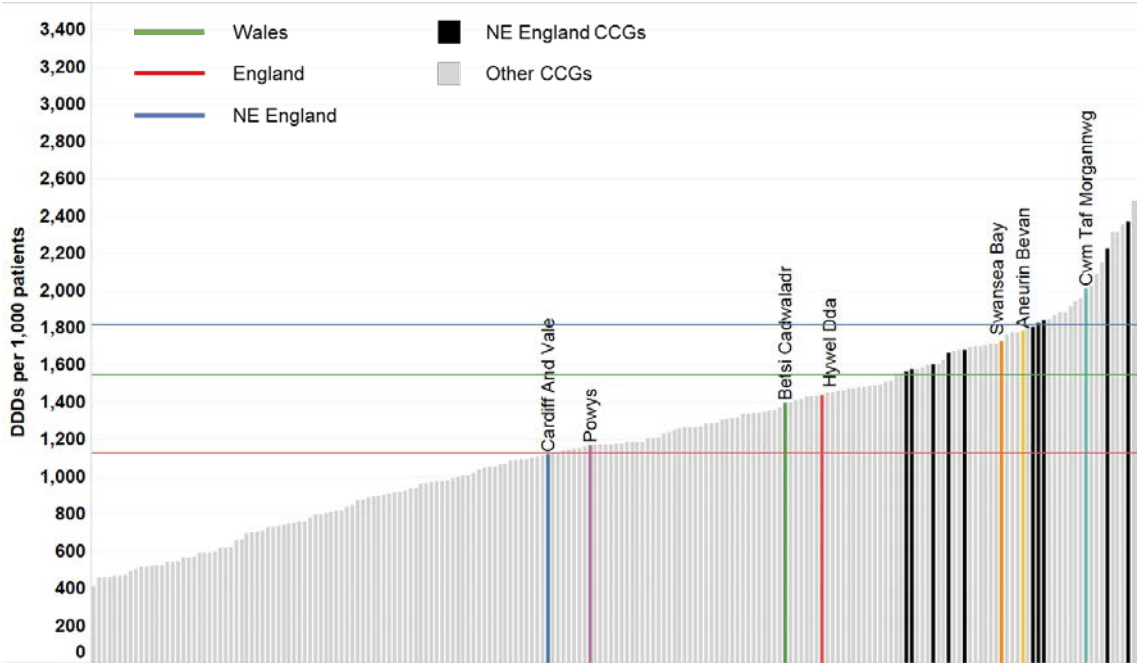


Figure 7. Gabapentin and pregabalin DDDs per 1,000 patients Welsh health boards and English CCGs – Quarter ending September 2019



Background and evidence

NICE recommends gabapentin or pregabalin as first-line options in the treatment of neuropathic pain, along with amitriptyline and duloxetine[27]. Gabapentin is licensed for peripheral neuropathic pain and epilepsy[28-30], whilst pregabalin is licensed for peripheral and central neuropathic pain, in addition to epilepsy and as a third line option for the treatment of generalised anxiety disorder (GAD)[31-34]. In April 2019, gabapentin and pregabalin were reclassified as Schedule 3 controlled drugs in response to recommendations made by the Advisory Council on the Misuse of Drugs, due to concerns regarding the potential risk of dependence, misuse and diversion[35].

There has been increasing use of gabapentin and pregabalin in primary care with prescribing data from the quarter ending June 2019, compared with the quarter ending June 2014, demonstrating an increase of over 65% in prescription items across Wales[18]. Current prescribing of gabapentin and pregabalin in Wales is high in comparison with England, with 1,549 DDDs per 1,000 patients in Wales[18], compared with 1,128 DDDs per 1,000 patients in England[36] for the quarter ending September 2019. During the same period, the number of deaths where gabapentin or pregabalin was mentioned on the death certificate has also increased. The number of deaths has risen from a total of 64 in England and Wales in 2014, to 280 deaths in 2018. In Wales alone, there were a total of 21 deaths in 2018, compared to a total of 2 deaths in 2014[19].

Dependence, diversion and misuse

The Summaries of Product Characteristics (SPCs) for both gabapentin and pregabalin highlight that cases of misuse, abuse and dependence have been reported. Caution should be exercised in prescribing either drug for patients with a history of substance abuse, and patients should be monitored for symptoms of misuse or dependence[28-33]. A Welsh Health Circular in 2016 noted that patients should be made aware of the risk of harms, including dependence[37]. Their mechanism for producing dependence is not yet well understood, though there may be direct or indirect effects on the dopaminergic 'reward' system[38]. An NHS Scotland resource, *Gabapentinoid Prescribing for Chronic Pain in Primary Care*, highlights that there appears to be more evidence of misuse than for dependence[38].

Misuse of gabapentin and pregabalin has been noted for some years in clients attending substance misuse services, and within prisons; currently, pregabalin appears to be more sought after for misuse than gabapentin[37]. Pregabalin may have a higher abuse potential than gabapentin due to its rapid absorption, faster onset of action and higher potency[35]. Pregabalin causes a 'high' or elevated mood in users[35], and individuals misusing gabapentin and pregabalin describe improved sociability, euphoria, relaxation and a sense of calm[39]. Pregabalin misusers achieve these effects by taking large quantities, ranging from 200 mg to 5 g as a single dose[39].

Individuals at risk of misusing or diverting gabapentinoids may include those with a history of substance misuse; patients who make specific requests for initiation of either gabapentin or pregabalin, particularly after release from prison; patients who repeatedly make requests for an early prescription or repeatedly report lost medication, and those who contact out of hours services for supplies of medication[38]. Prescribers must give careful consideration to the individual patient when prescribing gabapentinoids to minimise the risk of misuse, dependence and diversion and assessment of the risks and benefits is essential[38].

In September 2019, Public Health England published an evidence review; *Dependence and withdrawal associated with some prescribed medicines*, which noted that gabapentinoids have come to be used for a wider range of indications than is supported by the evidence or their licensing, and they have sometimes been prescribed in place of opioids or benzodiazepines in the likely-mistaken belief that they are less liable to misuse or dependence, and lack of awareness of the withdrawal problems that can arise when prescribing is stopped[7]. This is concerning given the increase in number of deaths associated with gabapentin and pregabalin, and highlights the importance of appropriate initiation, review, and tapering and stopping of medication where the patient is not benefitting or there are concerns regarding misuse or diversion.

With prevalence of neuropathic pain estimated to be between 7% and 10%[40], estimated prevalence of GAD estimated to be 5.9%[41] and prevalence of epilepsy at 1.0%[42], it is likely that the majority of gabapentin and pregabalin prescribed is for neuropathic pain, however the same considerations regarding the potential for dependence, misuse and diversion apply when prescribing for patients with GAD, and The Advisory Council on the Misuse of Drugs issued advice to prescribers in 2016 noting the importance of appropriate prescribing to minimise these risks[35].

Neuropathic pain

Neuropathic pain can be defined as pain that arises as a direct consequence of a lesion or diseases affecting the somatosensory nervous system[43], and can be very challenging to manage with only a minority of people experiencing a clinically relevant benefit from any one intervention[40].

Before initiating any treatment for neuropathic pain, it is good practice to assess the type, severity and impact of pain to guide management and gauge its success, and there are brief and well-validated tools available for use in non-specialist settings[44]. Tools to aid assessment of neuropathic pain include the Leeds assessment of neuropathic symptoms and signs (LANSS)[45] and the Pain Detect pain questionnaire[46].

No single drug works for all neuropathic pain, and given the diversity of pain mechanisms, patient's responses and diseases, treatment must be individualised[47]. When agreeing a treatment plan with the patient, pain severity, the underlying cause of pain, comorbidities, concurrent medications and vulnerability to adverse effects should be taken into account[27]. Patients should be informed that response to drug treatment in neuropathic pain is often inadequate, with no more than 40–60% of people obtaining partial pain relief[48]. A 2015 systematic review and meta-analysis found that the number

needed to treat (NNT) for 50% pain relief was 7.2 for gabapentin and 7.7 for pregabalin[49], A recent Cochrane systematic review of pregabalin for neuropathic pain in adults concluded that pregabalin at daily oral doses of 300 mg to 600 mg can provide good levels of pain relief for some people with post-herpetic neuralgia and painful diabetic neuropathy, however evidence for use in other types of neuropathic pain is very limited. In addition, the review noted that more than half of patients treated with pregabalin will not attain worthwhile pain relief, and around 6 or 7 out of 10 will experience at least one adverse event[40].

NICE guidance on neuropathic pain in adults recommends early assessment once treatment has commenced. This should be followed by regular clinical reviews to assess and monitor effectiveness, including pain control, impact on lifestyle, physical and psychological wellbeing, adverse effects and continued need[27]. If the patient has not shown sufficient benefit within eight weeks of reaching the maximum tolerated dose, drug treatment should be reduced and stopped[47]. The SPCs for both gabapentin and pregabalin indicate that they can be discontinued gradually over a minimum of one week, independent of indication[29,32]; however, a more gradual dose taper allows observation of emergent symptoms that may have been controlled by the drug. Public Health England suggests reducing the daily dose by a maximum of 300 mg every four days in the case of gabapentin and by a maximum of 50–100 mg per week in the case of pregabalin[39].

If pain does not appear to be neuropathic in nature and is not currently well controlled, consider a change of treatment as gabapentin and pregabalin are only licensed for neuropathic pain[47]. Both gabapentin and pregabalin are commonly prescribed for non-neuropathic pain syndromes; however, there is little evidence to support this practice[39]. A 2017 Canadian systematic review and meta-analysis highlighted that gabapentin and pregabalin are increasingly being used for non-specific chronic lower back pain, despite the significant risk of adverse effects without any demonstrated benefit[50]. This highlights the need for treatment to be reviewed when either pregabalin or gabapentin are prescribed outside of their licensed indications.

Neuropathic pain management is often complex and prescribers need to make evidence-based, informed decisions based on the individual needs of the patient. Overall, treatment gains in neuropathic pain with even the most effective of available treatments are modest[40]. Prescribers should be aware not only of the potential benefits of gabapentin and pregabalin, but also that they may be misused or diverted. Individuals who are misusing analgesics need to be distinguished from those who are using higher or more frequent doses because their symptoms are not being adequately treated. It is vitally important that any individual whose condition warrants an increase in pain relief is reassessed and subsequently receives the appropriate evidence-based prescribing[51]. The reclassification of gabapentin and pregabalin as class C controlled substances has resulted in stronger controls with regards to the prescribing and supply of these items and it is now illegal to be in possession of these drugs without a prescription.

This NPI promotes a prudent approach to prescribing gabapentin and pregabalin, taking into account the risks and benefits, and encouraging timely review.

Useful resources

- AWMSG (2016) Persistent pain resources
- PrescQIPP (2016) Neuropathic pain: Pregabalin and gabapentin prescribing
- Public Health England (2014) Advice for prescribers on the risk of the misuse of pregabalin and gabapentin
- SIGN (2019) SIGN 136. Management of chronic pain

1.2 ANTICOAGULANTS IN ATRIAL FIBRILLATION

***Purpose*:**

To encourage the appropriate use and review of anticoagulants in patients with Atrial Fibrillation (AF).

Units of measure:

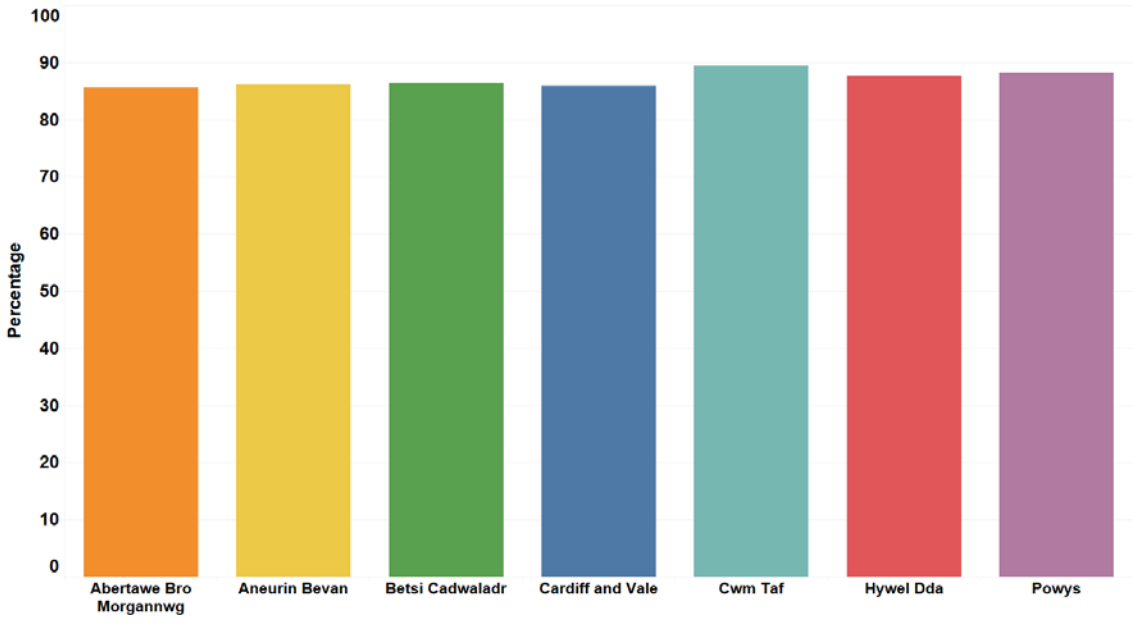
The number of patients diagnosed with AF who:

1. Have a CHA_2DS_2-VASc score of 2 or more who are currently prescribed an anticoagulant as a percentage of all patients diagnosed with AF.
2. Are currently prescribed an anticoagulant and have received an anticoagulant review (read codes 8BT3, 6A9, or 66QB) within the last 12 months, as a percentage of all patients diagnosed with AF who are prescribed an anticoagulant.
3. Are prescribed antiplatelet monotherapy, as a percentage of all patients diagnosed with AF.

Targets for 2020–2021:

1. To increase the number of patients with AF and a CHA_2DS_2-VASc of 2 or more prescribed an anticoagulant.
2. To increase the number of patients with AF who are prescribed an anticoagulant and have received an anticoagulant review (read codes 8BT3, 6A9, or 66QB) within the last 12 months.
3. To reduce the number of patients with AF prescribed antiplatelet monotherapy.

Figure 8. Percentage of patients with AF and a CHA_2DS_2-VASc score of 2 or more who are currently treated with anticoagulant therapy – quarter ending March 2019[52*]



* Please note, this graph is based on data provided by NWIS for the Quality Assurance and Improvement Framework (QAIF). This data is currently only available up to March 2019 in the old health board structures.

Figure 9. Percentage of patients with AF who are prescribed an anticoagulant and have received an anticoagulant review within the last 12 months – September 2019[52]

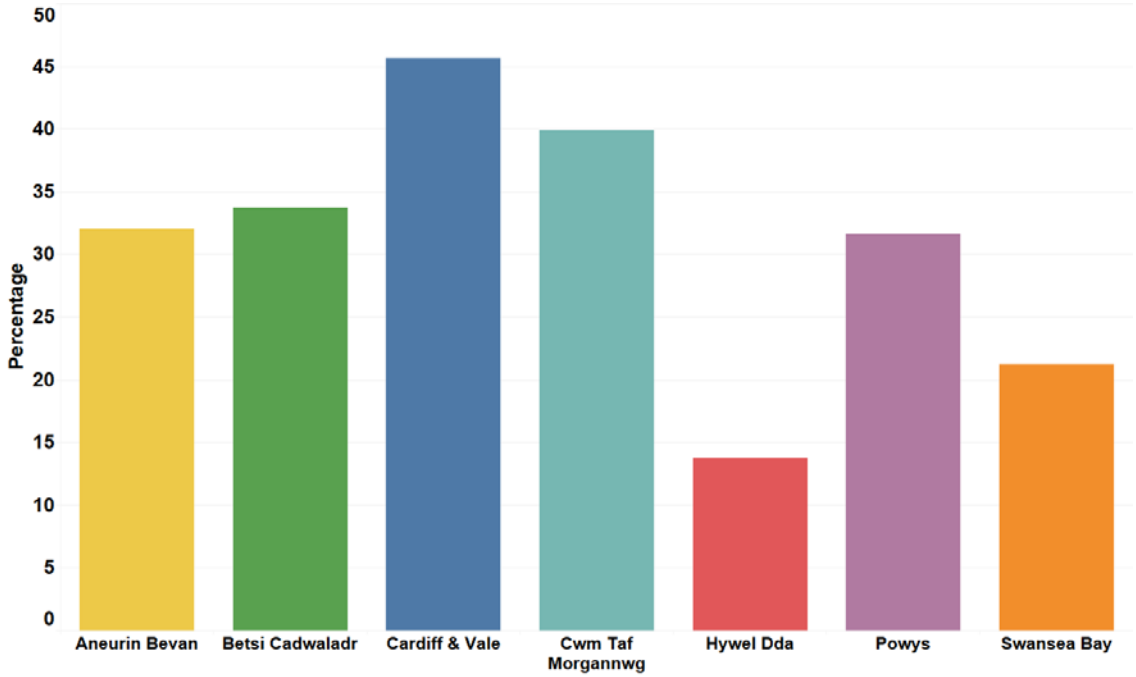
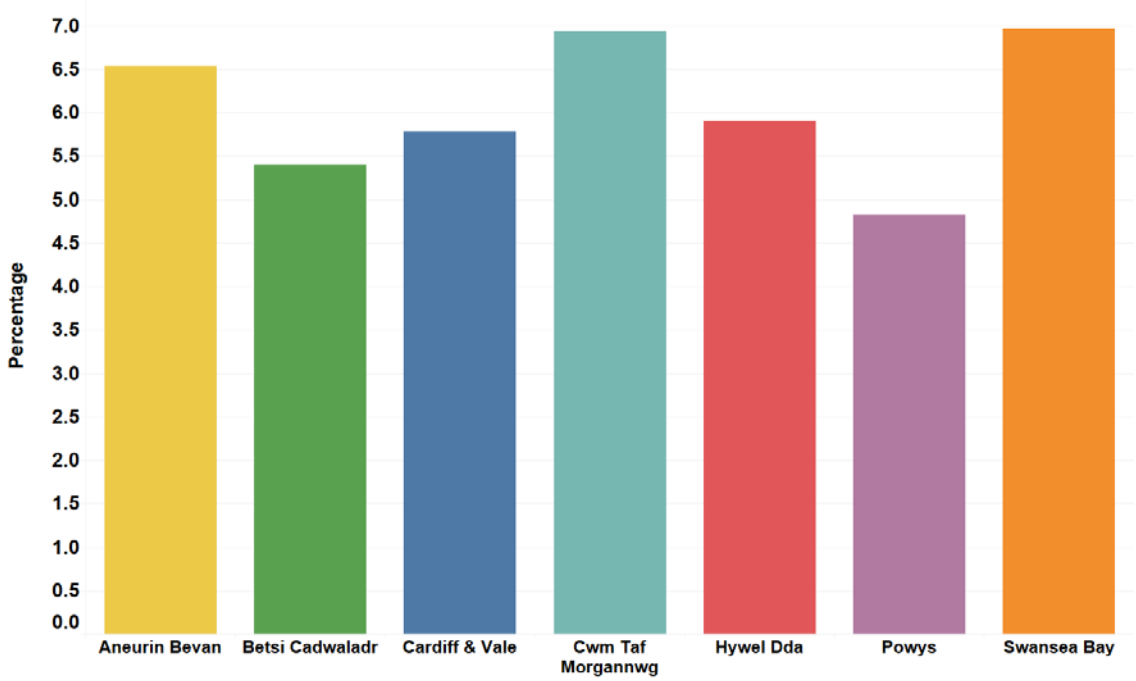


Figure 10. Percentage of patients with AF who are prescribed antiplatelet monotherapy – September 2019[52]



Background and evidence

This priority area contains a number of measures looking at the use of anticoagulants and antiplatelets in patients with a diagnosis of AF, with the aim of ensuring that patients are appropriately treated and receive a review of their anticoagulant medication. These indicators support the implementation of a number of the quality statements produced by NICE in relation to AF. In addition, the indicators align with the Stop a Stroke project aim to support health boards in Wales in the initiation of a sustainable approach to reviewing the treatment of patients with AF to reduce the risk of having a stroke.

AF is a supraventricular tachyarrhythmia resulting from irregular, disorganised electrical activity and ineffective contraction of the atria[53]. AF is the most common sustained cardiac arrhythmia[53] with about 1.2 million people in the UK diagnosed with the condition[54]. GP practice data for September 2019 demonstrates that there are over 75,000 patients with AF in Wales[52], and statistics consistently highlight that people living in Wales have the highest prevalence for AF across the UK[55].

Anticoagulation

AF causes around 20% of strokes, however this can be reduced by about two thirds if people are anticoagulated[56]. The NICE guideline *Atrial fibrillation: management* recommends that patients with persistent or permanent AF are assessed for stroke risk using the CHA_2DS_2VASc score[57], which takes into account risk factors including age, gender and co-morbidities. Adults with non-valvular AF and a CHA_2DS_2VASc score of 2 or above are at a much higher risk of having a stroke than the general population, however anticoagulation therapy can help to prevent strokes by reducing the likelihood of a blood clot forming.

For patients with a CHA_2DS_2VASc of 2 or above, NICE recommends that anticoagulation should be offered[57]. The patient's bleeding risk should be taken into account in reaching a decision about anticoagulation, however for most people, the benefit of anticoagulation outweighs the bleeding risk[58]. NICE guidance recommends anticoagulation with either apixaban, dabigatran etexilate, rivaroxaban or a vitamin K antagonist[57], however since publication of the guidance an additional anticoagulant, edoxaban, has been licensed and recommended as a treatment option for preventing stroke and systemic embolism in adults with AF[59].

The Sentinel Stroke National Audit Programme (SSNAP) measures the quality and organisation of stroke care in the NHS and includes a range of measures which can be used to improve the quality of care that is provided to patients. The audit programme captures data from secondary care regarding patients admitted with a stroke[56]. Data from the 2018–2019 SSNAP clinical audit report highlights that nearly 61.1% of patients across Wales, England and Northern Ireland with known AF prior to admission to hospital with a stroke, were on anticoagulant medication[56]. Table 3 details the breakdown of this audit data for each health board in Wales. All health boards have made substantial improvements since the first year of SSNAP reporting in 2013–2014, however work still needs to be done to ensure that all patients who would benefit from anticoagulants are prescribed them, as increasing the proportion of people with AF on anticoagulants will reduce the number of people having a stroke[56].

Table 3. Percentage of patients with AF before stroke on anticoagulant medication 2018–2019[60]

Health board	Percentage of patients with AF before stroke on anticoagulant medication
Abertawe Bro Morgannwg	55.9%
Aneurin Bevan	62.0%
Betsi Cadwaladr	63.1%
Cardiff and Vale	46.4%
Cwm Taf	54.3%
Hywel Dda	63.5%
Powys	65.4%

Anticoagulation review

The review of patients with AF who are taking an anticoagulant is vital. The use of any anticoagulant is associated with some drug-drug interactions which may increase the risk of serious bleeding or diminish stroke prevention[61]. Warfarin has well known food and drug interactions, and treatment with Direct Oral Anticoagulants (DOACs) and warfarin requires vigilance due to potentially severe complications, particularly as the target population tends to be of an older age and with increased frailty[61]. The NICE guideline *Atrial fibrillation: management* highlights the need to review anticoagulation and the quality of anticoagulation at least annually, or more frequently if clinically relevant events occur affecting anticoagulation or bleeding risk[62]. Quality Statement 3 within the NICE Quality Standard for *Atrial fibrillation* states that adults with AF who are prescribed anticoagulation should discuss the options with their healthcare professional at least once a year[58]. Patients should have the opportunity to discuss the choice of suitable anticoagulants with their healthcare professional, in order to improve adherence to treatment. Adherence to anticoagulation can help to prevent stroke by reducing the likelihood of a blood clot forming[58].

Antiplatelet monotherapy

Antiplatelet medication, i.e. aspirin or clopidogrel, is no longer recommended in patients with AF. Despite this, data from the SSNAP audit highlights that 15% of stroke patients across Wales, England and Northern Ireland with AF are still prescribed antiplatelet drugs[56]. Quality Statement 2 within the NICE Quality Standard for *Atrial fibrillation* states that adults with AF should not be prescribed aspirin as monotherapy, as the risks of taking aspirin outweigh any benefits[58]. However, prescribers should be aware that adults with AF may need to take aspirin for other indications[58].Table 4 shows the percentage of patients in Welsh health boards, with AF, admitted to hospital with a stroke who were on antiplatelet medication.

Table 4. Percentage of patients with AF before stroke on antiplatelet medication 2018–2019[60]

Health board	Percentage of patients with AF before stroke on antiplatelet medication
Abertawe Bro Morgannwg	18.8%
Aneurin Bevan	16.2%
Betsi Cadwaladr	15.7%
Cardiff and Vale	15.9%
Cwm Taf	14.8%
Hywel Dda	18.2%
Powys	17.3%

Useful resources

- AWMSG (2020) All Wales Advice on Oral Anticoagulation for Non-valvular Atrial Fibrillation
- NICE (2014) CG180: Atrial fibrillation: management
- NICE (2014) CG180: Patient decision aid and user guide
- NICE (2018) Quality Standard Atrial fibrillation
- Stop a Stroke website

1.3 ANTIMICROBIAL STEWARDSHIP

Antimicrobial resistance (AMR) is a growing threat to global health, and sporadic outbreaks of untreatable 'super-bugs' now a reality in hospitals across the UK. It is currently estimated that approximately 700,000 people a year die from infection caused by these organisms globally, and left unchecked, that figure could rise to 10 million by 2050, eclipsing the number of deaths caused by cancer and malaria. The financial impact on the global economy would be extreme, at an estimated cost of $100 trillion[63].

In 2015, member states of the World Health Organisation endorsed a Global Action Plan (GAP) on Antimicrobial Resistance, encompassing five key strategic objectives[64]. This provides a framework from which National Action Plans (NAP) can be developed and delivered by individual member states. The GAP was adopted a year later at the 71st session of the United Nations General Assembly, and an Intra-Agency Coordination Group was put in place by the UN Secretary General to develop a framework for action and monitor progress[65].

The UK was one of the first countries to establish a National Action Plan, with strategies and action plans in place since 2000, pre-dating the UN GAP. The previous UK NAP, the 2013-2018 AMR Strategy, focused on seven key areas including infection prevention and control; antimicrobial prescribing; education, training and public engagement; and better access to and use of surveillance data[66]. In Wales, this plan was reflected in the Antimicrobial Resistance (AMR) Delivery Plan for NHS Wales, which ran from 2016 – 2019[67].

In 2018, the four devolved administrations of the UK worked together to produce a new 20 year vision, designed to deliver the key strategies of the UN GAP. The vision was published in January 2019[68] along with the first of four 5-year National Action Plans (NAP)[69]. The 20-year vision aims to contain, control and mitigate AMR by 2040 through lowering the burden of infection, optimising the use of antimicrobials and developing new diagnostics, therapies and vaccines. These documents are 'one-health', reflecting a need for coordinated action across human health, animal health, agriculture and the environment.

The UK 2019-2024 NAP contains four overarching targets aimed at human health:

- To halve the number of healthcare associated Gram-negative blood stream infections
- To reduce the number of specific drug-resistant infections by 10% by 2025
- To reduce the UK antimicrobial use in humans by 15% by 2024
- To be able to report on the percentage of antimicrobial prescriptions supported by an appropriate diagnostic test or decision support tool by 2024

In support of the new UK 5-year NAP, Welsh Government will be releasing annual Welsh Health Circulars (WHCs), designed to provide sequential targets to the NHS in Wales, enabling them to meet the overall UK targets. Each of the four devolved administrations will align their targets and metrics, allowing each devolved administration to adjust their targets to reflect local need. In July 2019, the Welsh Government published the latest WHC, which contained the following ambitions[70]:

Primary care
The overarching UK AMR strategy ambition is to reduce antimicrobial consumption in primary care by 25%, by 2024, against a baseline year of 2013.

Improvement goal:

- To reflect the UK AMR strategy target, primary care services in Wales will be expected to achieve a 25% reduction in antimicrobial prescribing, compared with the baseline year of 2013, by 2024.

Secondary care

The overarching UK AMR strategic ambition is to reduce prescribing of antibiotics in the WHO 'Watch' and 'Reserve' categories by 10%. The four devolved administrations are currently working on defining this target.

Improvement goals:

- Increase the proportion of antibiotics prescribed within the WHO 'Access' category of antibiotics to ≥55% of total antibiotic consumption (measured as DDDs)
- Reduce the total consumption of antimicrobials in hospital care by 1% against a baseline of 2018-19.

1.3.1 Total antibacterial items

***Purpose*:**
To encourage the appropriate prescribing of all antibiotics in primary care.
Unit of measure:
Total antibacterial items per 1,000 STAR-PUs.
Target for 2020–2021:
Health board target: a quarterly reduction of 5% against a baseline of data from April 2018–March 2019. GP practice target: maintain performance levels within lower quartile, or show a reduction towards the quartile below.

Note
Comparative trends for antimicrobial NPIs should be interpreted with caution, with particular respect to seasonal variation.

Table 5. Health board baseline data: total primary care antibacterial items per 1,000 STAR-PUs 2018–2019[71]

	June 2018	September 2018	December 2018	March 2019
Aneurin Bevan	278	264	304	310
Betsi Cadwaladr	275	257	290	292
Cardiff and Vale	263	244	277	279
Cwm Taf Morgannwg	313	299	335	340
Hywel Dda	288	266	314	312
Powys	233	222	253	261
Swansea Bay	309	289	332	327
Wales	**283**	**266**	**303**	**306**

Figure 11. Trend in total primary care antibacterial items per 1,000 STAR-PUs to quarter ending September 2019

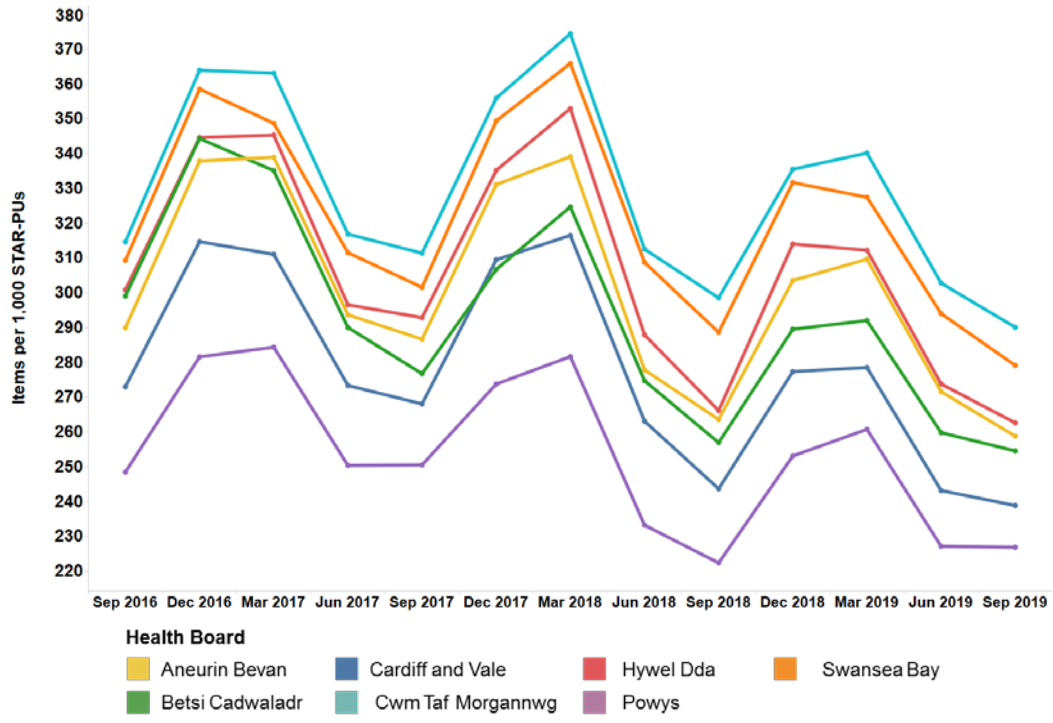
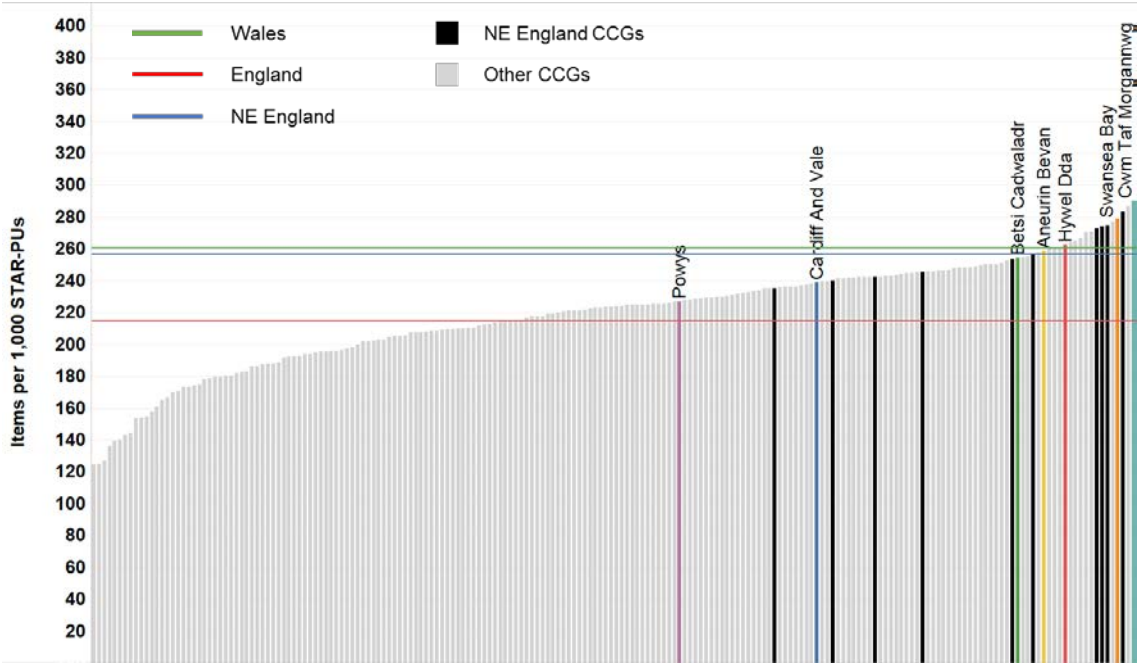


Figure 12. Total primary care antibacterial items per 1,000 STAR-PUs Welsh health boards and English CCGs – Quarter ending September 2019



Background and evidence

The widespread and often excessive use of antimicrobials is one of the main factors contributing to the increasing emergence of AMR. Within Wales, antimicrobial usage and AMR have been increasing year on year for at least the last 7 years in acute hospital settings[67], although during the 5-year period 2013–2014 to 2017–2018, there was an 11.9% reduction in total antibacterial usage across GP practices in Wales[72]. This is a step in the right direction; however, variation still exists. For the quarter ending June 2019, primary care prescribing rates varied from 227 to 303 items per 1,000 STAR-PUs across Welsh health boards[71].

The Public Health Wales report *Antibacterial Resistance in Wales 2008–2017* presents the different AMR patterns across Wales[73]. The report shows resistance trends in Wales for drug-bug combinations compared with UK aggregate rates, and finds that while there are small differences, generally the trends are comparable. However, in some cases there is considerable variability in resistance rates between different areas and hospitals[73].

NICE Guideline 15 – *Antimicrobial stewardship: systems and processes for effective antimicrobial medicine use* – makes recommendations for organisations on antimicrobial stewardship programmes, antimicrobial stewardship interventions and communication strategies[74]. In addition it makes recommendations for individual prescribers in both primary and secondary care. Key recommendations include:

- Follow local or national guidelines, prescribing antibiotics for the shortest effective course at the most appropriate dose;
- Consider the risk of antimicrobial resistance for individual patients and the population as a whole;
- Document the clinical diagnosis in the patient's record and the reason for prescribing, or not prescribing, an antimicrobial[74].

Ultimately, indiscriminate or inappropriate use of antibiotics is a key driver in the spread of antibiotic resistance[66]. Therefore, the ultimate aim has to be the reduction in inappropriate prescribing, measured as volume of antimicrobials.

1.3.2 4C antimicrobials

***Purpose*:**
To reduce the prevalence of healthcare associated infection (HCAI), including *Clostridioides difficile* infection and *Staphylococcus aureus* bacteraemia caused by MRSA, by encouraging a reduction in variation and reduce overall prescribing of the 4C antimicrobials (co-amoxiclav, cephalosporins, fluoroquinolones and clindamycin) in primary care.
Unit of measure:
Co-amoxiclav, cephalosporin, fluoroquinolone and clindamycin items combined, per 1,000 patients.
Target for 2020–2021:
Health board target: a quarterly reduction of 10% against a baseline of data from April 2018–March 2019. GP practice target: maintain performance levels within lower quartile, or show a reduction towards the quartile below.

Note
Comparative trends for antimicrobial NPIs should be interpreted with caution, with particular respect to seasonal variation.

Table 6. Health board baseline data: 4C antimicrobials per 1,000 patients 2018–2019[71]

	June 2018	September 2018	December 2018	March 2019
Aneurin Bevan	10.8	10.4	10.6	10.1
Betsi Cadwaladr	15.1	15.4	14.6	13.4
Cardiff and Vale	10.4	9.95	10.1	9.96
Cwm Taf Morgannwg	17.9	17.8	17.1	16.8
Hywel Dda	17.0	16.8	16.8	15.7
Powys	12.7	12.5	12.6	11.8
Swansea Bay	17.9	16.6	16.1	16.0
Wales	**14.4**	**14.1**	**13.8**	**13.2**

Figure 13. Trend in 4C antimicrobial items per 1,000 patients to quarter ending September 2019

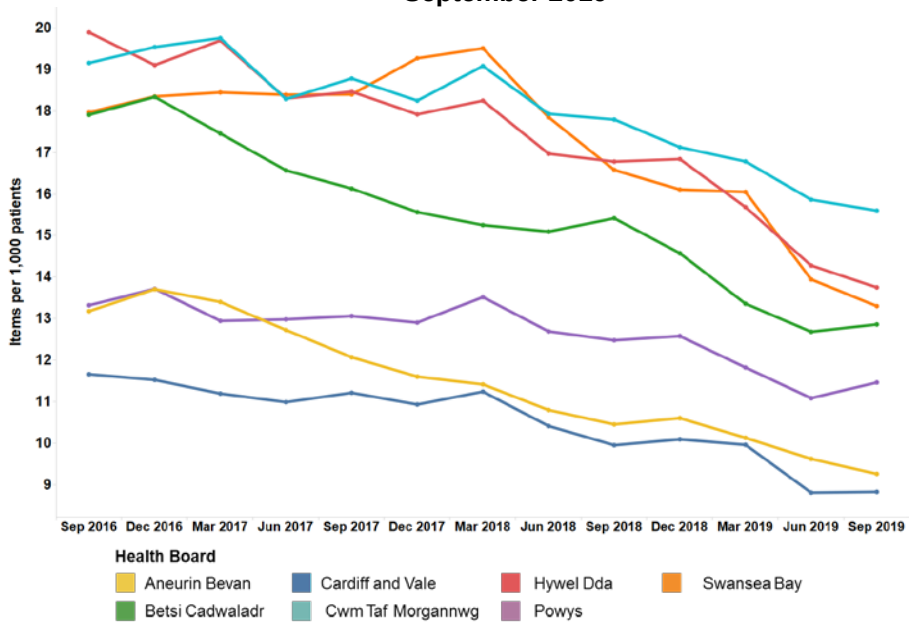
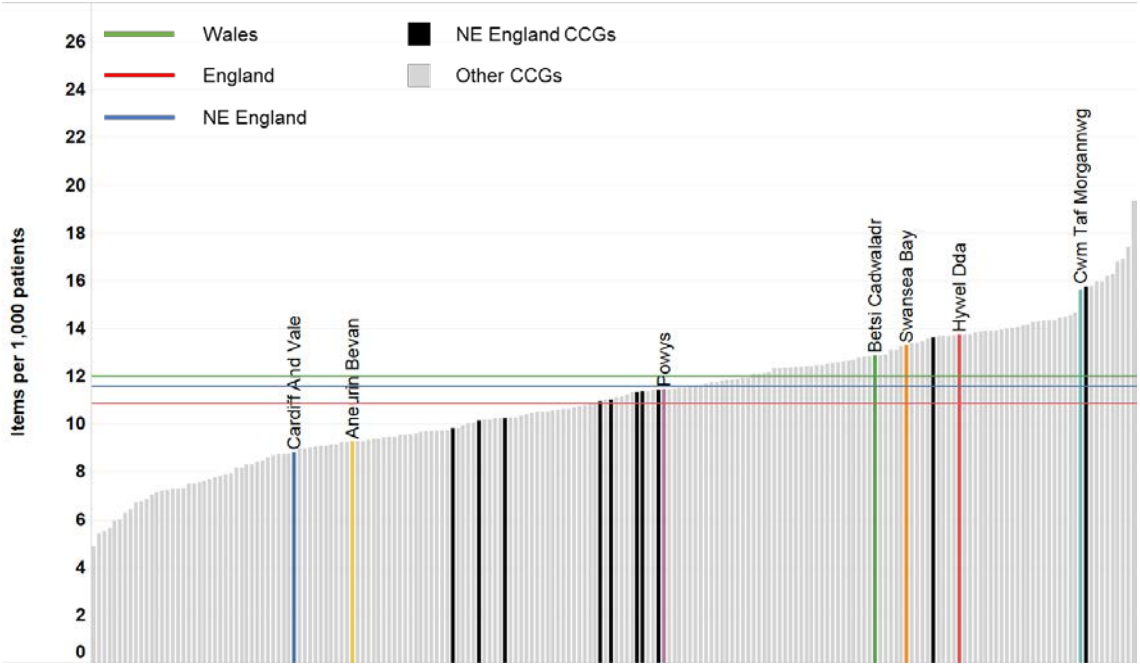


Figure 14. 4C antimicrobial items per 1,000 patients Welsh health boards and English CCGs – Quarter ending September 2019



Background and evidence

Public Health England guidance states "Use simple generic antibiotics if possible. Avoid broad spectrum antibiotics (e.g. co-amoxiclav, quinolones and cephalosporins) when narrow spectrum antibiotics remain effective, as they increase the risk of *C. difficile*, methicillin-resistant *Staphylococcus aureus* (MRSA) and resistant urinary tract infections"[75]. The guidance advises when it may be appropriate to consider a broad-spectrum antibiotic.

The term '4C antimicrobials' refers collectively to four broad-spectrum antibiotics, or groups of antibiotics: co-amoxiclav, cephalosporins, fluoroquinolones and clindamycin. The use of simple generic antibiotics and the avoidance of these broad-spectrum antibiotics preserve them from resistance and reduce the risk of *C. difficile*, MRSA and resistant UTIs. Compared with narrow-spectrum antibiotics, broad-spectrum antibiotics are more likely to significantly change the gut flora, potentially allowing other bacteria, such as *C. difficile,* to become established[76]. *C. difficile* may be found in the gut of people with no symptoms. When the normal bacteria in the gut are disrupted (for example, by antibiotics) the numbers of *C. difficile* bacteria may increase to unusually high levels, particularly in people whose immune system is compromised. Symptoms of *C. difficile* infections vary from mild, self-limiting diarrhoea to severe complications, including pseudomembranous colitis, toxic megacolon, perforation of the colon, sepsis and death[76]. The most commonly implicated antibiotics in *C. difficile* infection include clindamycin, cephalosporins (in particular second and third generation cephalosporins), fluoroquinolones and co-amoxiclav[76]. However, these antimicrobials have a very useful role in specific clinical situations, so should be reserved for use as per local guidelines.

In March 2019, a Drug Safety Update from the MHRA informed prescribers of new restrictions and precautions for use of fluoroquinolone antibiotics due to very rare reports of disabling and potentially long-lasting or irreversible side effects. Following an EU-wide review of safety, new restricted indications have been introduced for ciprofloxacin; levofloxacin; moxifloxacin and olfloxacin[77]. The marketing authorisation for the quinolone nalidixic acid, licensed for UTIs, has been suspended[78]. Fluoroquinolones should not be prescribed for treatment of mild to moderate infections unless other antibiotics that are commonly recommended for such infections are considered inappropriate. Patients should be advised to stop treatment at the first signs

of a serious adverse reaction involving muscle pain, weakness, joint pain or swelling, peripheral neuropathy and central nervous system effects, and to contact their doctor immediately for further advice. Fluoroquinolones should be prescribed with special caution for people over 60 years and for those with renal impairment or solid-organ transplants as they are at higher risk of tendon injury[77].

Useful resources

- AWMSG (2015) Primary care antimicrobial guidelines
- AWMSG (2013) CEPP National Audit: Focus on Antibiotic Prescribing
- WeMeReC (2012) Bulletin: Appropriate antibiotic use – whose responsibility?
- RCGP TARGET Antibiotics toolkit

2.0 SUPPORTING DOMAINS

2.1 SAFETY

2.1.1 Prescribing Safety Indicators

***Purpose*:**

To identify patients at high risk of adverse drug reactions and medicines-related harm in primary care.

Units of measure:

Prescribing Safety Indicators related to acute kidney injury (AKI)

- Number of patients on the CKD register (CKD stage 3–5) who have received a repeat prescription for an NSAID within the last 3 months.
- Number of patients who are not on the CKD register but have an eGFR of < 59 ml/min and have received a repeat prescription for an NSAID within the last 3 months.
- Number of patients with concurrent prescriptions of an NSAID, renin-angiotensin system (RAS) drug and a diuretic.
- Number of patients aged 75 and over with a current prescription for an ACE Inhibitor or loop diuretic without a check of renal function and electrolytes in the previous 15 months.

Prescribing Safety Indicators related to bleeds

- Number of patients with a peptic ulcer who have been prescribed NSAIDs without a PPI.
- Number of patients with concurrent prescriptions of warfarin and an oral NSAID.
- Number of patients with concurrent prescriptions for a DOAC and an oral NSAID.
- Number of patients aged 65 years or over prescribed an NSAID plus aspirin and/or clopidogrel but without gastroprotection (PPI or H_2-receptor antagonist).
- Number of patients with concurrent prescriptions of an oral anticoagulant (warfarin or DOAC) and an SSRI.

Prescribing Safety Indicators related to cognition

- Number of patients aged 65 years or over prescribed an antipsychotic.
- Number of patients aged 75 and over with an Anticholinergic Effect on Cognition (AEC) score of 3 or more for items on active repeat.

Prescribing Safety Indicators specific to females

- Number of female patients with a current prescription of oestrogen-only hormone replacement therapy (HRT) without any hysterectomy READ/SNOMED codes.
- Number of female patients with a past medical history of venous or arterial thrombosis who have been prescribed combined hormonal contraceptives.
- Number of female patients aged 14–45 with a prescription for sodium valproate.
- Number of female patients aged 14-45 with a prescription for oral retinoids.

Prescribing Safety Indicators related to 'other'

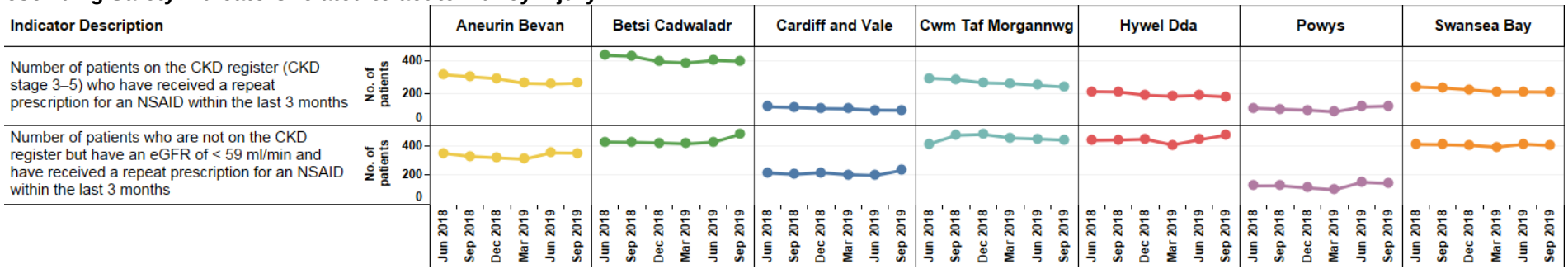
- Number of patients under 16 with a current prescription of aspirin.
- Number of patients with asthma who have been prescribed a beta-blocker.
- Number of patients with concurrent prescriptions of verapamil and a beta-blocker.

Target for 2020–2021:

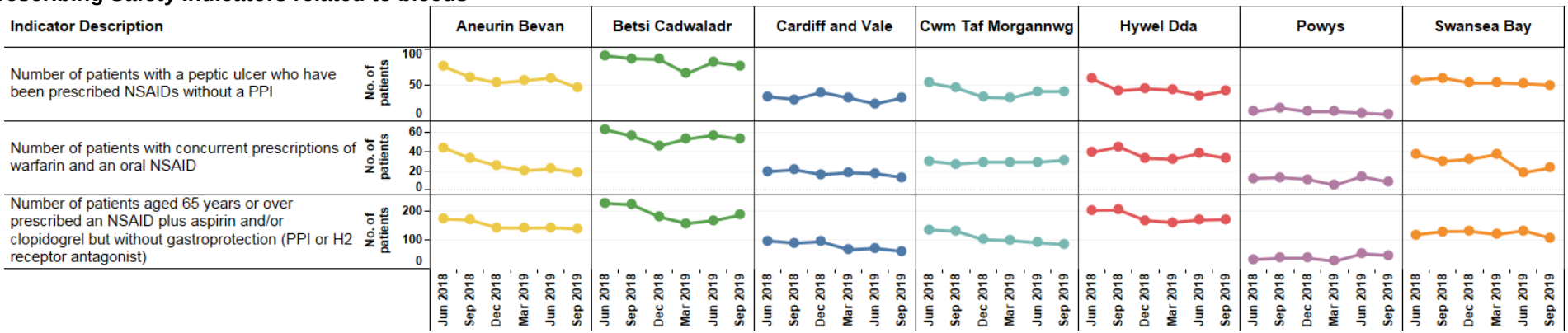
No target set

Figure 15. Prescribing Safety Indicators for 2019–2020*

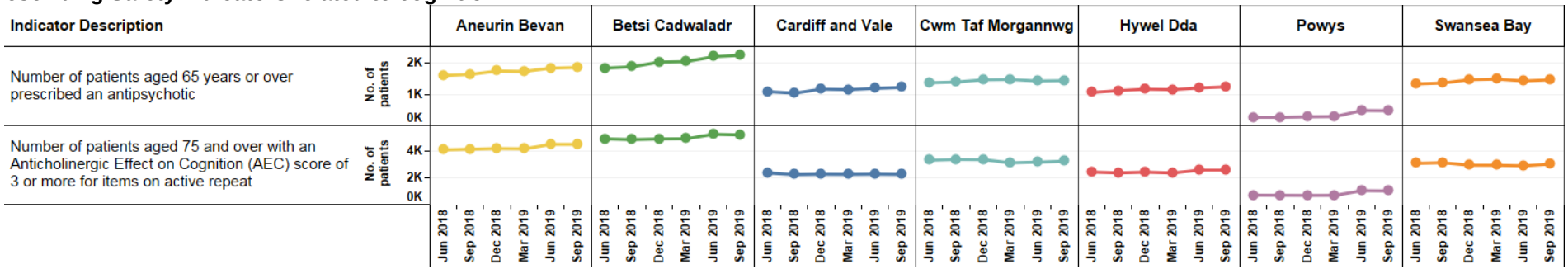
Prescribing Safety Indicators related to acute kidney injury



Prescribing Safety Indicators related to bleeds

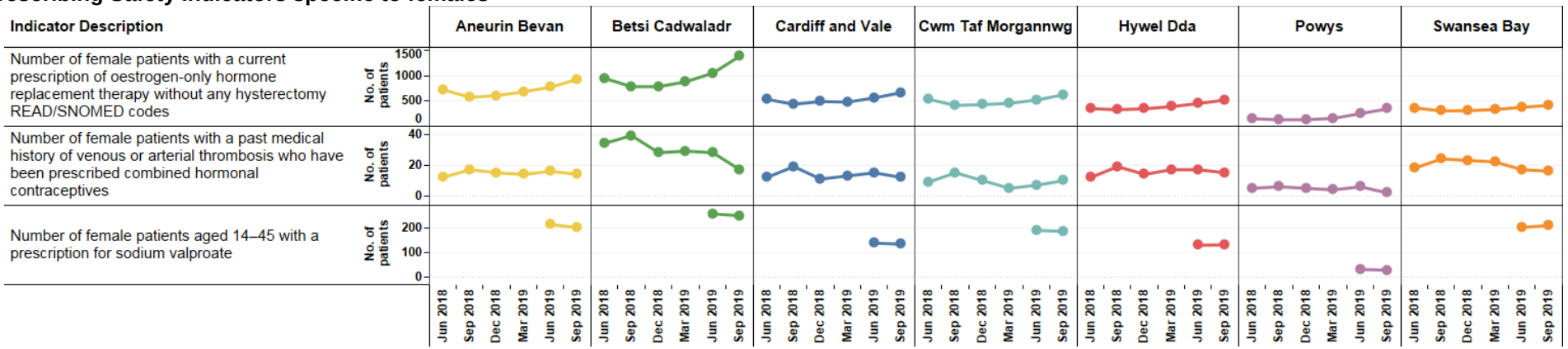


Prescribing Safety Indicators related to cognition

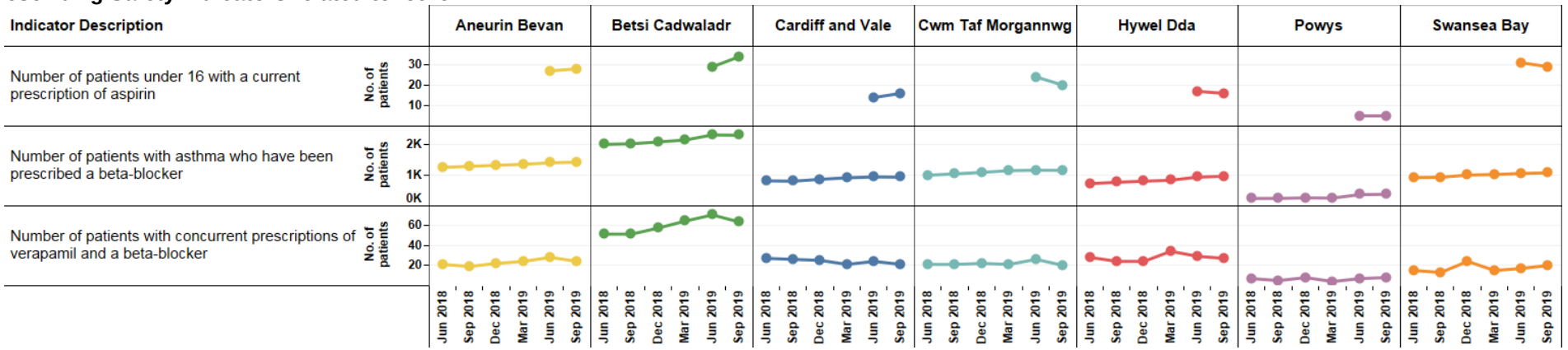


*A number of prescribing safety indicators listed in this document are new for 2020–2021, and therefore no baseline data is currently available.

Prescribing Safety Indicators specific to females



Prescribing Safety Indicators related to 'other'



Background and evidence
As adverse drug reactions can often be predictable, a system to identify patients at risk can enable potential problems to be identified and addressed before actual patient harm occurs[79]. The Prescribing Safety Indicators (PSIs) identify groups of patients within the GP practice, enabling intervention and avoidance of harm. Patients identified via the PSIs should be reviewed and/or monitored as appropriate.

These indicators support the third WHO Global Patient Safety Challenge: *Medication Without Harm*, launched in 2017, which aims to reduce severe avoidable medication-related harm by 50% globally, within 5 years[80].

PSIs related to Acute Kidney Injury (AKI)
AKI is a term covering a range of injury to the kidneys, resulting from a number of different causes. It is characterised by a decline in renal excretory function over hours or days that can result in failure to maintain fluid, electrolyte and acid based homeostasis[81].

One of the most common causes of AKI is reduced perfusion of the kidneys leading to decreased glomerular filtration rate (GFR). This can be caused by drugs that reduce blood pressure, circulating volume or renal blood flow, for example ACE inhibitors, ARBs, NSAIDs and loop diuretics[81]. AWMSG *Polypharmacy Guidance* notes that use of an ACE inhibitor or ARB and diuretic, in conjunction with an NSAID is a high risk drug combination[82]. Groups of patients most at risk of developing AKI include those aged over 65 years; patients with CKD; use of nephrotoxic drugs within the last week and people with a history of AKI[81]. NICE guidance *Chronic kidney disease in adults: assessment and management* highlights that in patients with CKD, the long-term use of NSAIDs may be associated with disease progression. The guideline recommends caution and monitoring of the effects on GFR, when using NSAIDs in people with CKD over prolonged periods of time[83].

Regular review of the ongoing need for treatment with drugs which may contribute to AKI, ensuring systems are in place for regular monitoring of renal function, in addition to reassessment of the risk versus benefit is appropriate, and processes for this should be in place.

PSIs related to bleeds
NSAIDs have been shown to be the medicine group most likely to cause an adverse drug reaction requiring hospital admission due to events such as gastrointestinal bleeding and peptic ulceration[79]. A PPI can be considered for gastroprotection in patients at high risk of gastrointestinal complications with an NSAID[13].

NSAIDs can reduce platelet aggregation which can worsen any bleeding event in patients on an anticoagulant[13]. Wherever possible, patients taking anticoagulants should avoid concomitant use of NSAIDs[84]. AWMSG *Polypharmacy Guidance* notes that NSAIDs plus an oral anticoagulant is a potential high risk drug combination[82] which should be avoided.

Hospital admission due to gastrointestinal bleeding has been associated with aspirin and clopidogrel, as well as NSAIDs[79]. The harmful consequences of bleeds due to antiplatelet therapy increase with age[85] and PPIs are recommended in older patients undergoing antiplatelet treatment[85,86]. PPIs are the preferred option to reduce GI adverse effects in people taking low dose aspirin, as the level of suppression provided by traditional doses of H_2-receptor antagonists may not prevent NSAID related ulcers[87].

SSRIs are associated with increased risk of bleeding, especially in the elderly, or those taking drugs which damage the GI mucosa/interfere with clotting such as aspirin,

NSAIDs and warfarin[82]. Anticoagulants are likely to increase the risk of bleeding events used in conjunction with SSRIs[13].

PSIs related to cognition

Use of antipsychotics in patients with dementia have a significant risk of harm, with only a limited benefit in treating behavioural and psychological symptoms of dementia[88]. The Welsh Government *Dementia Action Plan for Wales 2018–2022* calls for health boards to demonstrate a reduction in the percentage of people with a diagnosis of dementia prescribed an antipsychotic medication, and a reduction in the duration of treatment[89].

The harms associated with antipsychotic use in patients with dementia include a clear increased risk of stroke and a small increase in risk of death[90]; falls; gait disturbances; dehydration; chest infection and cognitive decline[82]. Antipsychotics should be avoided in patients with dementia unless the person is at risk of harming themselves or others, or experiencing agitation, hallucinations or delusions that are causing them severe distress[91]. Completion of the AWMSG National Audit *Antipsychotics in Dementia* can help to ensure appropriate prescribing.

An increasing number of studies report that medicines with anticholinergic effects are associated with an increased risk of cognitive impairment, dementia and falls in older people, with research also suggesting a link to increased mortality with the number and potency of anticholinergic agents prescribed. Anticholinergic medicines are used for a variety of conditions, including Parkinson's disease, overactive bladder, COPD and depression. Risk of adverse clinical outcomes in older people prescribed anticholinergic medications increases with increasing anticholinergic exposure[92], and a number of rating scales are available to asses overall anticholinergic burden. The Anticholinergic Effect on Cognition (AEC)[93] scale is used for this indicator and it is good practice, where possible, to use drugs with AEC scores of zero and to avoid those scored 1, 2 or 3. Encouraging timely review to reduce the anticholinergic burden in older people by avoiding or reducing doses and deprescribing medicines with anticholinergic activity where clinically possible will help minimise potential medication-related risks.

PSIs specific to females

Oestrogen-only hormone replacement therapy without a record of hysterectomy

Where hormone replacement therapy is indicated, hysterectomy status of the woman will determine which type is appropriate. All women with an intact uterus require a progestogen component in their hormone replacement therapy to prevent endometrial hyperplasia, which can occur after as little as six months of unopposed oestrogen therapy[94], however there may be instances where patients with an intact uterus may be prescribed oestrogen-only HRT in conjunction with a separate progestogen for progestogenic opposition of oestrogen HRT. Conversely, women who have undergone a hysterectomy should not receive a progestogen component[94].

Combined hormonal contraceptives in thrombosis patients

There is an increased risk of venous thromboembolic disease and a slight increase in the risk of arterial thromboembolism in people using combined hormonal contraceptives[13]. Any patients with a history of venous or arterial thrombosis who have been prescribed combined hormonal contraceptives are therefore at an increased risk[13].

Sodium valproate in females of child bearing age
In March 2018, the Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh)* endorsed new measures to avoid exposure of babies to valproate medicines in the womb, because exposed babies are at high risk of malformations and developmental problems[95]. The MHRA have published a Drug Safety Update stating that valproate must no longer be used in any women or girl able to have children unless she has a Pregnancy Prevention Programme in place[96] to ensure that patients are fully aware of the risks and the need to avoid becoming pregnant[97].

Oral retinoids in females of child bearing age
Oral retinoids are highly teratogenic and there is an extremely high risk that foetal exposure to isotretinoin will result in life-threatening congenital abnormalities. Any use of oral acitretin, alitretinoin, and isotretinoin in women and girls of childbearing potential must be in accordance with the conditions of a Pregnancy Prevention Programme[98].

PSIs related to 'other'

Aspirin in under 16s
Reye's syndrome is a very rare disorder that can cause serious liver and brain damage. If it is not treated promptly, it may lead to permanent brain injury or death. Reye's syndrome mainly affects children and young adults under 20 years of age[99]. Owing to an association with Reye's syndrome, aspirin should not be given to children under the age of 16, unless specifically indicated e.g. for Kawasaki disease[13,100].

Beta-blockers in asthma patients
Beta-blockers should be avoided in patients with asthma due to the potential to precipitate bronchospasm[13]. If the benefits of using a beta-blocker in an asthma patient are justified the patient should be monitored closely[13].

Verapamil in combination with beta-blockers
Beta-blockers are associated with adverse drug reactions such as bradycardia and atrio-ventricular conduction disturbances[13]. A co-prescription of a calcium channel blocker, such as verapamil, with a beta-blocker is generally not recommended due to an increased negative effect on heart function compared with beta-blocker therapy alone[13].

Useful resources
- WeMeReC (2015) Medicines-related admissions
- AWMSG (2014) Polypharmacy: Guidance for Prescribing
- AWMSG (2017) CEPP National Audit: Medicines Management for CKD
- AWMSG (2015) CEPP All Wales Audit: Towards Appropriate NSAID Prescribing
- MHRA (2014) Antipsychotics e-learning module
- AWMSG (2018) Antipsychotics in dementia audit
- PrescQIPP (2016) Bulletin 140: Anticholinergic drugs
- South London and Maudsley NHS Foundation Trust (2017) Medichec: The Anticholinergic Effect on Cognition Tool (Android Medichec app available, app for iOS due out shortly)
- Sanofi (2018) Guide for healthcare professionals: Information on the risks of valproate▼ use in girls (of any age) and women of childbearing potential

*The CMDh is a medicines regulatory body representing the European Union (EU) Member States, Iceland, Liechtenstein and Norway.

2.1.2 Proton pump inhibitors

***Purpose*:**
To encourage appropriate use of proton pump inhibitors (PPIs) in primary care.
Unit of measure:
PPI DDDs per 1,000 PUs
Target for 2020–2021:
Maintain performance levels within the lower quartile, or show a reduction towards the quartile below

Figure 16. Trend in PPI DDDs per 1,000 PUs to quarter ending September 2019

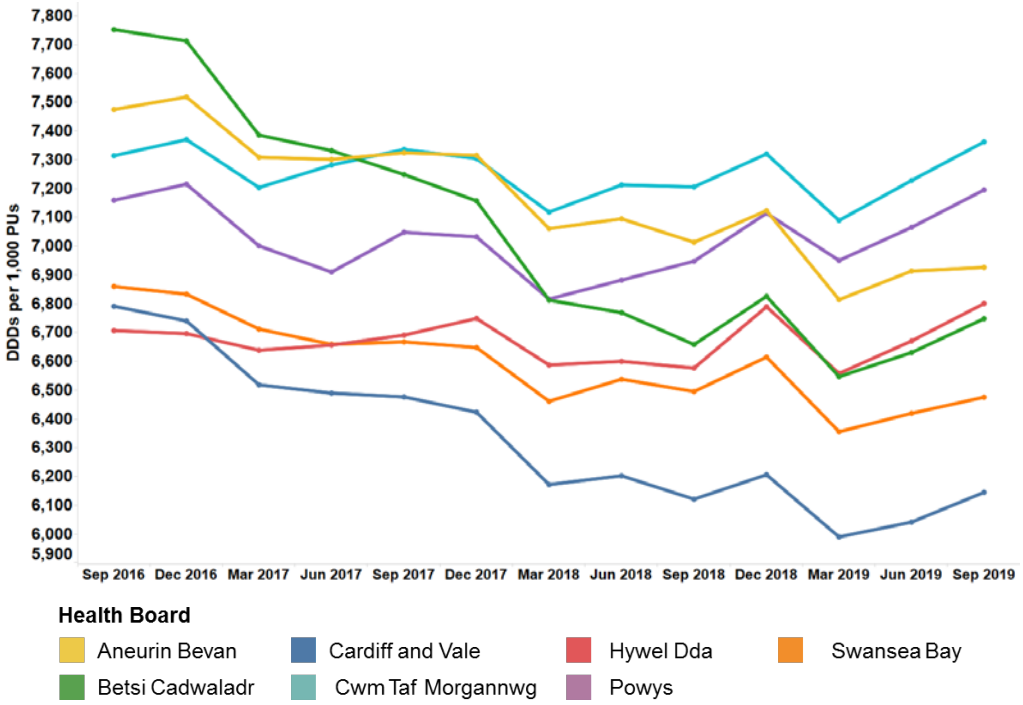
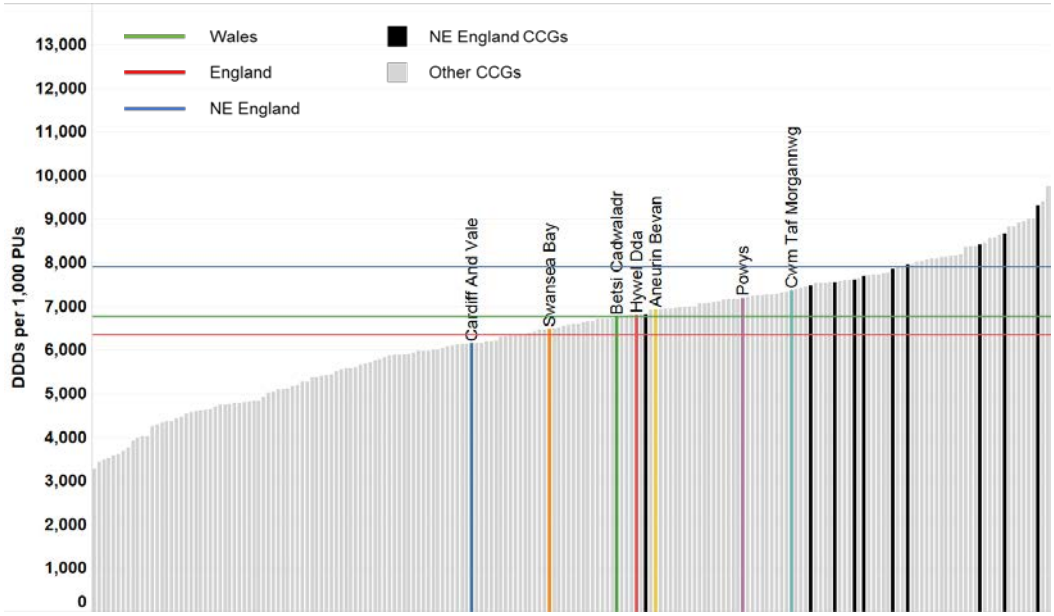


Figure 17. PPI DDDs per 1,000 PUs Welsh health boards and English CCGs Quarter ending September 2019



Background and evidence

PPIs should only be considered for short courses (4 weeks) where needed. If symptoms continue or recur, a PPI can be continued at the lowest dose possible to control symptoms or on an 'as-required' basis[101], ensuring that the indication is clearly recorded in the patient's record.

PPIs are generally well tolerated, with a low incidence of short-term adverse effects. There is, however, increasing evidence regarding the potential consequences of long-term treatment with PPIs, including *C. difficile* infection, fractures and hypomagnesaemia[102].

Long-term PPI prescriptions should be reviewed at least annually and patients should be advised that it may be appropriate for them to return to self-treatment with antacid and/or alginate therapy[101]. When the potential adverse effects are taken into consideration, the possible risks of treatment may outweigh the potential benefits, particularly in patients without a clear indication for a PPI, or when the patient is at increased risk of medicine-related adverse effects, e.g. frail, older people, or those with significant co-morbidities[102]. Patients may be more willing to try self-care to improve their symptoms if they are aware of the potential long-term effects of PPIs[102].

Ranitidine supply disruption

Due to the disruption to the supply of ranitidine from October 2019 and the recommendation to switch to omeprazole, rather than an alternative H_2-receptor antagonist where ongoing treatment is still required and the patient cannot be stepped down to an antacid or alginate[103], there may be a resultant increase in PPI prescribing.

Useful resources

- AWMSG (2018) Safe Use of Proton Pump Inhibitors
- WeMeReC (2015) Proton pump inhibitors bulletin
- PrescQIPP (2015) Bulletin 92: Safety of long term PPIs
- WeMeReC (2010) Stopping Medicines - Proton Pump Inhibitors

2.1.3 Hypnotics and anxiolytics

***Purpose*:**
To encourage a reduction in the inappropriate prescribing of hypnotics and anxiolytics in primary care.
Unit of measure:
Hypnotic and anxiolytic UDG ADQs per 1,000 STAR-PUs.
Target for 2020–2021:
Maintain performance levels within the lower quartile, or show a reduction towards the quartile below.

Figure 18. Trend in hypnotic and anxiolytic ADQs per 1,000 STAR-PUs to quarter ending September 2019

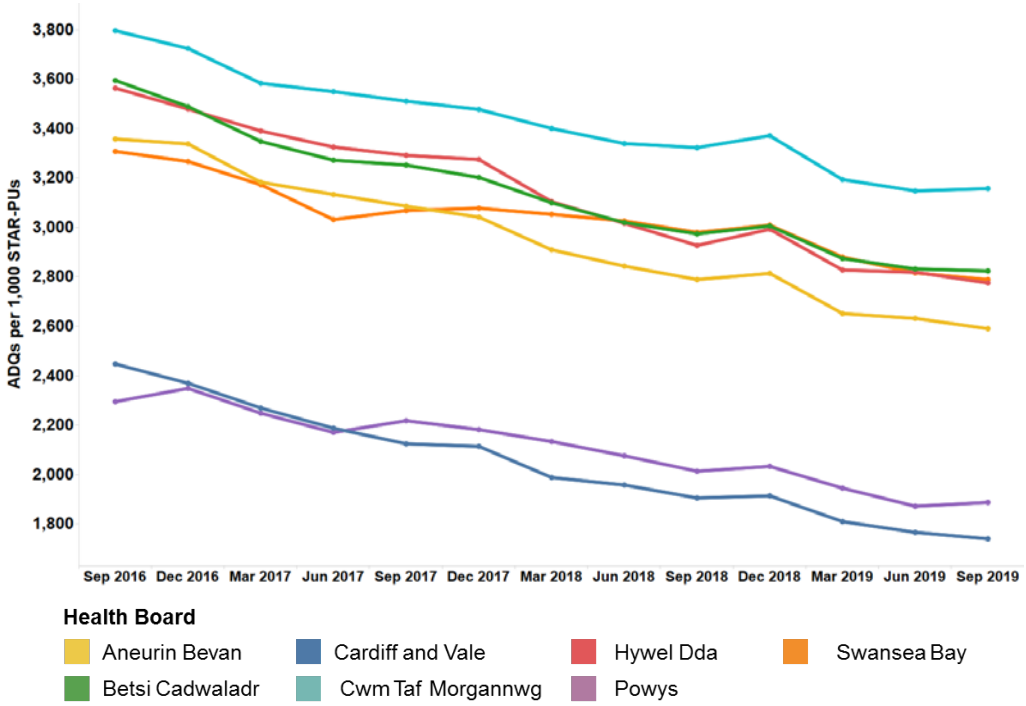
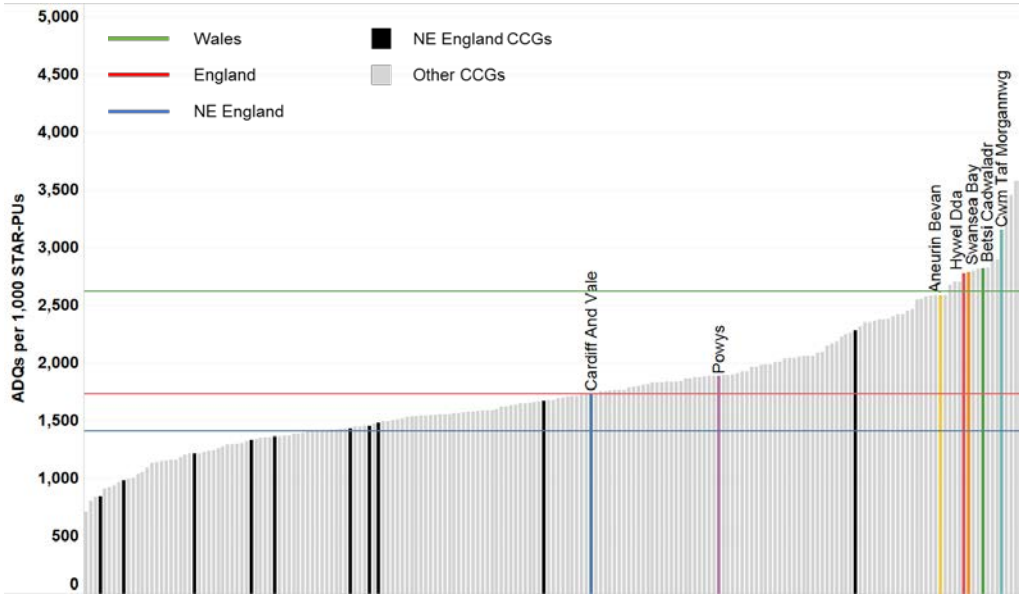


Figure 19. Hypnotic and anxiolytic ADQs per 1,000 STAR-PUs Welsh health boards and English CCGs – Quarter ending September 2019



Background and evidence

There has been concern with regard to the high level of hypnotic and anxiolytic prescribing in NHS Wales, with the substance misuse strategy of the Welsh Government, *Working together to reduce harm*, calling for the reduction of inappropriately prescribed benzodiazepines[104]. Although the prescribing volume of hypnotics and anxiolytics in Wales has declined over recent years, there is considerable variation in prescribing rates across health boards and between GP practices. Prescribing in Wales is still high in comparison to England, with five out of seven health boards in Wales within the highest prescribing quartile when compared with CCGs in England[18,36]. Despite a reduction in prescribing, there has been a 19% increase in the number of drug-related deaths where any benzodiazepine is mentioned on the death certificate (deaths registered in England and Wales) compared with 2017.

The problems associated with benzodiazepines (such as development of tolerance and dependence, and falls) are well known. It is recommended that benzodiazepines should not be used for more than two to four weeks for insomnia and anxiety, and only if it is severe, disabling, or subjecting the individual to unacceptable distress[105]. NICE guidance on the management of insomnia advises that if, after non-drug therapies have been explored, hypnotics are considered appropriate, they should be used in the lowest effective dose possible for the shortest duration possible in strict accordance with their licensed indications[106,107]:

AWMSG has developed an *Educational Pack: Material to Support Appropriate Prescribing of Hypnotics and Anxiolytics across Wales*, which provides examples of practice protocols to allow clinicians to agree a consistent approach for the prescribing and review of hypnotics and anxiolytics. The pack also provides materials to support the review and discontinuation of hypnotic and anxiolytic treatment. Analysis of primary care dispensing data has shown that the trend in Z-drug usage reduced significantly across Wales in the 12-month period following introduction of the pack in 2011[108].

Useful resources

- Bruyère Research Institute (2019) Benzodiazepine & Z-Drug (BZRA) Deprescribing Algorithm
- AWMSG (2016) Educational Pack: Material to Support Appropriate Prescribing of Hypnotics and Anxiolytics across Wales
- WeMeReC (2015) Bulletin: Sedative medicines in older people
- AWMSG (2014) Polypharmacy: Guidance for Prescribing

2.1.4 Yellow Cards

***Purpose*:**

To encourage an increase in the number of Yellow Cards submitted in Wales.

Unit of measure:

Number of Yellow Cards submitted, per GP practice, per health board and per hospital.
Number of Yellow Cards submitted by Community Pharmacies, per health board.

Target for 2020–2021:

GP practices: Submit one Yellow Card per 2,000 practice population.
Health boards:

- Submit one Yellow Card per 2,000 health board population
- Demonstrate a 20%, or greater, increase from baseline (2019–2020), for Yellow Cards submitted by secondary care
- Demonstrate a 50%, or greater, increase from baseline (2019–2020), for Yellow Cards submitted by members of the public

Community pharmacy: no target set

Figure 20. Percentage of GP practices meeting the target of one Yellow Card per 2,000 practice population 2018–2019

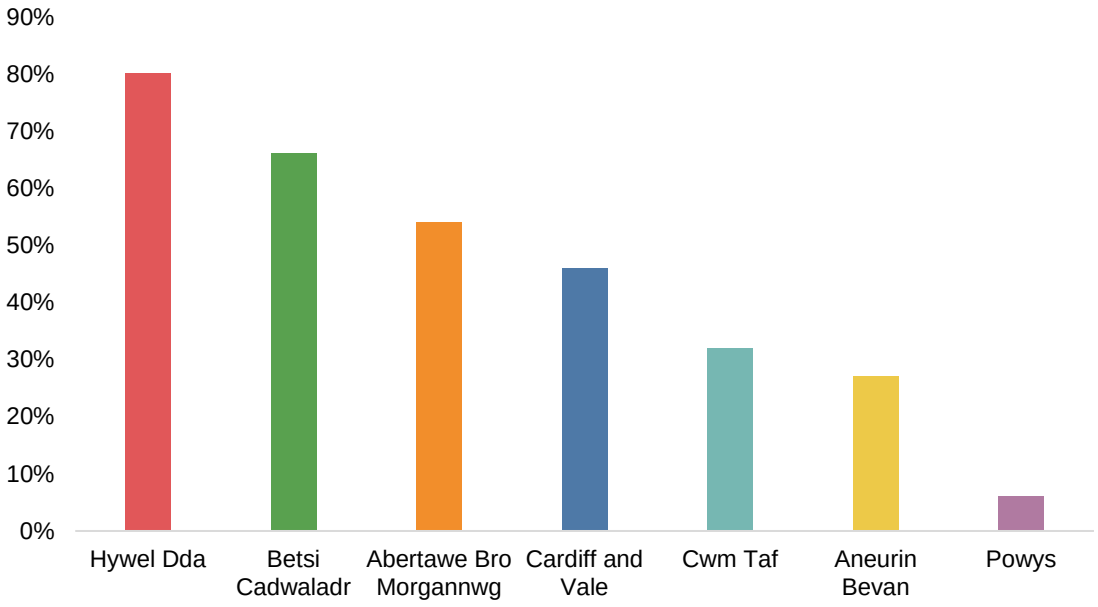


Table 7. Yellow Card data showing total number of reports, number of secondary care reports and number of member of public reports in 2018–2019

Health board	Total number of reports	Secondary care reports	Member of public reports
Aneurin Bevan	375	84	56
Betsi Cadwaladr	929	188	77
Cardiff and Vale	479	106	73
Cwm Taf Morgannwg	315	47	40
Hywel Dda	704	95	59
Powys	57	8	15
Swansea Bay	346	52	34
Velindre	17	17	N/A

Background and evidence

Adverse drug reactions (ADRs) are a significant clinical problem, increasing morbidity and mortality. Studies have shown that ADRs are the cause of up to around 6.5% of hospital admissions in adults and 2.1% in children[79,109]. An ADR has been defined as *"a response to a medicinal product that is noxious and unintended resulting not only from the authorised use of a medicinal product at normal doses but also from medication errors and uses outside the terms of the marketing authorisation, including the misuse and abuse of the medicinal product"*[110]. The Yellow Card Scheme is vital in helping the MHRA monitor the safety of all healthcare products in the UK, to ensure they are acceptably safe for those that use them.

Prior to April 2013, the number of reports from GPs across Wales had been in decline. In April 2013, Yellow Card reporting was included as a Clinical Effectiveness Prescribing Programme (CEPP) Local Comparator and in April 2014 it became an NPI. In 2018–2019, the number of Yellow Cards submitted by GP practices in Wales increased by 8.5% compared with the previous year, to 2,149. This NPI also monitors the number of Yellow Cards submitted by all reporters per health board population. In 2018–2019, the number of Yellow Cards submitted by health boards in Wales increased by 6% compared with the previous year, to 3,221. It is anticipated that continuing to monitor Yellow Card reporting as an NPI for 2020–2021 will further increase reporting rates.

In 2018–2019, 597 Yellow Card reports were submitted across Wales from secondary care settings. This represents an 8% decrease on the number reported in the previous year. The purpose of this measure is for health boards to compare how their secondary care sites are progressing each quarter, it is not intended to measure performance between health boards due to the varying size and nature of the services provided.

Yellow Cards submitted by patients have been shown to provide a more complete indication of the *"profound effect that an ADR can have on people"*[111]. In 2018–2019, 354 Yellow Card reports were submitted across Wales by members of the public. Continued monitoring of the number of Yellow Cards submitted by patients, their carers and/or parents will aim to ensure that reporting continues to increase.

Community pharmacists are required to ask patients about ADRs as part of the essential (batch repeat dispensing) and advanced (medicines use review [MUR] and discharge medicines review [DMR]) elements of the community pharmacy contract[112,113]. As a result, community pharmacists are ideally placed to make a significant contribution to the number of Yellow Cards submitted. In 2018–2019, a total of 68 Yellow Card reports were submitted from community pharmacies across Wales. This NPI will measure the total number of reports submitted from community pharmacies in each health board.

Useful resources

- Yellow Card champions are available in each health board to provide training. Contact YCCWales@wales.nhs.uk for more information
- Yellow Card reports can be completed online – Yellow Card website
- Health Professional Guidance on Reporting
- MHRA website
- YCC Wales website
- NHS Education for Scotland e-learning modules on ADRs
- Health Education and Improvement Wales (HEIW) e-Learning module on the Yellow Card Scheme

Download the Yellow Card App:

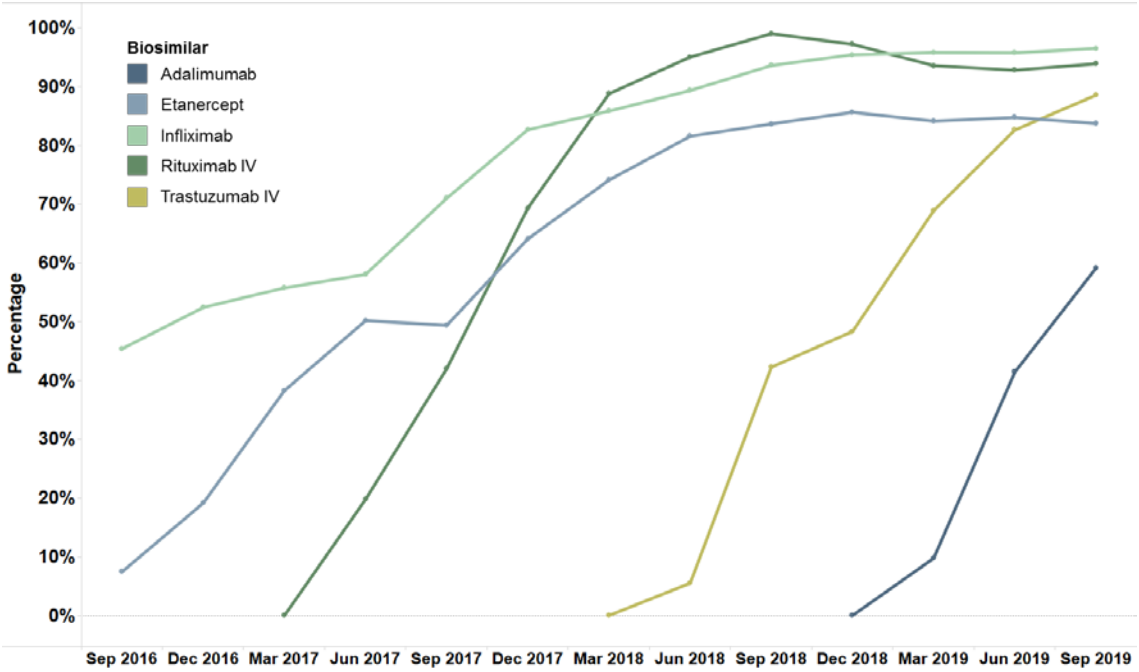
- Android
- Apple

2.2 EFFICIENCIES

2.2.1 Best value biological medicines

***Purpose*:**
To ensure prescribing of best value biological medicines supports cost-efficient prescribing in primary and secondary care in Wales.
Unit of measure:
Quantity of best value biological medicines prescribed as a percentage of total 'biosimilar' plus 'reference' product.
Target for 2020-2021:
Increase the appropriate use of cost-efficient biological medicines, including biosimilar medicines.

Figure 21. Trend in biosimilar percentage to quarter ending September 2019



Background and evidence

Biological medicines account for a significant expenditure within the NHS. Continuing development of biological medicines, including biosimilar medicines, creates increased choice for patients and clinicians, increased commercial competition and possible enhanced value propositions for individual medicines. This indicator supports the ongoing work within NHS Wales to increase the use of the best value intervention wherever possible within healthcare.

The list of biological medicines being reported on will be determined by the requirements of the service. The biological medicines with biosimilar versions available for use within NHS Wales that are currently being reported on within this NPI in 2020–2021 are:

- Infliximab – Inflectra®
- Etanercept – Benepali®▼, Erelzi®▼
- Rituximab – Truxima®▼
- Trastuzumab – Ontruzant®▼
- Adalimumab – Amgevita®▼, Hulio®▼, Hyrimoz®▼, Imraldi®▼
- Teriparatide – Movymia®▼, Terrosa®▼

Within this efficiency indicator, 'best value' is primarily derived from cost data as any meaningful outcome data is not retrievable from within the current prescribing systems. Currently, for all of the biological medicines being reported on, the 'best value' option is the biosimilar version. The prices of the biosimilar and reference options for each of these biological medicines are monitored on a regular basis, and the 'best value' option will be highlighted within the quarterly reports and biosimilar efficiencies dashboard.

It is the responsibility of the clinician, in consultation with the patient, to make the decision about whether to prescribe a biological medicine and whether that should be the original reference medicine or a biosimilar medicine. Switching between a reference product and its biosimilar (and indeed amongst biosimilar medicines) should be managed at the discretion of the individual prescriber in partnership with the patient, and with appropriate monitoring in place. The NHS England publication *What is a biosimilar medicine?* provides supportive information for the use of biosimilar medicines[114].

Where AWMSG or NICE has already recommended the reference biological medicine, the same guidance will normally apply to any biosimilars[115,116]. However, where a review of the evidence for a biosimilar medicine is considered necessary, NICE will consider producing a further evidence summary[115].

Useful resources

- AWTTC (2019) Biosimilar Best Practice Day
- AWTTC (2019) SPIRA – Biosimilar Efficiencies
- European Medicines Agency (2017) Biosimilars in the EU
- European Commission (2016) What I need to know about Biosimilar Medicines: Information for patients
- NHS England (2019) What is a Biosimilar Medicine?
- The Cancer Vanguard (2017) Biosimilars frequently asked questions for healthcare professionals
- AWMSG (2019) Position statement for biosimilar medicines
- NICE Position statement for biosimilar medicines
- NICE (2018) Key Therapeutic Topic 15: Biosimilar medicines
- MHRA (2008) Drug safety update. Biosimilar products
- European Medicines Agency (2018) European public assessment reports
- The Cancer Vanguard (2018) Biosimilars adoption

2.2.2 Insulin

***Purpose*:**
To encourage a reduction in the prescribing of long-acting insulin analogues in primary and secondary care in line with NICE guidance to maximise cost-effectiveness in Wales.
Unit of measure:
Items/number of long-acting insulin analogues as a percentage of total long- and intermediate-acting insulin prescribed.
Target for 2020–2021:
Reduce prescribing of long-acting insulin analogues and achieve prescribing levels below the Welsh average.

Table 8. Use of long-acting insulin analogues as a percentage of long- and intermediate-acting insulin in primary and secondary care across NHS Wales for 2017–2019

	2017–2018				2018–2019			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Percentage of long-acting insulin analogues (primary care)	88.9	88.5	88.3	88.1	88.1	87.9	88.0	88.1
Percentage of long-acting insulin analogues (secondary care)	79.2	80.1	81.8	82.0	81.2	81.9	81.3	81.8

Figure 22. Trend in long-acting analogue prescribing as a percentage of total long- and intermediate-acting insulin prescribed in primary care to quarter ending September 2019

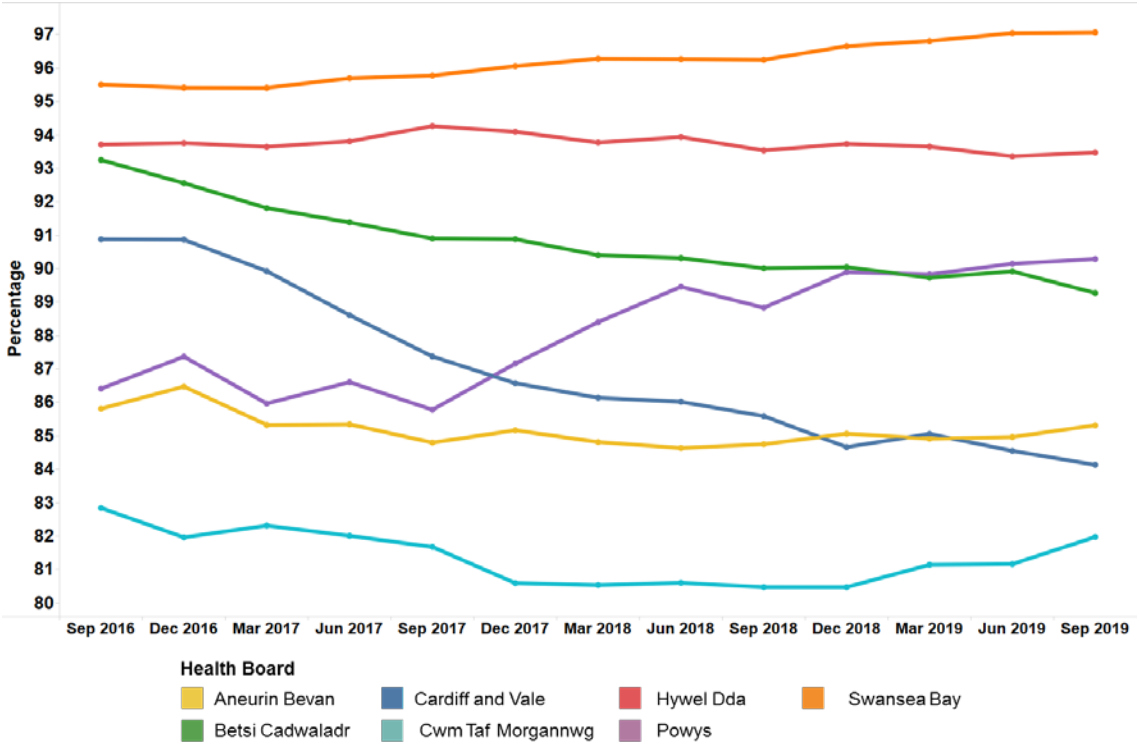
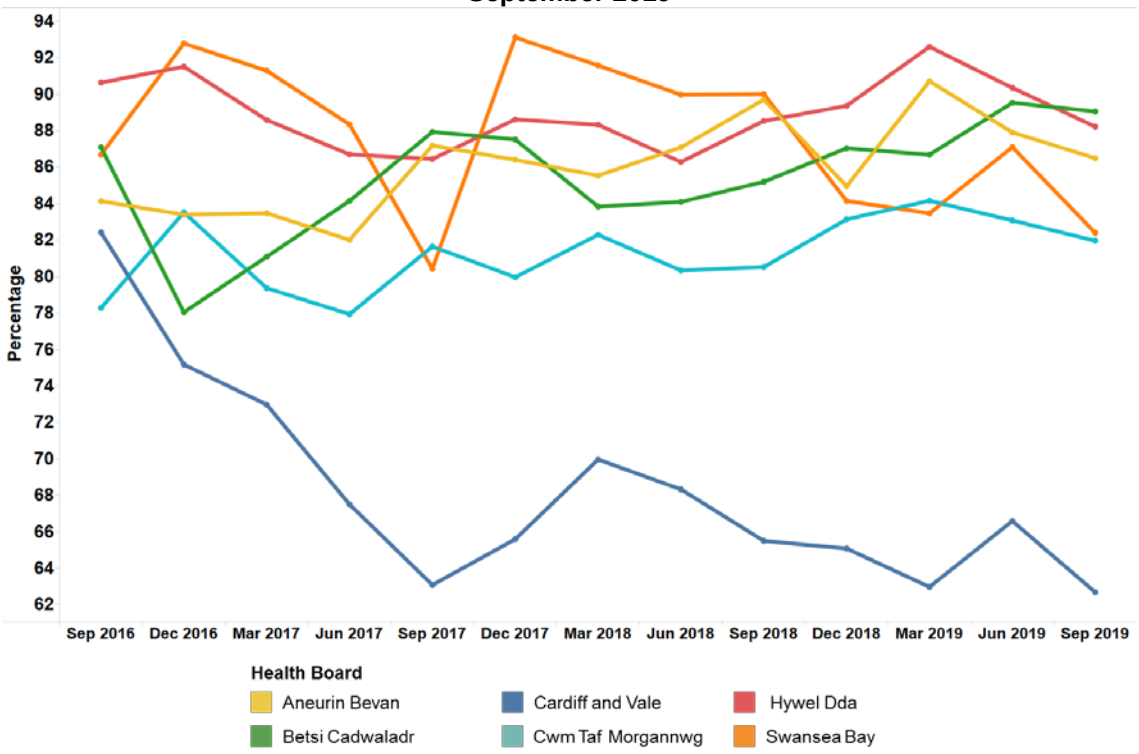


Figure 23. Trend in long-acting analogue prescribing as a percentage of total long- and intermediate-acting insulin prescribed in secondary care to quarter ending September 2019



Background and evidence

The 2015 NICE Guideline (NG) 28 on the management of type 2 diabetes mellitus recommends that when control of blood glucose remains or becomes inadequate on oral anti-diabetic therapy, then insulin should be considered as the next treatment option. In the absence of evidence to suggest the superiority of the long-acting insulin analogues over neutral protamine Hagedorn (NPH) insulin in terms of improved safety, glycaemic control or reduction of long-term diabetic complications, a cautious approach to prescribing the long-acting insulin analogues is advised[117].Therefore, human isophane (NPH) insulin is recommended as the first-choice regimen for the majority of people[118]. Despite the recommendations outlined in NG28, the prescribing cost for long-acting insulin analogues was approximately £9.46 million across NHS Wales in 2018–2019[18,119].

The majority of insulin prescribing is initiated by a specialist clinician within secondary care and therefore review of hospital prescribing practice will affect the primary care prescribing trend. Prescribing will often continue in the primary care setting and it is therefore important to consider data for primary and secondary care.

Useful resources

- AWTTC Best Practice Day 2019 Presentation by Lindsay George: Prudent prescribing of human versus analogue insulin (YouTube)
- NICE (2015) NG28: Type 2 diabetes in adults: management
- Cochrane (2007) Long-acting analogues versus NPH insulin (human isophane insulin) for type 2 diabetes mellitus

2.2.3 Low value for prescribing

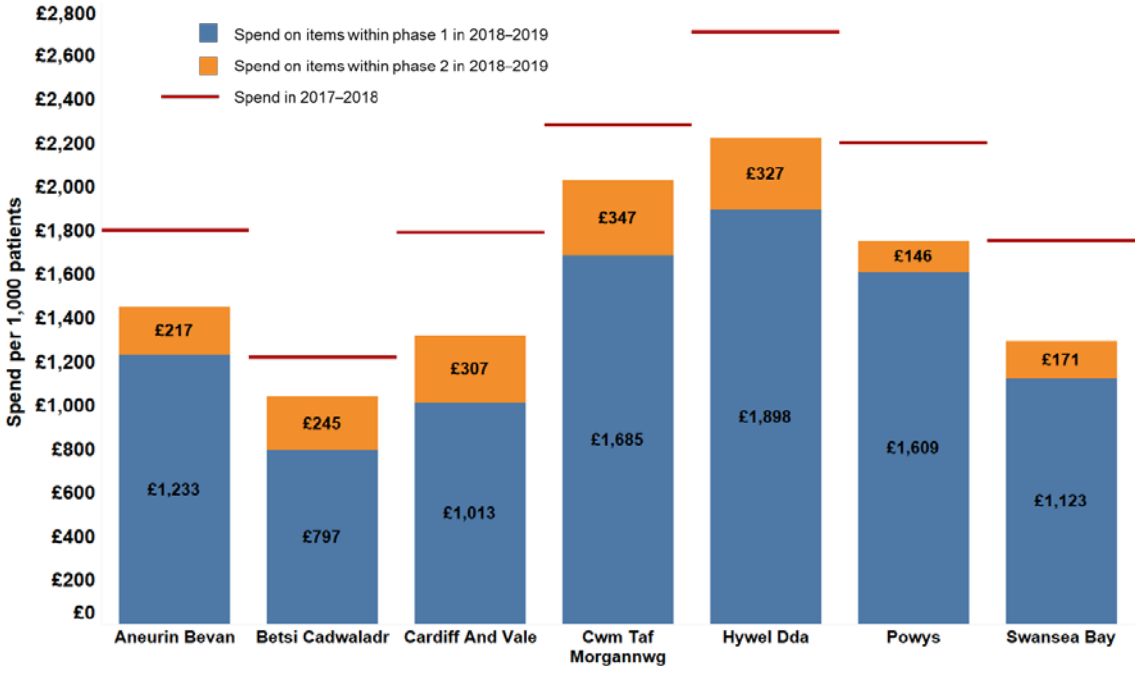
***Purpose*:**
To drive a reduction in the prescribing of items considered as not suitable for routine prescribing in Wales
Unit of measure:
Low value for prescribing UDG spend per 1,000 patients
Target for 2020–2021:
Maintain performance levels within the lower quartile or show a reduction towards the quartile below

The aim of the *Low Value for Prescribing in NHS Wales* initiative is to minimise the prescribing of items that offer a limited clinical benefit to patients and where more cost-effective treatments *may be* available. The first paper in the initiative, entitled *Medicines Identified as Low Priority for Funding in NHS Wales* was endorsed by AWMSG in 2017, and the second paper was endorsed in 2018[120,121]. Five items/item groups were identified for the purposes of the first phase of this initiative, with an additional four included in the second phase. The paper detailing the items included in the third phase of this initiative will be endorsed and published in February 2020.

Within 2018–2019 there has been a decrease achieved in the overall spend on these items of £1.12m. Although this cannot be taken as a direct overall saving to the NHS in Wales it does confirm a decreased spend on the items identified as not suitable for routine prescribing.

Figure 24 illustrates the differences in spend between 2017–2018 and 2018–2019 for the nine items/item groups within the low priority for funding initiative by health board. Also indicated is how the items within phase 1 and phase 2 make up the total spend within 2018–2019.

Figure 24. Spend per 1000 patients on the medicines identified as low value for prescribing by health boards in 2018–2019, compared to 2017–2018



Useful resources

- AWMSG (2017) Medicines Identified as Low Priority for Funding in NHS Wales – paper 1
- AWMSG (2018) Medicines Identified as Low Priority for Funding in NHS Wales – paper 2
- AWMSG (2020) Items Identified as Low Value for Prescribing in NHS Wales – paper 3
- AWTTC (2020) SPIRA - Low Value for Prescribing Dashboard

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APPENDIX 1. ANTICHOLINERGIC EFFECT ON COGNITION (AEC) SCORE[93]

Drugs with AEC score of 0		Drugs with AEC score of 1	Drugs with AEC score of 2	Drugs with AEC score of 3
Alprazolam	Lorazepam	Amiodarone	Amantadine	Alimemazine (trimeprazine)
Amlodipine	Losartan	Aripiprazole	Chlorphenamine	Amitriptyline
Amoxicillin	Lovastatin	Bromocriptine	Desipramine	Atropine
Aspirin	Lurasidone	Carbamazepine	Dicycloverine (dicyclomine)	Benztropine
Atenolol	Meloxicam	Citalopram	Dimenhydrinate	Chlorpromazine
Atorvastatin	Metoclopramide	Diazepam	Diphenhydramine	Clemastine
Bupropion	Metopralol	Domperidone	Disopyramide	Clomipramine
Cephalexin	Moclobemide	Fentanyl	Levomepromazine	Clozapine
Cetirizine	Morphine	Fluoxetine	Olanzapine	Cyproheptadine
Chlordiazepoxide	Naproxen	Fluphenazine	Paroxetine	Dothiepin (dosulepin)
Cimetidine	Omeprazole	Hydroxyzine	Pethidine	Doxepin
Ciprofloxacin	Paracetamol	Iloperidone	Pimozide	Hyoscine hydrobromide
Clopidogrel	Pantoprazole	Lithium	Prochlorperazine	Imipramine
Darifenacin	Pravastatin	Mirtazepine	Promazine	Lofepramine
Diclofenac	Propranolol	Perphenazine	Propantheline	Nortriptyline
Diltiazem	Rabeprazole	Prednisolone	Quetiapine	Orphenadrine
Enalapril	Ranitidine	Quinidine	Tolterodine	Oxybutynin
Entacapone	Risperidone	Sertindole	Trifluoperazine	Procyclidine
Fexofenadine	Rosiglitazone	Sertraline		Promethazine
Fluvoxamine	Simvastatin	Solifenacin		Trihexyphenidryl (benzhexol)
Furosemide	Theophylline	Temazepam		Trimipramine
Gabapentin	Thyroxine (levothyroxine)			
Gliclazide	Tramadol			
Haloperidol	Trazodone			
Ibuprofen	Trimethoprim			
Ketorolac	Trospium			
Lamotrigine	Venlafaxine			
Levadopa	Valproate			
Lisinopril	Warfarin			
Loperamide	Ziprasidone			
Loratadine	Zolpidem			

Score 3	Review and withdraw or switch
Score 2	Review and withdraw or switch
Score 1	Caution required
Score 0	Safe to use

APPENDIX 2. OPIOID EQUIVALENCE TABLE

(Values are approximate – see notes below)

Reproduced with kind permission from a resource developed by Emma Davies, Advanced Pharmacist Practitioner in Pain Management, Swansea Bay University Health Board.

<table>
<tr><th>Morphine</th><th>Oxycodone</th><th>Fentanyl</th><th>Buprenorphine</th><th>Codeine phosphate/ Dihydrocodeine</th><th>Tramadol</th><th>Tapentadol (Palexia® SR)</th></tr>
<tr><th>Oral (mg)</th><th>Oral (mg)</th><th>Transdermal patch (mcg/hr)</th><th>Transdermal patch (mcg/hr)</th><th>Oral (mg)</th><th>Oral (mg)</th><th>Oral (mg)</th></tr>
<tr><td>24hr total dose</td><td>24hr total dose</td><td>Patch strength
STABLE PAIN ONLY</td><td>Patch strength
STABLE PAIN ONLY</td><td>24hr total dose</td><td>24hr total dose</td><td>24hr total dose</td></tr>
<tr><td>5</td><td rowspan="3"></td><td rowspan="5"></td><td></td><td>60</td><td>50</td><td rowspan="4"></td></tr>
<tr><td>10</td><td rowspan="2">5</td><td>120</td><td>100</td></tr>
<tr><td>15</td><td></td><td>150</td></tr>
<tr><td>20</td><td>10</td><td rowspan="2">10</td><td>240</td><td>200</td></tr>
<tr><td>30</td><td>15</td><td rowspan="6"></td><td>300</td></tr>
<tr><td>40</td><td>20</td><td rowspan="2">12</td><td>20</td><td>400</td><td rowspan="2">100</td></tr>
<tr><td>60</td><td>30</td><td rowspan="2">35</td><td rowspan="5"></td></tr>
<tr><td>80</td><td>40</td><td rowspan="3">25</td><td rowspan="2">200</td></tr>
<tr><td>100</td><td>50</td><td rowspan="2">52.5</td></tr>
<tr><td>120</td><td>60</td><td>300</td></tr>
<tr><td colspan="7">Doses above this level are not recommended in chronic pain
If patient is still complaining of pain despite opioids at this level, then opioids are not working and should be reduced and stopped even if there is no other treatment available.</td></tr>
<tr><td>140</td><td>70</td><td rowspan="2">37</td><td rowspan="2">70</td><td rowspan="6"></td><td rowspan="6"></td><td></td></tr>
<tr><td>160</td><td>80</td><td rowspan="2">400</td></tr>
<tr><td>180</td><td>90</td><td rowspan="2">50</td><td rowspan="4">105</td></tr>
<tr><td>200</td><td>100</td><td>500</td></tr>
<tr><td>240</td><td>120</td><td>62</td><td rowspan="4"></td></tr>
<tr><td>280</td><td>140</td><td rowspan="2">75</td></tr>
<tr><td>320</td><td>160</td><td rowspan="2">140</td></tr>
<tr><td>360</td><td>180</td><td>100</td></tr>
</table>

Each row is roughly equivalent e.g.: 60 mg bd oral morphine = 30 mg bd oral oxycodone = 25 mcg/hr fentanyl patch

NB: This is to be used as a guide rather than a set of definite equivalences. Some doses suggested may be 'off-licence', but are based on clinical experience. Refer to the Summary of Product Characteristics for further details. Most data on doses are based on single-dose studies so it may be less accurate in chronic use where similar data are unavailable. Consider that individual patients may metabolise different drugs at varying rates. **The advice is to always calculate doses using morphine as standard and to adjust them to suit the patient and the situation – consider making a reduction in morphine equivalence dose of 20–50% when changing drugs.** Caution should be used in renal and hepatic failure. Avoid patch use in unstable pain.