This report 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 2071 6900

This document should be cited as:
GLOSSARY

ADQs – average daily quantity
ADRs – adverse drug reactions
AEC – Anticholinergic Effect on Cognition
AWMSG – All Wales Medicines Strategy Group
AWTTC – All Wales Therapeutics and Toxicology Centre
BTS – British Thoracic Society
CEPP – Clinical Effectiveness Prescribing Programme
CKD – chronic kidney disease
COX2 – cyclooxygenase-2
DDDs – defined daily doses
DVLA – Driver and Vehicle Licensing Agency
GFR – glomerular filtration rate
GI – gastrointestinal
ICS – inhaled corticosteroids
MHR – Medicines and Healthcare products Regulatory Agency
MRSA – methicillin-resistant Staphylococcus aureus
NICE – National Institute for Health and Care Excellence
NPH – neutral protamine Hagedorn
NPI – National Prescribing Indicators
NSAIDs – non-steroidal anti-inflammatory drugs
PHW – Public Health Wales
PPIs – proton pump inhibitors
PPS – Point Prevalence Survey
PUs – prescribing units
RCGP – Royal College of General Practitioners
SIGN – Scottish Intercollegiate Guidelines Network
SSRIs – selective serotonin reuptake inhibitors
STAR-PUs – specific therapeutic group age-sex related prescribing units
UTI – urinary tract infection
WAPSU – Welsh Analytical Prescribing Support Unit
WeMeReC – Welsh Medicines Resource Centre
YCC – Yellow Card Centre
PROTON PUMP INHIBITORS

**Purpose:** To encourage appropriate use of PPIs.

**Unit of measure:** PPI DDDs per 1,000 PUs.

**Why?**

- Safety concerns regarding long-term use, e.g. *Clostridium difficile* infection, increased risk of bone fractures, and increased risk of mortality in older people.

**How?**

- Ensure that people with dyspepsia are initially offered lifestyle advice on healthy eating, weight reduction, smoking cessation and avoiding food and drink associated with dyspepsia (e.g. alcohol, coffee, chocolate and fatty foods).
- Review medications for possible causes of dyspepsia (e.g. calcium antagonists, nitrates, theophyllines, bisphosphonates, corticosteroids).
- If medication is required, first-line treatment should be with an alginate either ‘as required’ or regularly. 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.
- All patients receiving a PPI should be offered an annual review and are encouraged to step down from treatment doses where appropriate.
- Tapering the dose of PPIs in patients who have been taking them for a long time is recommended to reduce the risk of rebound hypersecretion; in addition, reassuring patients on how to manage this with simple antacids might avoid the re-initiation of the PPI.
- 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.

**Useful resources**

- WAPSU (2013) All Wales PPI and Dyspepsia Resource Pack
- AWMSG (2014) Polypharmacy: Guidance for Prescribing
- WeMeRec (2015) Proton pump inhibitors bulletin

INHALED CORTICOSTEROIDS

**Purpose:** To encourage the routine review of ICS in people with asthma, particularly those on high doses, encouraging step down of the dose when clinically appropriate.

**Unit of measure:** High-strength ICS items as a percentage of all ICS prescribing.

**Why?**

- Prolonged use of high-dose ICS carries a risk of systemic side effects, such as adrenal suppression or crisis, growth retardation in children and young people, decrease in bone mineral density, cataracts and glaucoma. In addition, the prolonged use of high doses of ICS carries the risk of a range of psychological or behavioural effects (e.g. psychomotor hyperactivity, sleep disorders, anxiety, depression and aggression).

(Taken from NPS MedicinesWise ICS dose–response [2014])

**How?**

- To minimise side effects from ICS in people with asthma, the BTS/SIGN British guideline on the management of asthma recommends that the dose of ICS should be titrated to the lowest dose at which effective control of asthma is maintained. ICS dose reduction should be considered every three months, decreasing the dose by approximately 25–50% each time.

**Useful resource**

SIGN (2016) SIGN 153: British guideline on the management of asthma
HYPNOTICS AND ANXIOLYTICS

**Purpose:** To encourage a reduction in the inappropriate prescribing of hypnotics and anxiolytics.

**Unit of measure:** Hypnotic and anxiolytic ADQs per 1,000 STAR-PUs.

**Why?**
- There has been concern with regard to the high level of hypnotic and anxiolytic prescribing within NHS Wales, with the substance misuse strategy of the Welsh Government (*Working together to reduce harm*) calling for the reduction of inappropriately prescribed benzodiazepines.
- The problems associated with benzodiazepines (development of tolerance, dependence potential and withdrawal causing rebound insomnia) are well known.
- Hypnotics and anxiolytics are known to significantly increase the risk of falls.

**How?**
- Hypnotics should only be considered after non-drug therapies have been explored. Hypnotics should be used in the lowest dose possible, for the shortest duration possible and in strict accordance with their licensed indications: no more than 4 weeks.
- Benzodiazepines should not be offered for the treatment of generalised anxiety disorder except as a short-term measure during crises.
- Consider reducing hypnotics and anxiolytics where appropriate.

**Useful resources**
- AWMSG (2016) *Educational Pack: Material to Support Appropriate Prescribing of Hypnotics and Anxiolytics across Wales*
- AWMSG (2014) *Polypharmacy: Guidance for Prescribing*

ANALGESICS

1. **Purpose:** To encourage the appropriate use and review of tramadol, minimising the potential for diversion and misuse.

**Unit of measure:** Tramadol DDDs per 1,000 patients.

**Why?**
- While there is a recognised place in pain management for tramadol, there are concerns regarding abuse, dependence and deaths involving tramadol, in addition to the risks associated with misuse and diversion.
- Tramadol produces analgesia by two mechanisms: an opioid effect and an enhancement of the serotonergic and adrenergic pathways. This unique dual-action pharmacological profile of tramadol increases the risk of adverse effects seen in overdose.
- Hallucinations, confusion and convulsions, as well as rare cases of dependence and withdrawal symptoms, have been reported with tramadol at therapeutic doses.
- Tramadol should be used with caution in patients taking concomitant medicines that can lower the seizure threshold, such as tricyclic antidepressants or SSRIs. The use of tramadol is contra-indicated in uncontrolled epilepsy and in patients receiving, or who have recently discontinued (within the previous two weeks) monoamine oxidase inhibitors.

**How?**
- 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 seizures, hallucinations and anxiety.
- To encourage patient engagement and concordance, a suggested approach would be to reduce the dose at each reduction step, e.g. by one 50 mg dose, and to titrate by how the patient manages, rather than by setting time limits for the next reduction.

**Useful resources**
- AWMSG (2013) *Tramadol Educational Resource Materials*
- AWMSG (2016) *Persistent pain resources*
2. **Purpose:** To encourage the appropriate use and review of opioid patches.

*Unit of measure:* Opioid patch items as a percentage of all opioid prescribing

**Why?**
- Modified-release morphine is the first-line choice when treatment with a strong opioid is required.
- Fentanyl patches have been associated with a number of life-threatening reactions and fatalities occurring as a result of inappropriate strength of fentanyl prescribed in opioid naive patients.
- Fentanyl and buprenorphine patches are not suitable for acute pain, or for patients whose analgesic requirements are changing rapidly.

**How?**
- Reserve the use of opioid patches for patients in whom oral opioids are unsuitable and whose analgesic requirements are stable.
- Fentanyl patches should only be used in patients who have previously tolerated opioids because of the risk of significant respiratory depression in opioid naive patients.
- Ensure the initial dose of opioid patch is based on a patient’s opioid history.
- Where an opioid patch is indicated, the patch with the lowest acquisition cost should be initiated.

**Useful resources**
- AWMSG (2016) [Safeguarding Users of Opioid Patches by Standardising Patient/Caregiver Counselling](#)
- PrescQIPP (2014) [Opioid patches](#)
- AWMSG (2016) [Persistent pain resources](#)

3. **Purpose:** To encourage the appropriate use and review of gabapentin and pregabalin, minimising the potential for diversion and misuse.

*Unit of measure:* Gabapentin and pregabalin DDDs per 1,000 patients

**Why?**
- While there is a recognised place in pain management for pregabalin and gabapentin, there are concerns regarding the risks associated with misuse and diversion. The number of drug-related deaths involving gabapentin or pregabalin in England and Wales is increasing, from 48 deaths in 2013 to 137 deaths in 2015.

**How?**
- If the patient has not shown sufficient benefit within eight weeks of reaching the maximum tolerated dose, gabapentin and pregabalin should be gradually reduced over a minimum of one week and then stopped.
- Caution should be exercised in prescribing pregabalin for patients with a history of substance abuse.
- Neuropathic pain management is complex, and prescribers need to make evidence-based, informed decisions based on the individual needs of the patient.

**Useful resources**
- PrescQIPP (2014) [Pregabalin in neuropathic pain](#)
- Public Health England (2014) [Advice for prescribers on the risk of the misuse of pregabalin and gabapentin](#)
- AWMSG (2016) [Persistent pain resources](#)
ANTIMICROBIAL STEWARDSHIP

Purpose: To encourage the appropriate prescribing of antibiotics.

Units of measure:
1) Total antibacterial items per 1,000 STAR-PUs.
2) Co-amoxiclav items per 1,000 patients.
   Co-amoxiclav items as a percentage of total antibacterial items.
3) Cephalosporin items per 1,000 patients.
   Cephalosporin items as a percentage of total antibacterial items.
4) Fluoroquinolone items per 1,000 patients.
   Fluoroquinolone items as a percentage of total antibacterial items.

Why?
- Overprescribing of antibiotics leads to resistance.
- The use of simple generic antibiotics and the avoidance of broad-spectrum antibiotics (e.g. co-amoxiclav, fluoroquinolones and cephalosporins) preserve these from resistance and reduce the risk of C. difficile, MRSA and resistant UTIs.

How?
- If there is evidence of bacterial infection, prescribe according to national or local guidelines.
- Where an antibiotic is indicated, prescribe the shortest effective course at the most appropriate dose.
- Document the clinical diagnosis with the reason for prescribing, or not prescribing, an antimicrobial.

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

ANTICHOLINERGIC BURDEN

Purpose: To encourage a review of patients with an AEC score of 3 or more, with the aim of reducing anticholinergic use where appropriate.

Unit of measure: Number of patients aged 75 and over with an AEC score of 3 or more for items on active repeat, as a percentage of all patients aged 75 and over.

Why?
- 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 suggesting a link to increased mortality with the number and potency of anticholinergic agents prescribed.
- Many medicines commonly prescribed to older people are not routinely recognised as having anticholinergic activity and are prescribed based on their anticipated therapeutic benefits, overlooking the risk of cumulative anticholinergic burden.

How?
- During medication review consider anticholinergic burden with the aim of avoiding, reducing doses and deprescribing medicines with anticholinergic activity where clinically possible.

Useful resources
- PrescQIPP (2016) Anticholinergic drugs bulletin
- AWMSG (2014) Polypharmacy: Guidance for Prescribing
# NON-Steroidal Anti-Inflammatory Drugs

**1) Purpose:** To ensure that the risks associated with NSAIDs are minimised by appropriate use.

**Unit of measure:** NSAID ADQs per 1,000 STAR-PUs

| Why? | There are longstanding and well recognised renal and GI safety concerns with all NSAIDs.  
|      | Additionally, there have been increasing cardiovascular safety concerns with some NSAIDs, particularly COX-2 inhibitors and diclofenac. |
| How? | If an oral NSAID is indicated, prescribing should be based on the safety profiles of individual NSAIDs or selective COX-2 inhibitors, and on individual patient risk profiles (e.g. GI and cardiovascular).  
|      | Patients should be prescribed the lowest effective dose, for the shortest duration necessary to control symptoms, in order to minimise adverse effects.  
|      | A patient’s need for symptomatic relief and response to treatment should be re-evaluated periodically. |

**Useful resources**
- AWMSG (2015) CEPP All Wales Audit: Towards Appropriate NSAID Prescribing

**2) Purpose:** To encourage appropriate use and review of NSAIDs for patients on the CKD register, and patients who are not on the CKD register but who may have CKD.

**Unit of measure:**
- Number of patients on the CKD register (CKD 3–5) who have received a repeat prescription for an NSAID within the last 3 months, as a percentage of all patients on the CKD register.  
- 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, as a percentage of all patients who are not on the CKD register but have an eGFR of < 59 ml/min.

| Why? | In patients with CKD, the chronic use of NSAIDs may be associated with disease progression, and acute use is associated with reversible decrease in GFR. |
| How? | For patients with CKD, regular review of the ongoing need for an NSAID and reassessment of the risk versus benefit is appropriate, and processes for this should be in place. |

**Useful resources**
- AWMSG (2017) CEPP National Audit: Medicines Management for CKD
YELLOW CARDS

Purpose: To encourage an increase in the number of Yellow Cards submitted by GP practices in Wales.

Unit of measure: Number of Yellow Cards submitted per practice and per health board.

Why?
- ADRs are a significant clinical problem, increasing morbidity and mortality.
- 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.
- Yellow Card reporting supports the identification and collation of ADRs, which might not have been known about before.

How?
- A strong safety culture requires good reporting of adverse events and critical incidents from across all professions and healthcare settings, as well as from patients.
- Reports can be made for all medicines including vaccines, blood factors and immunoglobulins, herbal medicines and homeopathic remedies, and all medical devices available on the UK market.

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 on-line – Yellow Card website
- MHRA web pages
- WeMeReC (2013) Pharmacovigilance Bulletin
- YCC Wales website
- NHS Scotland e-learning modules on ADRs
SECONDARY CARE

INSULIN PRESCRIBING

**Purpose:** Ensure long-acting analogue insulin prescribing in type 2 diabetes mellitus is in line with NICE guidance to maximise cost-effective prescribing within Wales.

**Unit of measure:** Items/number of long-acting insulin analogues expressed as a percentage of total insulin prescribed within primary and secondary care.

**Why?**
- In type 2 diabetes mellitus when blood glucose control is inadequate on oral anti-diabetic therapy, insulin should be considered as the next treatment option.
- Human isophane (NPH) insulin is recommended as the first choice regimen.
- There is an absence of evidence to suggest superiority of the long-acting insulin analogues over NPH insulin.

**How?**
- Patients should have the opportunity to make informed decisions about their care and treatment. Discuss with the patient the comparative effectiveness of NPH insulin to the long-acting insulin analogues and ascertain any preference for a specific insulin type.
- When patients are commenced on an insulin therapy, a structured programme employing active dose titration should be employed. This programme should encompass injection technique, continuing telephone support, self-monitoring, dose titration to target levels, dietary understanding, DVLA guidance, management of hypoglycaemia, management of acute changes in plasma glucose control, and support from an appropriately trained and experienced healthcare professional.

**Useful resources**
- NICE (2015) NG28: Type 2 diabetes in adults: management
- Cochrane (2007) Long-acting analogues versus NPH insulin

PRESCRIBING OF BIOSIMILARS

**Purpose:** Ensure prescribing of biological medicines is in line with AWMSG guidance and supports cost-effective prescribing within Wales.

**Unit of measure:** Quantity of biosimilar medicines prescribed as a percentage of total ‘reference’ product plus biosimilar.

**Why?**
- Biological medicines account for a significant expenditure within NHS Wales. Biosimilar medicines are biological medicines that have been developed as highly similar and clinically equivalent to their ‘reference’ or ‘originator’ medicine.
- A number of ‘reference’ biological medicines have lost, or will lose, their patent protection within the next five years, creating increased commercial competition.
- Although individual health boards’ contracting prices for biosimilar and reference medicines may vary, there are expected to be significant cost-saving opportunities from the use of the most cost-effective biological medicine.

**How?**
- Where AWMSG or NICE have recommended the ‘reference’ medicine, the same guidance will normally apply to the biosimilar.
- At the time of dispensing there must not be automatic substitution of the reference product with a biosimilar medicine. Therefore, the clinician in consultation with the patient should make the decision on whether the reference or biosimilar biological medicine will be prescribed for the patient.
- All biological medicines, including biosimilars, must be prescribed by brand name.
- Current biosimilar medicines for use within NHS Wales are:
  - Infliximab – Inflectra®
  - Filgrastim – Nivestim®, Zarzio®
  - Insulin glargine – Abasaglar®
  - Etanercept – Benepali®

**Useful resources**
ANTIBIOTIC SURGICAL PROPHYLAXIS

**Purpose:** To encourage the appropriate prescribing of antibiotics. The development of NPIs for antibiotic prescribing supports one of the key elements of the Welsh Antimicrobial Resistance Programme: to inform, support and promote the prudent use of antimicrobials.

**Unit of measure:** Proportion of elective colorectal patients receiving surgical prophylaxis for more than 24 hours.

**Why?**
- The use of antibiotics for infection prophylaxis carries a risk of adverse drug reactions (including *C. difficile* associated diarrhoea) and increased prevalence of antibiotic resistant bacteria.
- For patients undergoing colorectal surgery, a single therapeutic dose of intravenous antibiotic is suitable in the majority of cases. Certain circumstances may require a longer course of antibiotic prophylaxis up to a maximum of 24 hours.
- PPS data in 2015 reported 26% of antibiotic surgical prophylaxis, for a range of surgery types, was administered for greater than 24 hours.

**How?**
- Antibiotic choice should reflect local, disease-specific information about the common pathogens and their antimicrobial susceptibility. Narrow-spectrum, less expensive antibiotics should be the first choice.
- Any additional prophylactic antibiotic doses should be confirmed and justified within the patient’s notes.

**Useful resources**
- PHW (2016) [Antimicrobial Usage in Secondary Care in Wales](#)
- PHW (2016) [Report on the PPS of Antimicrobial Prescribing in Secondary Care in Wales](#)
- PHW (2016) [Antibacterial Resistance in Wales](#)

**NOTES**
Implementation of the 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.