All Wales Medicines Strategy Group

Grŵp Strategaeth Meddyginiaethau Cymru Gyfan

National Prescribing Indicators 2018–2019

Supporting Information for Prescribers

February 2018

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).

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NHS WALES GIG CYMRU

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GLOSSARY

ADQ – 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
CEPP – Clinical Effectiveness Prescribing Programme
CHC – combined hormonal contraceptive
CKD – chronic kidney disease
DDD – defined daily dose
DVLA – Driver and Vehicle Licensing Agency
eGFR – estimated glomerular filtration rate
MHRA – Medicines and Healthcare products Regulatory Agency
MRSA – methicillin-resistant *Staphylococcus aureus*
NICE – National Institute for Health and Care Excellence
NPH – neutral protamine Hagedorn
NPIs – National Prescribing Indicators
NSAIDs – non-steroidal anti-inflammatory drugs
PHW – Public Health Wales
PPIs – proton pump inhibitors
PPS – Point Prevalence Survey
PU – prescribing unit
RCGP – Royal College of General Practitioners
SIGN – Scottish Intercollegiate Guidelines Network
SSRIs – selective serotonin reuptake inhibitors
STAR-PU – specific therapeutic group age-sex related prescribing unit
WAPSU – Welsh Analytical Prescribing Support Unit
WeMeReC – Welsh Medicines Resource Centre
YCC – Yellow Card Centre

1.0 SAFETY INDICATORS

1.1 PRESCRIBING SAFETY INDICATORS

***Purpose*:** To identify patients at high risk of ADRs and medicines-related harm in primary care.
Unit of measure:

- Number of patients with a peptic ulcer who have been prescribed NSAIDs without a PPI as a percentage of all patients.
- Number of patients with asthma who have been prescribed a beta-blocker as a percentage of all patients.
- Number of patients with concurrent prescriptions of verapamil and a beta-blocker as a percentage of all patients.
- Number of female patients with a past medical history of venous or arterial thrombosis who have been prescribed combined hormonal contraceptives, as a percentage of all female patients.
- Number of female patients with a current prescription of oestrogen-only hormone replacement therapy without any hysterectomy READ/SNOMED codes, as a percentage of all female patients.
- Number of patients with concurrent prescriptions of warfarin and an oral NSAID as a percentage of all patients.
- Number of patients under 12 with a current prescription of aspirin, unless due to a specialist recommendation, as a percentage of all patients.
- 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), as a percentage of all patients aged 65 years or over.
- Number of patients aged 65 years or over prescribed an antipsychotic, as a percentage of all patients aged 65 years or over.
- 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.
- 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, 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?

- This NPI is facilitating the move towards a more patient-focussed approach considering whether the right patients are getting the right medicines. This is intended to reduce the number of ADRs experienced by patients.
- In the UK, it is estimated that around 6.5% of hospital admissions are related to ADRs.
- ADRs can often be predictable, making it possible to identify potential causes and address them before actual patient harm occurs. Therefore a process of identifying patients electronically could enable intervention and help avoid harm.
- The PINCER study demonstrated that such an approach is an effective method for reducing the frequency of a range of medication errors.

How?

- Review patients identified as being at high risk of ADRs and medicines-related harm.
- No target has been set for the 2018–2019 NPI as this can provide a baseline for future years.

Useful resources

- The Lancet (2012) PINCER study
- MHRA (2014) Antipsychotics learning module
- WeMeReC (2015) Medicines-related admissions
- AWMSG (2014) Polypharmacy: Guidance for Prescribing
- PrescQIPP (2016) Bulletin 140: Anticholinergic drugs
- AWMSG (2015) CEPP All Wales Audit: Towards Appropriate NSAID Prescribing
- AWMSG (2017) CEPP National Audit: Medicines Management for Chronic Kidney Disease (CKD)

1.2 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 ADQs per 1,000 STAR-PUs.

Why?

- 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.
- The problems associated with benzodiazepines (e.g. tolerance, dependence, withdrawal causing rebound insomnia) are well known, and the number of deaths associated with benzodiazepines has increased.
- 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

1.3 ANALGESICS

1.3.1 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.

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 ADRs. 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 according to 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

1.3.2 OPIOID PATCHES

***Purpose*:** To encourage the appropriate use and review of opioid patches in primary care, minimising the potential for diversion, misuse and ADRs.

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.
- There have been reports of life-threatening reactions and fatalities from fentanyl overdose, with a number of incidents occurring as a result of inappropriate strength of fentanyl patches 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

1.3.3 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

Why?

- While there is a recognised place in pain management for gabapentin and pregabalin, there are concerns regarding the risks associated with dependence, diversion and misuse.
- There has been an increase in the number of deaths where gabapentin or pregabalin was mentioned on the death certificate in England and Wales, from 12 deaths registered in 2012 to 170 deaths registered in 2016.

How?

- 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 relief.
- If the patient has not shown sufficient benefit within eight weeks of reaching the maximum tolerated dose, pregabalin should be reduced and stopped.
- Gabapentin and pregabalin can be reduced over a minimum of one week; however, a more gradual dose taper reducing the daily dose by a maximum of 300 mg every four days for gabapentin and by a maximum of 50–100 mg per week for pregabalin, allows observation of emergent symptoms that may have been controlled by gabapentin or pregabalin.
- Caution should be exercised in prescribing gabapentin or 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 (2016) Neuropathic pain: Pregabalin and gabapentin prescribing
- Public Health England (2014) Advice for prescribers on the risk of the misuse of pregabalin and gabapentin
- AWMSG (2016) Persistent pain resources

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.

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

2.0 ANTIMICROBIAL STEWARDSHIP INDICATORS

2.1 TOTAL ANTIBACTERIAL ITEMS

***Purpose*:** To encourage the appropriate prescribing of all antibiotics in primary care.
Units of measure: Total antibacterial items per 1,000 STAR-PUs.

Why?
- The widespread and often excessive usage of antimicrobials in one of the main factors contributing to the increasing emergence of antimicrobial resistance.

How?
- 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 and 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

2.2 4C ANTIMICROBIALS

Purpose: To encourage a reduction in variation and reduce overall prescribing of the 4C antimicrobials (co-amoxiclav, cephalosporins, fluoroquinolones and clindamycin).
Unit of measure:
4C items combined, per 1,000 patients.
4C items combined, as a percentage of total antibacterial items.

Why?
- The use of simple generic antibiotics and the avoidance of broad-spectrum antibiotics (e.g. co-amoxiclav, cephalosporins, fluoroquinolones and clindamycin) preserve these from resistance and reduce the risk of *C. difficile*, MRSA and resistant urinary tract infections.
- 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.
- The most commonly implicated antibiotics in *C. difficile* infection include clindamycin, cephalosporins, fluoroquinolones and co-amoxiclav.

How?
- These antimicrobials have a very useful role in specific clinical situations and should be reserved for use as per local guidelines.

2.3 PROPHYLACTIC ANTIBIOTICS IN COLORECTAL SURGERY

Purpose: To encourage appropriate antimicrobial prophylaxis for colorectal surgical patients in secondary care.
Unit of measure: Proportion of elective colorectal patients receiving a single dose antimicrobial for surgical prophylaxis.

Why?
- The use of antibiotics for infection prophylaxis carries a risk of ADRs (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.

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 in 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

3.0 EFFICIENCY INDICATORS

3.1 PROTON PUMP INHIBITORS

Purpose: To encourage appropriate use of PPIs in primary care.

Unit of measure: DDDs per 1,000 PUs.

Why?

- Safety concerns associated with long-term PPI use have been raised, e.g. *C. difficile* infection, fractures and hypomagnesaemia.
- Other possible serious adverse effects include acute interstitial nephritis, vitamin B_{12} deficiency and rebound acid hypersecretion syndrome.

How?

- Only consider for short courses (4 weeks) where needed.
- If symptoms continue or recur, a PPI can be continued at the lowest possible dose to control symptoms or on an 'as-required' basis.
- 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.
- 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

- AWMSG (2018) Safe Use of Proton Pump Inhibitors [Link when published]
- AWMSG (2014) Polypharmacy: Guidance for Prescribing
- WeMeReC (2015) Proton pump inhibitors bulletin
- PrescQIPP (2015) Bulletin 92: Safety of long term PPIs

3.2 BIOSIMILARS

Purpose: To ensure prescribing of biological medicines supports cost-effective prescribing in 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 in 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 their patent protection, or will lose it within the next five years, creating increased commercial competition.
- Although individual health boards' contracting prices, as well as national 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 has 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 biological medicines with biosimilar versions for use in NHS Wales that will be reported on for the NPI in 2018–2019 are:
  - Infliximab – Inflectra®▼
  - Etanercept – Benepali®▼
  - Rituximab – Truxima®▼
  - Insulin glargine – Abasaglar®▼

Useful resources

- NHS England (2015) What is a biosimilar medicine?

3.3 INSULIN

Purpose: To encourage a reduction in the prescribing of long-acting insulin analogues in line with NICE guidance to maximise cost-effectiveness in Wales.

Unit of measure: Items/number of long-acting insulin analogues expressed as a percentage of total long- and intermediate-acting insulin prescribed in 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 the specific insulin types and ascertain any preference.
- When patients are started on an insulin therapy, a structured programme of active dose titration should be employed. In addition this programme should also cover injection technique, continuing telephone support, self-monitoring, 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

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.