NORTHERN IRELAND
MEDICINES MANAGEMENT

Health and Social Care Board

Deprescribing Supplement

May 2019

Background

Multimorbidity is a major issue facing general practice: one in four adults in the UK have two or more long term conditions (multimorbidity), rising to two in three in people aged over 65 years. For the patient, this can mean that they are taking a large number of medicines (polypharmacy). Clinical guidelines and care pathways have contributed to this increase in polypharmacy, where patients are prescribed many medicines on a continuous basis, often with insufficient or no review.

It is important to recognise that polypharmacy can be appropriate (well-managed and results in improved health outcomes) or problematic (associated with a high risk of interactions, adverse events, etc.). Therefore, polypharmacy requires an individualised, patient-centred approach.

Deprescribing is an important element of medicines optimisation and involves identifying the point at which drugs are no longer providing a worthwhile benefit (and may actually be causing harm).

The purpose of this newsletter supplement is to highlight therapeutic areas that could be targeted for a medication review, with the possibility of stopping or reducing the medicine(s). This list is not exhaustive.

Benefits of deprescribing

- Reduces potentially problematic polypharmacy
- Improves quality of life
- Avoids worsening of disease
- Reduces pill burden
- Reduces risk of adverse effects and drug interactions

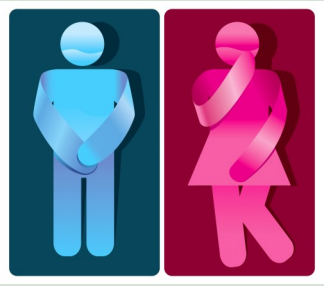
Areas of focus

- Drugs for over-active bladder
- Antidepressants
- Bisphosphonates
- Betahistine
- Mucolytics
- Benzodiazepines

Pain medicines:

- Pregabalin and Gabapentin
- Opioids
- Co-proxamol
- Lidocaine plasters
- Methocarbamol

Drugs for overactive bladder



Overactive bladder (OAB) is the term given to a group of symptoms of urinary urgency, with or without urgency urinary incontinence, usually with increased daytime frequency and nocturia. The incidence of OAB is estimated at 11.8% and, like many chronic diseases, OAB is a challenging condition to manage. Similar to other chronic conditions, the management of OAB should provide holistic care with adequate patient counselling and support. Guidelines emphasise the importance of conservative treatment including lifestyle advice and careful assessment including the use of a voiding diary. Ideally patients should be referred to community continence advisers before treatment is initiated. Clinicians and patients should consider carefully the risks and benefits before commencing treatment with medication.

What's the problem?

Antimuscarinics prescribed for OAB contribute to the overall anticholinergic burden of a patient's medicine regimen. Common adverse effects associated with anticholinergic medicines include increased risk of cognitive impairment, dementia, falls and mortality.

Action:

- Regularly review patients taking long-term bladder antimuscarinics to assess the continued risk / benefit of treatment and offer the option of a trial period without medication. The review should consider:
  - ◊ The wishes of the patient.
  - ◊ Clinical indication and expected benefit of the medicine.
  - ◊ Whether the medicine is still appropriate.
  - ◊ Co-morbidities and in particular co-prescribing of other medicines which contribute to the overall anticholinergic burden (ACB) score.
  - ◊ NICE guidance NG97 (June18) Dementia recommends minimising the use of drugs associated with increased anticholinergic burden.
- Offer patients referral to community continence advisers for lifestyle management (at any stage in their treatment journey).
- A review tool for use within GP practices is available on the Primary Care Intranet and relevant newsletter supplements can be found on the NI Formulary website.

Antidepressants

Antidepressants play an important role in the treatment of depression, and some other conditions. It is important that antidepressants are clinically indicated and that patients are regularly reviewed.

What's the problem?

- Place in therapy: antidepressants are not routinely recommended first-line in recent onset, mild depression or persistent sub-threshold depressive symptoms.
- Risk of adverse effects – examples include:
  - ◊ Gastrointestinal (GI) bleeding: avoid SSRIs if possible, or use with caution, in patients over 80 years, those with prior upper GI bleeding, or in those also taking aspirin or another NSAID
  - ◊ Hyponatraemia: should be considered in patients (usually the elderly) taking antidepressants (particularly SSRIs) who develop drowsiness, confusion or convulsions.
  - ◊ Anticholinergic burden: tricyclic antidepressants (TCAs) (except lofepramine) may be less suitable in the elderly due to the antimuscarinic or cardiotoxic effects.
- Interactions: consider drugs likely to affect cardiac rate, electrolyte balance, and QT prolongation. Consider risk of serotonin syndrome when co-prescribing medications that raise serotonin levels
- Risk of overdose.

Antidepressants (cont.)

Action:

Antidepressant therapy should be reviewed regularly in a face to face consultation. **People who benefit from their medication should continue for at least 6 months after remission. Those at risk of relapse should continue treatment for at least 2 years. Deprescribing is not appropriate for patients who are in the active or maintenance phase of their treatment.** The course of the illness and patient factors should influence deprescribing, e.g. deprescribing is not advised during a stressful time of the year such as an anniversary of an event, Christmas or just before a holiday. Deprescribing may however be considered in certain circumstances, e.g. no longer indicated or effective or when risk of adverse effects outweighs benefits.

At review:

- Consider ongoing appropriateness of treatment, e.g. choice of drug or dose may need to be amended as a result of a change in the patient's medical condition(s), or because of their age (e.g. lower doses of citalopram / escitalopram for patients aged over 65). Patients may require more frequent review in such circumstances.
- Consider withdrawal at 6 months or 2 years after remission of episodes depending on the course of illness. For some higher risk patients, e.g. with five lifetime episodes or two episodes in the past two years, at least 2 years treatment is advised and, for most of these, long-term treatment should be considered. If the decision is made to reduce or stop the antidepressant, this should be done slowly and the patient monitored closely. Patients may be carefully switched to another antidepressant where necessary via cross-titration, with close monitoring. Your local Medicines Information Department can provide guidance on protocols for switching antidepressants.
- Avoid polypharmacy where possible.
- Remember:
  - ◊ SSRIs are recommended first line due to their more favourable risk/benefit ratio (NICE). If a TCA is required, trimipramine should not routinely be prescribed due to availability of more cost-effective TCAs (i.e. trimipramine 25mg TDS costs over £600, *Drug Tariff May 2019*).
  - ◊ Dosulepin is NOT recommended for new patients due to the increased risk of heart problems and toxicity in overdose. Care should be taken if considering switching stable patients — seek specialist advice.
- Further guidance on the management of adults with depression in primary care and the appropriate use of antidepressants can be found at https://cks.nice.org.uk/depression.

Bisphosphonates

Bisphosphonate medication has shown efficacy in fracture risk reduction over 3 to 5 years of treatment, with the effect lasting for several years after treatment is stopped.

What's the problem?

Long term treatment with bisphosphonates has been noted in some cases to have caused atypical femoral fractures. The Medicines and Healthcare Products Regulatory Agency (MHRA) subsequently issued a warning of the risk of atypical femoral fractures with long term bisphosphonate use: '*The need for continued treatment should be re-evaluated periodically based on the benefits and potential risks of bisphosphonate therapy for individual patients, particularly after 5 or more years of use*.'

Patient review

A review tool is available on the Primary care intranet. Re-evaluation of patients receiving bisphosphonates may have various possible outcomes depending on the femoral neck T risk score. Prescribers need to consider the following outcomes if patients have been receiving treatment for between 5 and 10 years:

Bisphosphonates

Low Risk (T score > -2.0) – discontinue treatment or consider a drug holiday for 2-3 years (depending on the bisphosphonate).
Medium risk (T score ≥ -2.5) – reassess need / consider drug holiday / discontinue treatment.
High risk (T score < -2.5) – continue therapy and review. No prescribing should occur after 10 years. If necessary specialist advice should be sought for further treatment plans.

Action for GP practices:

- Re-evaluate patients taking an oral bisphosphonate for the management of osteoporosis.
- Offer a drug holiday or discontinue treatment as appropriate. A patient information leaflet on Drug Holidays is available in the Patient Zone section of the NI Formulary website.
- Re-assess fracture risk at a suitable time period after the drug holiday.
- If clinical circumstances change, an earlier review may be required.
- Following review, make a note in the patient's record to highlight the next re-evaluation date.

Action for community pharmacies:

- Support adherence to prescribed bisphosphonate therapy through patient advice.
- Provide patients with a patient information leaflet or signpost to the patient zone of the NI Formulary.
- Reinforce, as necessary, the advantages of the 'drug holiday' from oral bisphosphonate medication.

Betahistine

Betahistine is sometimes used to reduce the frequency and severity of recurrent attacks of nausea, hearing loss, tinnitus, and vertigo associated with Meniere's disease.

What's the problem?

Although betahistine is indicated for prevention of symptoms where there has been a proven diagnosis of Ménière's syndrome, evidence supporting its effectiveness in reducing symptoms or frequency of attacks is limited (at low or high dose). Furthermore betahistine can cause sedation and increase the risk of falls. Therefore, long-term treatment should be reviewed. If there are recurrent attacks despite its use, the patient should be referred to an ENT specialist.

To treat symptoms of an acute attack, short courses (7 days, 14 days if required previously) of prochlorperazine, or an antihistamine (e.g. cinnarizine) can be prescribed. Only short courses are used because regular, long-term use of vestibular suppressants may interfere with vestibular compensation.

Action:

- To determine if a patient can manage without betahistine, reduce doses of 16mg three times a day to 8mg three times a day. If the patient does not experience any symptoms, then a further reduction or trial without medication could be proposed with the patient reassured that the medication can be restarted should symptoms flare.

Mucolytics

Mucolytics may reduce exacerbation frequency and the duration of disability in people with chronic bronchitis or chronic obstructive pulmonary disease (COPD).

What's the problem?

NICE only recommends mucolytic therapy in people with stable COPD who have a chronic cough productive of sputum. However, the evidence that mucolytics can reduce the frequency of exacerbation is of very low quality. The 2016 GOLD Strategy noted that "although a few patients with viscous sputum may benefit from mucolytics, the overall benefits seem to be very small; the widespread use of these agents cannot be recommended at present."
HSCB have produced a Review Tool to help practices identify patients and assess if continued therapy is required, and can be found on the Primary care intranet.

Action:

- Only prescribe mucolytics to COPD patients with chronic cough productive of sputum.
- Stop if no symptomatic improvement after 4-6 weeks.
- Identify patients prescribed 'repeat' mucolytics and ensure therapy is appropriate and improvements have been demonstrated.
- Do not offer mucolytics for acute conditions (e.g. "chesty cough", URTI) or as a short term "cough bottle".

Benzodiazepines

Benzodiazepines are prescribed for a variety of conditions, particularly anxiety and insomnia. Z drugs (zopiclone/zolpidem) are normally prescribed for insomnia. Collectively these drugs are known as anxiolytics/hypnotics. Prescribing of these drugs in NI is significantly higher than other parts of the UK.

What's the problem?

Risks include falls, accidents, cognitive impairment, dependence, withdrawal symptoms, an increased risk of dementia and Alzheimer's disease and increased risk of death of any cause.
They are particularly dangerous when used in combination with other prescribed or illicit drugs such as pregabalin or heroin. They may increase the risk of suicide in some people and are often a factor in lethal overdose, alone or in combination.
The licenses for anxiety/insomnia extend to a maximum period of four weeks, which includes tapering off. However many patients use these medications on a long-term basis, exposing both the patient and the prescriber to significant risks.

Action:

- Use the "Good Relaxation Guide" or the "Good Sleep Guide" as an alternative first step for management of anxiety/insomnia. These are available in the Patient zone section of the Northern Ireland Formulary website.
- If it is essential to initiate one of these drugs, only prescribe a short supply and avoid putting it onto the patient's repeat record.
- Identify patients on these drugs long-term and review them to assess their suitability for reduction/ withdrawal. An audit tool is available on the Primary Care Intranet.
- Display the HSCB Benzo / Z poster to raise awareness of the risks and encourage patients to ask for help in reducing/stopping. This is available on the Primary Care Intranet along with a patient information leaflet.
- Consider strategies that the practice may employ to reduce prescribing, e.g. reducing quantities for those on repeat. Contact your pharmacy adviser for further support or advice.

Pain Medicines for Persistent Pain

The aim of treatment for persistent pain is to improve function and quality of life. Pain reduction from medication of 30-50% is considered a good outcome; it is unrealistic to expect 100% pain relief from any medication. To avoid unrealistic expectations, treatment goals should always be set, including self-management strategies. Resources to support both prescribers and patients are available in the Pain Section on the Primary Care Intranet and on the Live Well with Pain website: https://livewellwithpain.co.uk/.

Pregabalin and Gabapentin

The majority of prescribing of these drugs is for pain.

What's the problem?

Gabapentin and pregabalin were recently classified as Schedule 3 controlled drugs following the increasing abuse and misuse of these drugs, and their associated harm in society (33 deaths in NI in 2017).

No single drug works for all neuropathic pain and therefore treatment must be individualised. NICE recommends regular reviews for patients prescribed neuropathic agents, which should include factors such as pain control, adverse effects, impact on lifestyle and daily activities, and continued need for treatment.

Action:

1. When prescribing pregabalin or gabapentin for neuropathic pain:
   - NI Formulary Guidance should be followed and a worthwhile benefit* assessed after 2-4 weeks. Note: Gabapentin and pregabalin should not be used together.
     - ◊ **If there is no benefit from the drug, it should be stopped slowly over 4 weeks.**
     - ◊ After 6 months of successful treatment an attempt should be made to slowly reduce to the lowest effective dose, or stop the drug, as appropriate.
   - Review prescription quantities: although not a legal requirement, there is a strong recommendation that prescriptions are limited to a quantity necessary for up to 30 days' supply.

* e.g. improvement in pain, function or sleep.

2. Other points to consider at each review, and make adjustments as necessary, include:
   - Prescribing for non-neuropathic pain, i.e. outside licenced indication.
   - Prescribing for patients with a history of substance misuse, to those recently released from prison, and co-prescribing with opiates.
   - Signs of abuse and dependence.
   - Prescribing outside the therapeutic dose range (or twice daily frequency with pregabalin).
   - Compliance, for example, patients not taking the medication regularly may benefit from 'when required' use of other analgesia such as paracetamol or NSAIDs.
   - Risk of CNS depression with gabapentin which may be potentiated by opioids.

Note: A HSCB Gabapentinoids Pain Supplement is available for advice on stepping down.

Opioids

Opioids are often used for persistent non-malignant pain and should be initiated and titrated in line with the NI formulary.

What's the problem?

There is a lack of evidence that opioids are beneficial for **persistent non-malignant pain**. The aim of treatment for persistent pain is to improve function and quality of life. Opioids also have the potential to cause serious harm.

The following points should be considered:

- The risk of harm increases substantially at doses above an oral morphine equivalent of 120mg/day, but there is no increased benefit.
- If pain remains severe despite opioid treatment, this means the opioids are not working and should be stopped, even if no other treatment is available.
- More than one opioid should not be prescribed at any one time on a regular basis.
- Liquid and immediate–release opioids should be avoided due to increased risk of tolerance and dependence.

Action:

- Prioritise patients for review in line with guidance.
- Identify non-palliative patients prescribed ≥120mg/day oral morphine equivalent in total and aim to gradually reduce doses with careful monitoring. Individual reduction plans should be agreed, taking account of other supporting strategies, e.g. pain self-management skills. The following opioid dose calculator may be helpful particularly if patients are on a combination of opioids and/or strengths: http://www.paindata.org/calculator.php.
- Refer to *'Opioid Prescribing for Persistent Pain - Frequently Asked Questions'* for further details on appropriate prescribing and reduction on the Primary care intranet.

Co-proxamol

Co-proxamol (dextropropoxyphene 32.5mg and paracetamol 325mg) was gradually phased out between 2005 and 2007 after concerns that it was involved in a number of suicides and accidental poisonings. **As co-proxamol is now an unlicensed medicine, clinical and product liability lies solely with the prescriber**.

What's the problem?

- Dextropropoxyphene, **even at normal therapeutic doses**, has serious effects on the electrical activity of the heart, prolonging the P-R and Q-T intervals and widening QRS complexes.
- The lethal dose is relatively low and can be potentiated by alcohol and other CNS depressants.
- Death from co-proxamol overdose may occur **rapidly**. The **majority** of co-proxamol overdose deaths occur **before hospital treatment can be received**.
- Treating overdose is not straightforward due to the very long duration of action. Patients need to be monitored for a long period following overdose and additional doses of naloxone may be needed.
- The paracetamol content is lower than the standard 500mg strength per tablet.

Action:

- Carry out a review of patients still prescribed co-proxamol with a view to consider trying an alternative pain management regime.
- If there are exceptional individual patient circumstances in which the prescriber believes justify the prescribing of co-proxamol, document the discussion and the clinical reason(s) for continuing to prescribe co-proxamol.

Co-proxamol (cont.)

- Co-proxamol should not be used for:
  1. New patients
  2. Any acute pain indication
  3. Patients under 18 years of age
  4. Patients who are alcohol-dependent or who are likely to consume alcohol whilst taking co-proxamol
  5. Patients who are suicidal or have a history of addiction (risk of addiction and abuse associated with co-proxamol).

Lidocaine plasters

Lidocaine plasters are licensed for symptomatic relief of neuropathic pain associated with previous herpes zoster infection (post-herpetic neuralgia, PHN) in adults.

What's the problem?

Most prescribing of lidocaine plasters is for *unlicensed indications*. In these circumstances, the General Medical Council advises that the prescriber must: "*be satisfied that there is sufficient evidence or experience of using the medicine to demonstrate its safety and efficacy.*"

Evidence for use in non-neuropathic pain such as chronic back pain or rib fractures is limited. The NI regional expert group on pain management made the following recommendation regarding the use of lidocaine plasters: ***"lidocaine plasters should only be considered as third line treatment where satisfactory pain reduction is not achieved with second line oral treatment:***

- ***to treat post herpetic neuralgia***
- ***to treat localised allodynia (unlicensed use), e.g. painful scarring and***
- ***lidocaine plasters should not normally be used for treatment of back pain."***

Action:

- Treatment outcome should be re-evaluated after 2-4 weeks. If there has been no response after this period (during the wearing time and / or during the plaster-free interval), treatment must be discontinued as potential risks may outweigh benefits in this context.
- Review patients regularly to ensure that they are benefitting from the treatment.
- A patient information leaflet to aid deprescribing of lidocaine plasters is available on the NI Formulary website in the Deprescribing section.

Methocarbamol

Methocarbamol is licensed as a short-term adjunct to the symptomatic treatment of acute musculoskeletal disorders associated with painful muscle spasms.

What's the problem?

As evidence for use in muscle spasm or spasticity is limited, methocarbamol is listed in the BNF as 'less suitable for prescribing'. It is neither first nor second line in the NI formulary for skeletal muscle relaxants". Use in other musculoskeletal conditions has not been examined in rigorous RCTs and limited clinical trial evidence makes it difficult to evaluate its place in therapy. As such, it is on the NI Limited Evidence List.

Action:

- Review patients receiving repeat prescriptions for methocarbamol to ensure it is effective for the patient and is being prescribed appropriately. Remember that half of the maximum recommended dose (or less) may be sufficient to produce a therapeutic response in the elderly.
- A patient information leaflet to aid deprescribing of methocarbamol is available on the NI formulary website, in the Deprescribing section.

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