Grŵp Strategaeth Meddyginiaethau Cymru Gyfan
All Wales Medicines Strategy Group

Polypharmacy in older people

A guide for healthcare professionals

March 2023

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Contents

NICE defines medicines optimisation as a "*person-centred approach to safe and effective medicines use, to ensure people obtain the best possible outcomes from their medicines*[1]."

The following guide has been created in order to help support medicines optimisation in older patients who may be subject to inappropriate polypharmacy.

1.0 Introduction

The World Health Organization (WHO) describes polypharmacy as a major global problem and has set a global safety challenge to avoid medicine-related harm[2]. Patients being prescribed a higher number of medications has been associated with an increased risk of harm and is a strong predictor of hospitalisation due to adverse drug events[3,4].

Harm from medications results in 11% of unplanned hospital admissions, 70% of these patients being older patients prescribed multiple medications[5]. This presents a significant opportunity for intervention. The WHO Third Global Patient Safety Challenge, *Medication without Harm*, has included appropriate management of polypharmacy as a key area to address. The aim is to reduce severe avoidable medication related harm by 50% over 5 years globally[2].

In addition to potential harm, polypharmacy poses a huge financial pressure on the NHS. In the UK, 75% of people aged 75 years and over have more than one long-term condition[6], with over 85% of people in this age group in Wales estimated to have taken at least one prescription medicine within 12 months[7]. Despite this, only 50% of medications prescribed are taken as intended; costing the UK in 2007 up to £200 million each year in wasted medication[8]. A 2010 report also estimated that several hundred tonnes of medicines were disposed of by health service users per year[9]. Therefore, assessing polypharmacy and patient adherence to medication is imperative.

Polypharmacy can be defined as appropriate polypharmacy or problematic polypharmacy[10]:

- **Appropriate polypharmacy** – Prescribing of multiple medications for an individual with complex conditions or for multiple conditions in circumstances where medicines use has been optimised and prescribed in accordance to best evidence.
- **Problematic polypharmacy** – Prescribing of multiple medications inappropriately or where the intended benefit of the medication is not realised. The following examples would contribute to polypharmacy being considered inappropriate:
    - Use of a treatment is not evidence-based.
    - Risk of harm outweighs the benefits of treatment.
    - Drug interactions leading to unintended side-effects.
    - Unacceptable pill burden making it difficult to achieve clinically useful medicine adherence.

  - Prescribing medicines to treat side-effects of other prescribed medicines.

Appropriate polypharmacy can extend life and improve patient outcomes. However, problematic polypharmacy can increase risk of drug interactions and impair quality of life. Consequently, medication optimisation is essential.

Quantifying polypharmacy is difficult as there is no universal approach and patients should be assessed pragmatically using clinical judgement. A pragmatic approach to identifying high-risk polypharmacy in practice has been suggested by The King's Fund[10]:

- Patients with 10 or more regular medicines (for example, those medicines taken every day or every week).
- Patients receiving between four and nine regular medicines who also:
  - have at least one prescribing issue that meets criteria for potentially inappropriate prescribing;
  - have evidence of being at risk of a well-recognised potential drug-drug interaction or have a clinical contraindication;
  - have evidence from clinical records of difficulties with taking medicines, including problems with adherence;
  - have no or only one major diagnosis recorded in the clinical record (it might be expected that large numbers of medicines are unlikely to be justified in patients without multiple clinical conditions);
  - are receiving end-of-life or palliative care (where this has been explicitly recognised).

Good prescribing practice in older people should consider the following[11,12]:

- Use drugs that are familiar to the prescriber.
- Use the lowest effective dose and titrate up slowly.
- Prescribing should always be evidence-based for the specific age group.
- Anticipate drug interactions (including drug-drug, drug-food, drug-alcohol and drug-herbal).
- Be aware of and vigilant for adverse drug reactions and how pharmacology differs in older people.
- Monitor therapy (particularly high-risk medications e.g. digoxin).
- Be aware of medications that may be prescribed via specialist clinics and therefore not on the patient's record (e.g. memory clinic).
- Be aware of medication not prescribed such as over-the-counter medications, herbal products or someone else's medication.
- Avoid the prescribing cascade:
  - Optimise existing medication.
  - Consider introducing drugs as a trial – titrate dose and stop if ineffective.
  - Consider deprescribing to enable the safe and effective cessation of inappropriate medication.
- Promote adherence in collaboration with the patient:
  - Undertake shared decision making with the patient and involve carers where reasonable[13].

    - Keep the medication regimen simple, taking into account pill burden and timings.
    - Provide clear written instructions, a dosing schedule and information on why the medicine has been prescribed.
        - Avoid using the term, “as directed”.
    - Identify over-ordering/hoarding of medicines.
    - Consider advantages and disadvantages of compliance aids (N.B. monitored dosage systems should not be used first-line as they can have disadvantages; e.g. drug stability and difficulty in following directions such as ‘when required’ or with/after food etc.).
    - Don’t assume that the patient is taking medication as prescribed.
- Be aware of any transfer between care settings and changes to medication that may occur as a result. The community pharmacy discharge medicines review (DMR) service can provide support to patients recently discharged between care settings by ensuring that changes to patients’ medicines made in one care setting (e.g. during a hospital admission) are enacted as intended in the community[14].
- Be aware of the person's culture or social beliefs of the treatment or disease.
- Be aware that people of different races and ethnicities can have varying responses to medicines. The British National Formulary (BNF) or the individual medicine’s summary of product characteristics should always be consulted.
- Be aware of potential links between overprescribing, deprivation, ethnicity and inequalities and the impact this has on the health of the person[15].

"Another important challenge in the area of polypharmacy is that of working alongside patients to empower them to make informed choices about treatments and the burden of pills they are expected to consume. Increasingly, it is recognised that many people find their medication regimens an unpleasant chore and this can in its own right detract from their quality of life."

The King's Fund – Polypharmacy and Medicines Optimisation (2013)[10]

2.0 Frailty

Frailty is a multicomponent syndrome where individuals have a reduced resilience to external stressors such as infections and adverse drug reactions[16,17]. The multicomponent syndrome is made up of the five "geriatric giants" or frailty syndromes including[18,19]:

- falls;
- immobility;
- delirium;
- incontinence;
- susceptibility to adverse drug reactions.

Frailty has been estimated to occur in 10% of people aged over 65 years and in over 50% of people aged over 85 years[17]. Establishing frailty in individuals can be undertaken using a range of tools such as Frailty phenotype or PRISMA-7 questionaire[20,21]. There is also the clinical frailty index. However, this should only be used to quantify the extent of frailty following on from a comprehensive geriatric assessment. Frailty has been associated with poor outcomes with regard to mobility, frequent hospital admissions, institutionalisation and mortality, and is a dynamic process where improvements can be achieved with the correct interventions. Therefore, the gold standard intervention for diagnosis and the management of frailty is a comprehensive geriatric assessment[16].

Due to multimorbidity, polypharmacy is common in patients living with frailty, with studies highlighting that a significant number of medicines taken by frail patients have no clear indication. Also, due to the pharmacokinetic changes in older or frail patients such as reduced renal function, there is an increased sensitivity to medications with an increased likelihood of adverse drug reactions, falls, cognitive impairment and delirium. This leads to increased hospitalisation and morbidity in frail patients on multiple medications. Thus, undertaking a medication review is a beneficial intervention which forms part of the comprehensive geriatric assessment (CGA)[17]. A CGA is a multi-disciplinary, holistic assessment of an older person in order to formulate a plan and arrange interventions to tackle the problems that are of concern to that older person[22].

Undertaking a medication review and choosing the correct medication for frail patients requires a specific approach. The aims of treatment in this group of patients may predominantly be to reduce disease progression and improve symptom management to maintain function. Therefore, the aim of treatment along with factors such as pharmacokinetic changes, co-morbidities, efficacy, adherence and what is important to the patient should be kept in mind when reviewing medication[17]. Depending on the individual's level of frailty, a medication review may be different for

individuals of the same age; patients with a high frailty score indicating limited life expectancy may benefit less from medicines that have long-term preventative action[23].

A structured medication review can be undertaken following the guidance, tools and resources highlighted elsewhere in this document for frail patients. However, there are resources specifically related to frailty such as the STOPPFrail tool which highlights the classes of medicines that may need to be reviewed in frail patients with limited life expectancy (see Box 1)[23].

The STOPPFrail tool can be used to review medications as listed below in patients aged over 65 years that have ALL of the following[23]:

- End-stage irreversible pathology.
- Poor one-year survival prognosis (this can be gauged from the frailty score).
- Severe functional impairment and/or severe cognitive impairment.
- Symptom control is a priority over disease progression prevention.

Box 1. Medicines highlighted for review in frail patients with limited life expectancy as per the STOPPFrail toolkit[23].

- Lipid-lowering therapies
- Anti-platelets
- Neuroleptic antipsychotics
- Memantine
- Proton pump inhibitors (PPIs)
- H_2-receptor antagonists
- Gastrointestinal antispasmodics
- Theophyline
- Leukotriene antagonists in chronic obstructive pulmonary disease (COPD)
- Calcium supplementation
- Anti-resorptive medicines
- Selective oestrogen receptor modulators (SORMs) for osteoporosis
- Long-term non-steroidal anti-inflammatory drugs (NSAIDs)
- Long-term oral steroids
- 5-alpha reductase inhibitors
- Alpha-blockers
- Muscarinic antagonists
- Diabetic oral agents – aim for monotherapy
- Angiotensin-converting enzyme (ACE) inhibitors for diabetes
- Angiotensin receptor blockers for diabetes
- Systemic oestrogens for menopausal symptoms
- Multi-vitamin combination supplements
- Nutritional supplements
- Prophylactic antibiotics

Further detail on each of these drug classes can be found within the STOPP/FRAIL toolkit.

In frail patients, other factors such as medication risk versus benefit, difficulties with medicines administration, challenging monitoring of the medication or compliance should be taken into account when stopping or starting medication[23].

3.0 High-risk medication

A report published in 2000, *To Err is human, building a safer health system*, reported that there may be as many as 98,000 medication related-deaths per year in America, with some of those being preventable[24]. Elliot *et al*. estimated the cost to the NHS in England of preventable adverse drug reactions to be over £98 million; consuming over 181,000 bed days[25]. Thus, Hodkinson *et al*. published a paper in 2020 that undertook a systematic review and meta-analysis of the evidence at the time to highlight high-risk medicines that cause preventable harm[26], which correlates with Australian work who use the acronym APINCH to highlight high-risk medicines (see Table 1)[27]. Hodkinson *et al*. highlighted antihypertensives, diuretics and NSAIDs as some of the most common medicines to cause preventable harm, and also noted that geriatric units had a notably high prevalence of preventable medication harm[26].

Table 1: APINCH classification of high-risk medicines[27]

A	Antimicrobials
P	Potassium and other electrolytes
I	Insulin
N	Narcotics (opioids) and other sedatives
C	Chemotherapeutic agents
H	Heparin and other anticoagulants

Therefore, it is important to review these medications regularly to assess the risk versus benefit. There are a number of additional medications that are poorly tolerated and considered high risk in older people who are frail or have intellectual disabilities, including antipsychotics and anticholinergics. Tools exist to support identification of inappropriate medicines use in specific vulnerable population groups. Most notably, the STOPP/START tool identifies medicines inappropriate for prescribing in older and frail patients. STRIP (Systematic Tool to Reduce Inappropriate Prescribing) and STOMP (Stopping the Over Medication of People with a learning disability, autism or both) are specific approaches for reviewing inappropriate and overprescribing in people with intellectual disabilities and autism. More details on this can be found under the frailty section of the PrescQIPP *Polypharmacy and deprescribing* bulletin[28].

4.0 Sick day rules

Patients who become unwell and are unable to maintain adequate hydration are at risk of dehydration. Continuing to take certain medications when dehydration occurs can increase the risk of harm to the patient. It is therefore suggested to consider sick day rules. The following medications should be temporarily stopped during an illness that can result in dehydration[29]:

- **S**ulphonylurea;
- **A**CE inhibitors;
- **D**iuretics;
- **M**etformin;
- **A**ngiotensin receptor blockers (ARBs);
- **N**SAIDs;
- **S**odium-glucose cotransporter-2 (SGLT-2) inhibitors.

It is important to weigh up the risks and benefits of withholding these medications for each individual.

Patients should be advised to withhold these medications if they develop severe vomiting, diarrhoea or fever, and to restart taking the medication 24–48 hours after this has resolved. Refer to individual health board guidance for advice.

In addition to the above, patients receiving steroids should receive a dose escalation dependent on the steroid and indication for use during acute illness, trauma or surgery. Further information can be sought from the Welsh Endocrine and Diabetes Society.

5.0 Reviewing patient medication adherence

Patient assessment

As part of each patient assessment, the following questions should be addressed.

Who is responsible for administering medication?

- e.g. self-administration, family, healthcare support worker (HCSW), social care worker etc.

If medication is administered by social care workers or HCSWs:

- Do administration times align with planned care calls?
- When required (prn) medicines?
    - State reason e.g. for pain, constipation etc.
    - Specify dose i.e. avoid terms such as ‘one or two to be taken’.

How does the patient access their community pharmacy and/or GP to arrange order or delivery of medication?

Is the patient unable to manage their medication? For example, due to:

- complex dosage regimen;
- over-ordering/hoarding of medication;
- forgetful/diagnosis of dementia;
- chaotic lifestyle;
- swallowing difficulties;
- poor dexterity;
- poor mobility;
- poor sight;
- unable to hear, read or understand directions;
- unable to use medication device e.g. inhalers, eye drops etc.

Is the patient intentionally poorly adherent? For example, due to:

- medication no longer needed (particularly prn drugs) e.g. ongoing use of PPIs once long-term NSAIDs have stopped, painkillers etc.;
- ineffective medication;
- lack of understanding of indication/importance of treatment;
- patient beliefs surrounding their medication;
- lack of immediate visible effects/benefits e.g. for hypertension;
- unpleasant side-effects;
- directions unclear;
- complex administration instructions, e.g. bisphosphonates, warfarin.

Is the patient taking any over the counter or herbal medicines?

Potential Solutions

After the patient has been assessed, the following solutions to common issues may be considered.

- Can the regimen be simplified?
    - Consider call times if the patient receives a package of care.

- Is there any therapeutic duplication?
    - Any drugs of limited clinical value or drugs where long-term benefit is unlikely to be realised due to life expectancy (see Section 2.0)?

- Would they benefit from a further discussion with a community pharmacy professional?
    - Assess options and support required, e.g. compliance aids, reminder charts, alarms, dexterity aids.
    - The Equality Act 2010 requires the healthcare professional to assess patients with ‘disabilities’ and make ‘reasonable adjustments’ to support adherence with their medicine, without introducing additional risks. The final decision on which adjustment is required to the way that prescribed medicines are supplied will be the responsibility of the supplying pharmacist (or dispensing doctor).

- What support is available?
    - Under the discretion of the supplying pharmacy, this may include: child-resistant/wing-topped bottles, devices to aid popping tablets from blisters, devices to aid administration of eye drops/inhalers, large print labels/patient information leaflets, reminder charts, text alerts.
    - Monitored dosage systems (MDSs) are an option but should not be used first-line. It is important to note that there is no contractual requirement to supply an MDS to a care facility. Providing care workers are suitably trained, the supply of medicines in original packs should be promoted as standard. Please refer to National Guiding Principles for Medicines Support in the Domiciliary Care Sector for more information.

      Table 2 includes some of the key risks and benefits associated with an MDS.

Table 2. Risks and benefits associated with the use of monitored dosage systems (MDSs)[30,31]

Potential risks associated with an MDS	Potential benefits associated with an MDS
Medication becomes unlicensed when repackaged in an MDS	Can reduce the complexity of regimens for some patients
Stability data for medicines stored in an MDS not known in most cases	Can act as a memory aid for some patients
Adding a controlled drug (CD) to an MDS means the whole MDS needs to be treated as a CD	Can be more accessible to patients
Can reduce patient autonomy and understanding of medicines	Can support some people in maintaining independent healthy living
Can increase the risk of medication errors, some of which may be associated with an increased risk of harm to the patient	Can provide peace of mind to patients and/or carers
Not all medicines are suitable to be dispensed into an MDS	
Changes to medication requires new prescriptions to be issued and the entire MDS to be re-dispensed	
Not all MDSs are child-resistant	
For further information on the use of monitored dosage systems visit: Multi-compartment compliance aids (MCAs) – Royal Pharmaceutical Society (Accessible to members only)	

- Link with GP and community pharmacy to explore options for delivery and/or ordering of medicines.
    - It is worth noting that if a patient has medicines delivered, in an instance where they could have collected them themselves, they would miss potential opportunities for interactions with a community pharmacy professional.

- Address reasons for intentional poor adherence. For example:
    - With permission from the patient or carer, remove medication that is no longer needed or is now ineffective.
    - Utilise shared decision making through the use of patient decision aids.
    - Counsel patients appropriately.
    - Consider switching/stopping drugs with unpleasant side effects.

- If the patient has swallowing difficulties, would a liquid or soluble preparation be more appropriate?

- Consider cost implications, product licence etc.
- Be aware of unlicensed specials.

If tablets or capsules are being crushed/opened, consider the impact on product licence, stability, pharmacokinetics of the drug, coating etc.

6.0 A practical guide to stopping medication in older people

A four-step approach should be considered when stopping medication:

1. Recognise the need to stop.
2. Reduce or stop one medicine at a time.
3. Consider if the medicine can be stopped abruptly or should be tapered.
4. Assess risk benefit after each medicine has been stopped.

1. Recognise the need to stop
A lot of medications are not required for lifelong use and their need to continue should be reviewed frequently. Assessing whether the medication is still indicated and whether the risk outweighs the benefit should be part of this review.

When recognising medicines that may need to be stopped, utilise shared decision making with the patient and consider the patient's and/or carer's views on their medication[13,32,33].

2. Reduce or stop one medicine at a time
Reducing one medication at a time allows for identification of any issues that may occur as a result.

3. Consider if the medication can be stopped abruptly or should be tapered
Not all medication can be stopped abruptly as patients may develop withdrawal. It is important to taper some medication and monitor the patient's response closely. If medication is being stopped due to toxicity then the risk benefit should be assessed and a more ambitious withdrawal may be undertaken. Some medication may require close monitoring upon discontinuation and require tapering of doses. Specialist advice may be required to support the deprescribing of these medications[34]:

- Antidepressants
- Antipsychotics
- Anticonvulsants
- Centrally acting antihypertensives
- Corticosteroids
- Hypnotics and anxiolytics
- Opioid analgesics and gabapentinoids
- Anti-Parkinson's.

4. Assess risks and benefits after each medication has been stopped.
Review if there has been any benefit to stopping or reducing the medication as an aid to continue deprescribing. If the patient has experienced re-emergence of the initial symptoms of treatment, then consider whether to restart the medication and whether the patient can benefit from a lower dose.

Resources such as the STOPP/START tool exist to help highlight medication for review in the older population. Further information on individual medicines can be accessed via http://www.medicines.org.uk/ or from the individual pharmaceutical companies' medicines information departments.

The following sections have been created to help support the deprescribing of some of the medications that require tapering regimens and close monitoring.

6.1 Antihypertensives

Older patients are at higher risk of postural hypotension, making them particularly susceptible to adverse drug events such as falls[35].

6.1.1 When to consider stopping[12,35]

- Review if indication is still valid. Is blood pressure in range or too low?
- Is prescribing in line with national guidance[36]?
- Is the patient exhibiting signs of postural hypotension (defined as a drop in blood pressure [BP] – usually > 20/10 mmHg – within three minutes of standing)?
- Do adverse drug reactions outweigh possible benefits?
- Could the patient adopt lifestyle measures, such as losing weight, not misusing alcohol, exercising regularly and restricting consumption of salt?
- Does the patient have general frailty? Consider if length of treatment time required for benefit outweighs the risks.

6.1.2 Tapering guide

Consider indication and other drug properties when reviewing antihypertensives before deciding which to reduce or withdraw, e.g. rate-limiting properties of calcium channel blockers and cardio-protective properties of ACE inhibitors in heart failure.

- If more than one antihypertensive is used, stop one at a time maintaining the dose of the other antihypertensives.
- Monitor the person closely; recurrence of hypertension is most likely to happen in the first six months.
- Restart antihypertensives if BP increases above threshold stated in national guidelines[35].

6.1.3 Withdrawal effect

Withdrawal effects may be seen depending on drug and condition.

For an accurate list of withdrawal effects, please check individual drug summaries of product characteristics (SPCs) on www.medicines.org.uk.

6.2 Benzodiazepines and Z-drugs

6.2.1 When to consider stopping

Regular and prolonged use should be avoided as benzodiazepines and Z-drugs (e.g. zopiclone and zolpidem) are associated with an increased risk of tolerance, falls and cognitive impairment[37,38].

Patients should be prescribed the lowest possible dose for the shortest effective time. The maximum duration of treatment should be four weeks, including the tapering period[38].

Consider stopping if:

- there is no documented indication;
- patient is palliative/end-of-life (bear in mind that benzodiazepines or Z-drugs may be of benefit to palliative patients);
- benzodiazepines and Z-drugs are contraindicated, e.g. myasthenia gravis;
- the risk of harm outweighs the benefits, e.g. adverse drug reactions, patient is frail or patient has multimorbidity;
- the patient is not experiencing the intended outcome or benefit;
- the duration of treatment is longer than the licensed recommendation.

6.2.2 Tapering guide

If benzodiazepines or Z-drugs have been taken for longer than two weeks then there is a risk of withdrawal side-effects and the withdrawal should be conducted gradually with frequent review[39].

Withdrawal should be done gradually in steps of around 5–10% reduction weekly to fortnightly or one-eighth of the daily dose fortnightly[39].

Tapering down the dose of benzodiazepine or Z-drug can either be done on the person's current medication or by switching to an equivalent dose of diazepam.

Switching benzodiazepine to equivalent diazepam dose is recommended for: short-acting benzodiazepines; preparations that do not allow small dose reductions; and for people who will likely experience difficulty withdrawing directly from temazepam, nitrazepam and Z-drugs due to dependency.

Seek specialist advice before switching to diazepam in people with hepatic dysfunction.

When tapering with equivalent diazepam dose:

- Transfer the patient to equivalent daily dose of diazepam (see Table 3), preferably at night.
- Reduce the dose of diazepam gradually every two weeks and if withdrawal symptoms occur, maintain this dose until symptoms improve.
- If necessary, reduce dose further in smaller steps depending on withdrawal symptoms.
- Discontinuation can take 3–12 months and in some cases longer.

Table 3. Doses of oral benzodiazepines equivalent to oral diazepam 5 mg[37,40]

Temazepam 10 mg	Diazepam 5 mg
Chlordiazepoxide 12.5 mg–15 mg	
Loprazolam 0.5 mg–1 mg	
Lorazepam 0.5 mg	
Lormetazepam 0.5 mg–1 mg	
Nitrazepam 5 mg	
Oxazepam 10 mg–15 mg	
Clonazepam 0.25 mg	
Zolpidem 10 mg	
Zopiclone 7.5 mg	

The patient should be provided with information on tapering and the planned treatment regimen to help ensure their engagement and adherence.

6.2.3 Withdrawal effects

- Approximately 40% of people taking benzodiazepines for over six weeks followed by them being reduced or stopped will experience withdrawal effects[37].
- Withdrawal effects may occur within 24 hours with short-acting benzodiazepines, or over several days with and longer-acting drugs[37].
- Withdrawal effects may reach their maximum intensity between three and fourteen days and can continue for up to six weeks[37].
- Withdrawal symptoms are characterised by[39]:
    - insomnia;
    - anxiety;
    - loss of appetite and of body-weight;
    - tremor;
    - perspiration;
    - tinnitus;
    - perceptual disturbances.
- Symptoms may be similar to original complaint and encourage further prescribing.
- Some symptoms may continue for weeks after stopping benzodiazepines.
- For a list of full withdrawal effects please see individual drug on www.medicines.org.uk.

Seek advice from drug and alcohol services within your area

6.2.4 Additional resources

- Material to support appropriate prescribing of hypnotics and anxiolytics across Wales (AWMSG)
    - Includes examples of tapering regiments and a *Good sleep guide* for the management of insomnia.

6.3 Oral corticosteroids

6.3.1 When to consider stopping

In older patients, particularly in those receiving long-term treatment, the consequences of common adverse effects may be more serious (e.g. osteoporosis, diabetes, glaucoma, and gastrointestinal toxicity)[41].

6.3.2 Tapering guide

Be aware that too rapid a reduction of corticosteroid can lead to acute adrenal insufficiency, hypotension and death.

Dose reduction should be done on a case-by-case basis considering the underlying condition being treated, the likelihood of relapse and the duration of treatment.

Gradual withdrawal should be considered for people whose disease is unlikely to relapse and have one or more of the following[41]:

- Received a dose of 40 mg of prednisolone daily or higher for more than one week.
- Received repeated doses in the evening.
- Received more than three weeks of treatment.
- Recently received repeated courses; particularly if this has been for a period longer than three weeks.
- Received a short course within one year of stopping long-term therapy.
- Other possible causes of adrenal suppression.

During withdrawal, the dose of oral corticosteroids may be reduced rapidly down to physiological doses (approximately 7.5 mg prednisolone daily) and reduced more slowly thereafter[41].

If the problem has resolved and treatment has been given for only a few weeks reduce 2.5 mg equivalence prednisolone every 3–4 days to 7.5 mg daily then more slowly by 2.5 mg weekly, fortnightly or monthly[41].

If uncertain of disease resolution and/or therapy has been given for many weeks reduce by 2.5 mg equivalence of prednisolone every fortnight or month down to 7.5 mg daily then reduce by 1 mg every month[41].

If symptoms of disease are likely to recur on withdrawal reduce by 1 mg every month[41].

6.3.3 Withdrawal effects

Too rapid a reduction of corticosteroid can lead to acute adrenal insufficiency, hypotension and death.

Withdrawal symptoms include: Anorexia, hypotension, nausea, weakness, fever, myalgia, arthralgia, weight loss.

For a list of full withdrawal effects please see individual drug on www.medicines.org.uk.

6.4 Antidepressants

6.4.1 When to consider stopping[42]

- Review if the indication is still valid:
  - For a single episode of depression treat for six to nine months after remission of symptoms.
  - For multiple episodes treat for at least two years after remission of symptoms.
- Dosulepin should not routinely be prescribed.
- Consider stopping:
  - in cases where there is no documented or appropriate clinical indication, supported by discussions with the patient and/or carer;
  - when the known adverse drug reactions outweigh the possible benefits;
  - if tricyclic antidepressants are being taken with other medications that increase the patient's anticholinergic burden;
  - if the patient is end-of-life and reduction in pill burden is required;
  - if the patient has been treated at therapeutic dose for six weeks with no benefit. If partial benefit achieved treatment duration may need extending or a dose increase should be considered.

6.4.2 Tapering guide

Due to the pharmacology of the drugs[43], doses of antidepressants should be tapered proportionately (e.g. as a proportion of the **previous** dose), reducing by smaller and smaller amounts each time[44].

For people at a lower risk of withdrawal (e.g. patients who have been prescribed only short-term antidepressants) tapering can be carried out in increments of 50% dose reductions made every 2–4 weeks down to a final dose of approximately 1% of original dose (See citalopram example in the Royal College of Psychiatrists guidance)[45].

Longer tapering regimes will be required for patients who:

- develop distressing signs of withdrawal when trying to stop antidepressants;
- have been taking long-term antidepressants;
- have been taking antidepressants associated with a high risk of withdrawal effects (such as paroxetine, venlafaxine and duloxetine).

Such patients may need their doses reduced in increments of 10–25% of their previous dose every month, down to a final dose of approximately 1% of the original dose, or less. For patients at particularly high risk of withdrawal, increments of reduction may need to be as low as 5% of the previous dose every month (See paroxetine example in the Royal College of Psychiatrists guidance)[45].

Fluoxetine has a long half-life and active metabolites, making severe withdrawal less likely[45]. However, as any withdrawal symptoms may develop several days or even weeks after reducing the dose, and as we cannot predict who will get symptoms, a 50% dose reduction made every 2–4 weeks down to a final dose of about 1% of original dose is recommended.

Formulations other than widely available tablets will be required in order to accommodate the sort of tapering suggested in this section, because the doses required are not easily made. For higher doses, tablet cutters can be useful; however, this changes the licensed status of the medication. Tablet cutting is not suitable for all formulations as it may affect the pharmacokinetics of the drug. Therefore, it is important to assess this prior to initiating a regimen and discuss this with the patient

To make up lower doses some options include:

- liquids from the manufacturer – the NICE Guideline (NG222) *Depression in adults: treatment and management* states[46]: "*If, once very small doses have been reached, slow tapering cannot be achieved using tablets or capsules, consider using liquid preparations if available*";
- compounded liquids;
- compounded tablets (e.g. tapering strips).

"Every other day" dosing is not recommended. NICE Guideline (NG222) *Depression in adults: treatment and management* states: "*Advise people taking antidepressant medication that if they stop taking it abruptly, miss doses or do not take a full dose, they may have withdrawal symptoms*". "Every other day" or more infrequent dosing for drugs that have half-lives of about 24 hours will cause great changes in plasma levels leading to withdrawal effects. Fluoxetine's long half-life is the only exception to this and could be dosed up to every week.

Ultimately the speed and duration of withdrawal should be led by the patient and a further reduction only made when discontinuation symptoms have resolved.

6.4.3 Withdrawal effects

Not all individuals will experience discontinuation symptoms and they can also vary between individuals. Symptoms include dizziness, restlessness, problems sleeping, sweating, abdominal symptoms, nausea, changes in mood, akathisia, mania and suicide ideation[42].

Withdrawal symptoms can start 24–72 hours after medication is reduced or stopped; for some people symptoms can start after missing a single dose.

Sometimes withdrawal can be misdiagnosed as a return of the underlying condition[47]. The return of an underlying condition like anxiety or depression usually takes longer, typically weeks or months. Withdrawal symptoms include physical effects which are not present in depression or anxiety, such as "electric shocks" or "zaps". Patients will often say things like, "I have never experienced anything like this before"[45].

With fluoxetine, which has a long half-life, withdrawal can take longer to start and so is more difficult to distinguish from the underlying condition[45].

For a list of full withdrawal effects please see individual drug on www.medicines.org.uk.

Table 4. Risk of withdrawal symptoms with individual antidepressants[48]

Highest Risk	Moderate Risk	Low Risk	Lowest Risk
Amitriptyline	Citalopram	Bupropion	Agomelatine
Clomipramine	Escitalopram	Fluoxetine	
Paroxetine	Fluvoxamine		
Venlafaxine	Imipramine		
Duloxetine	Lofepramine		
	Nortriptyline		
	Mirtazapine		
	Reboxetine		
	Sertraline		
	Trazodone		
	Vortioxetine		

If an individual experiences mild discontinuation symptoms verbal reassurance to explain that most symptoms are short lived, along with safety netting advice, may be sufficient. Advise patients to seek help and contact a healthcare professional if their symptoms worsen.

More severe discontinuation symptoms may require re-starting the antidepressant at the previous dose, and attempting a slower reduction once symptoms have resolved. Withdrawal symptoms usually resolve quickly (in days or even hours) if the antidepressant is restarted[45].

Further advice on managing discontinuation symptoms can be found from the National Centre for Mental Health "Coming off antidepressants" fact sheet.

Useful information for patients coming off antidepressants can also be found on Mind's website (including a list of useful contacts and helplines).

6.5 Bisphosphonates

6.5.1 When to consider stopping

Review treatment following deprescribing algorithm (Figure 1).

The risks and benefits of bisphosphonate treatment for the patient should be reviewed regularly. Consider whether the benefits justify the risks of bisphosphonate use, particularly in cases where [49]:

- the patient has an eGFR less than 35 ml/min;
- the patient is at a low risk of falls e.g. immobile;
- the patient is not able to sit upright to take oral bisphosphonate;
- the patient has developed swallowing issues;
- the patient is demonstrating poor adherence despite counselling;
- the patient has limited life expectancy or frailty;
- the patient has osteonecrosis of jaw or external auditory canal has occurred;
- the use of bisphosphonates is now contraindicated.

Some of the adverse drug reactions associated with bisphosphonate use include:

- long-term use of bisphosphonates is associated with increased risk of atypical femoral fractures;
- intravenous bisphosphonates are associated with osteonecrosis of the jaw;
- long-term use of bisphosphonates has been associated with benign idiopathic osteonecrosis of the external auditory canal.

Prescribed a bisphosphonate and a proton pump inhibitor (PPI)?

Emerging evidence suggests a possible link between the use of PPIs (especially high doses for over one year) and an increased risk of fracture. The mechanism responsible for this increase and the strength of evidence has not yet been established; however, it may be prudent to ensure patients have a valid indication for a PPI and prescribed the lowest dose for the shortest duration. For further information see UK Medicines Information Q&A – *Is there an interaction between bisphosphonates and proton pump inhibitors?*[50].

6.5.2 Withdrawal effects

Withdrawal of oral bisphosphonate treatment is associated with decrease in bone mineral density and increased bone turnover after:

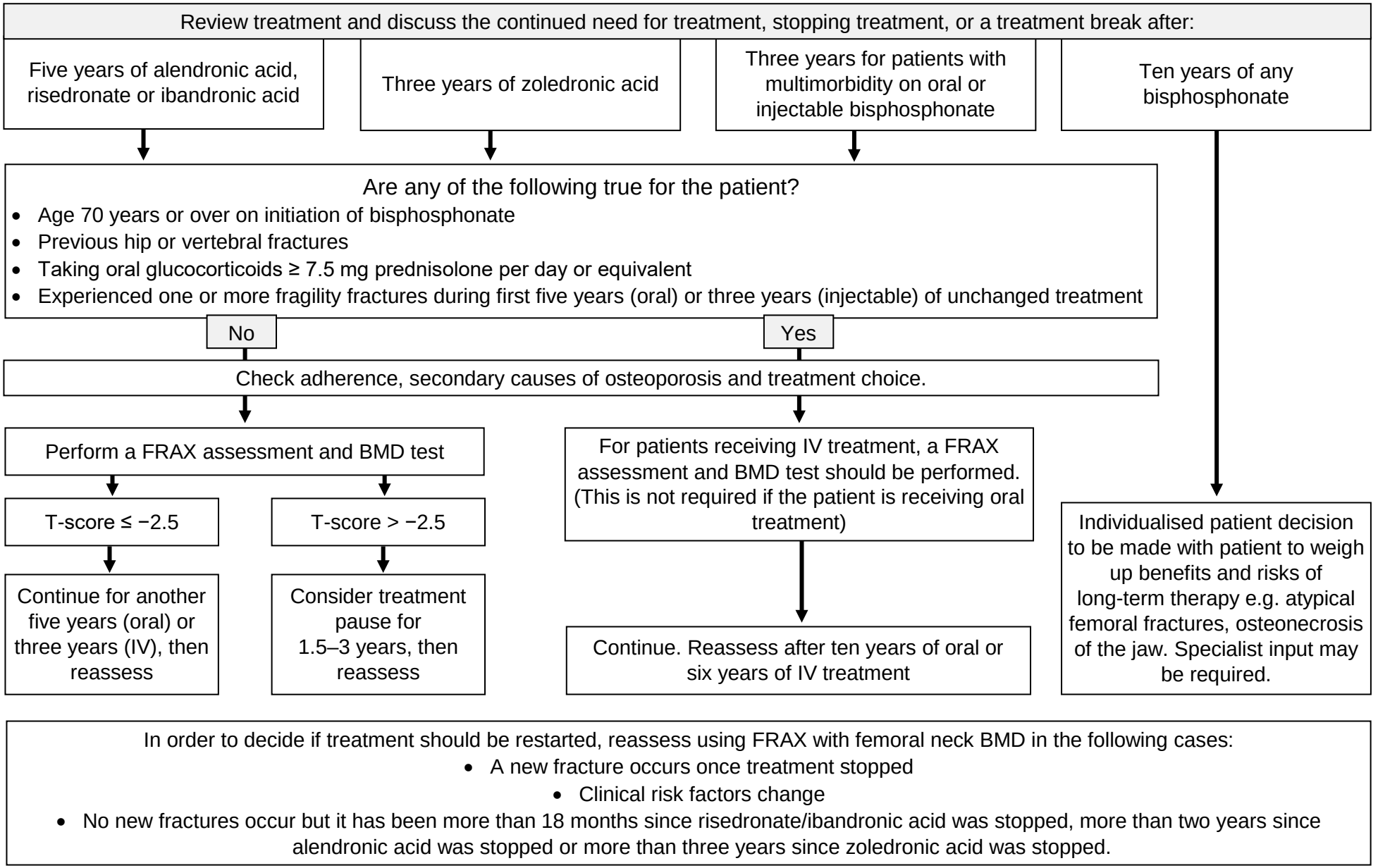
- 2–3 years for alendronic acid;
- 1–2 years for ibadronic acid and risedronate.

In the case of zoledronic acid, withdrawal after three years' treatment is associated with only a very small decrease in bone mineral density after a further three years without treatment[51].

See deprescribing algorithm (Figure 1) for advice on reassessment.

Further in-depth guidance can be found within the UK National Osteoporosis Guideline Group (NOGG) guideline[51].

Figure 1. Bisphosphonate deprescribing treatment algorithm[49,51]



BMD = bone mineral density; FRAX = fracture risk assessment tool; IV = intravenous.

6.6 Acid suppressants

6.6.1 When to consider stopping[52,53]

- Proton pump inhibitors (PPIs) are associated with an increased risk of the following and should be reviewed if the patient is experiencing adverse effects[54]:
    - infection including pneumonia and *Clostridioides difficile*;
    - bone fractures;
    - hyponatraemia;
    - hypomagnesaemia;
    - interstitial nephritis;
    - vitamin b12 deficiency.
- In addition, H_2 receptor antagonist (H_2RA) are associated with a number of risks including[12,55]:
    - increased risk of *Clostridioides difficile* infection;
    - the use of H_2RA could potentially mask gastric cancer;
    - the pharmacokinetics of certain drugs within this class (e.g. cimetidine) increase risk of drug-drug interactions.
- Is indication still valid?
    - Consider continuing in patients with a history of:
        - Barrett's oesophagus;
        - severe oesophagitis;
        - history of bleeding ulcer;
        - ongoing/uncontrolled gastro-oesophageal reflux disease (GORD).
    - Consider continuing in patients co-prescribed potentially ulcerogenic medicine e.g. long-term steroids or NSAIDs.
    - Consider deprescribing in patients with:
        - mild-to-moderate GORD treated for more than 4–8 weeks (symptoms controlled);
        - peptic ulcer disease treated for 2–12 weeks (from NSAID use; *Helicobacter pylori*);
        - upper GI symptoms without endoscopy, asymptomatic for three consecutive days;
        - ICU/surgery stress ulcer prophylaxis treated beyond a hospital admission;
        - uncomplicated *Helicobacter pylori* treated for two weeks and now asymptomatic.

6.6.2 Tapering guide

- Due to risk of rebound hypersecretion of gastric acid, tapering the dose of acid suppressant (PPI/H_2RA) is recommended.
- Review if PPI/H_2RA can be stopped or stepped down:
    - Step down: consider 'as needed (prn)' PPI/H_2RA treatment.
    - Stop: start gradual reduction with co-prescription of antacid and/or alginate for at least two weeks to reduce rebound hypersecretion.
    - Offer self-care advice.

6.6.3 Withdrawal effects

Monitor at four weeks and twelve weeks for heartburn, dyspepsia, regurgitation, epigastric pain, loss of appetite, or weight loss.

For a list of full withdrawal effects please see individual drug on www.medicines.org.uk.

6.6.4 Additional resources

- Safe use of proton pump inhibitors (AWMSG)

6.7 Opioids in non-cancer pain

6.7.1 When to consider stopping

Medicines for pain do not work for everyone with less than a third of those with chronic pain receiving benefit from treatment, in particular opioids. Pain medicines should form part of a holistic treatment plan which includes non-pharmacological management. The aim of pharmacological treatment is to form part of self-management to allow patients to function better by reducing pain intensity[56].

Opioids are associated with harm such as overdose and dependence, and adverse effects such as increased risk of infection (in particular pneumonia), constipation, vomiting, drowsiness, dizziness, osteoporosis and fracture, increased muscle tone and rigidity resulting in falls[57,58].

Older patients, those who are frail, have low body weight or renal/hepatic impairment require reduced doses of opioids for non-cancer/palliative pain[56]. Tramadol is particularly hazardous in older people due to its increased half-life and increased risk of serotonin side effects and opioid side effects due to its mechanism of action.

Transdermal opioids should be reserved for patients who are unable to receive oral medicines and should not be used for unstable pain until the efficacy of an opioid is established. Oxycodone is associated with higher rates of misuse and dependence[56]. Modified-release opioids should be avoided until benefit has been demonstrated.

The maximum recommended dose of opioid morphine equivalent is 120 mg daily for chronic non-malignant pain. Doses above this should be considered for tapering and/or discontinuation as they are unlikely to provide benefit but may increase risk of adverse effects[59].

The effectiveness of medicines for chronic pain should be reviewed regularly and a periodic dose taper can help to confirm any benefits of treatment and assess the natural history of the pain[56]

The timing of a review is partly dependent on the presenting complaint and the agreed goals of treatment. For newly initiated treatment a review should take place within 2–4 weeks of initiation or dose changes. For patients on long-term therapy, a review should take place every six months[56]. Increased review should be prompted following concerns regarding efficacy of treatment or problematic use and for patients with an increased overdose risk or who have indicators of dependence[44].

- Review diagnosis and type of pain, e.g. neuropathic pain, non-responsive.
- Review if indication still valid, e.g. has patient had intervention such as joint replacement? Has underlying condition resolved?
- Has patient developed intolerable side-effects.
- Review if pain is being managed; review if at least 30% pain reduction is not achieved.

Following initiation, if the patient doesn't describe a benefit of opioid use in the first 2–4 weeks they are unlikely to benefit long term. If the patient still complains of pain despite opioid use, this is an indication that the opioid is ineffective and they should be discontinued even if there are no other options. If a patient is not demonstrating benefit from a medicine it should be carefully tapered and stopped[56].

6.7.2 Tapering guide

Opioids should not be stopped abruptly and should be tapered down gradually with regular review. It is no longer best practice to consolidate all opioids a patient takes into a single, regularly prescribed modified-release preparation. It is easier to taper opioids that the patient is familiar with. "When required" opioid prescriptions should not be used during tapering and opioids should be managed via acute prescriptions. It is important to ensure that the patient's non-opioid pain management is optimised. Extra caution should be taken when considering the use of NSAIDs in frail, older people due to renal and cardiovascular side effects. Therefore, they should be used at the smallest dose for the shortest period of time. It is worth noting that the current evidence no longer supports the use for paracetamol in chronic pain conditions and that a dose reduction my need to be considered in older patients with low body weight, low oral intake or concurrent hepatotoxic medicines[56].

The dose of drug can be tapered by a maximum of 10% of the total daily dose weekly or two-weekly but will depend on the individual's response. Often this can be too big a dose reduction for many people and smaller dose reductions may be more successful[60]. When making small dose adjustments it is worth noting what formulations are available It may be beneficial changing to a different opioid formulation in order to make smaller reductions.

The rate and duration of taper should be adjusted to the patient's response, and once the lowest dose is reached the time interval can be extended[60,61].

Patients should be advised on non-pharmacological management strategies to improve function during opioid tapering such as exercise, physiotherapy and pacing activities[56].

6.7.3 Withdrawal effects

Stopping opioids suddenly can lead to withdrawal effects such as tiredness, diarrhoea, aching muscles, sweating, runny nose, and stomach cramps. Pain is also a withdrawal effect and can lead to patients remaining on opioids unnecessarily.

For a list of full withdrawal effects please see individual drugs on www.medicines.org.uk.

6.7.4 Additional resources

- Resources for pharmacological management of pain (AWMSG)
- Safeguarding users of opioid patches by standardizing patient and caregiver counselling (AWMSG)
- Live Well with Pain website

6.8 Gabapentinoids in neuropathic pain

6.8.1 When to consider stopping

Gabapentin and pregabalin can cause drowsiness and dizziness which can increase the risk of falls and confusion in older people[62]. It is also worth noting that as renal function declines in older people doses of these medicines may need to be adjusted depending on the extent of the impairment. See the individual drug's summary of product characteristics for guidance on dosing in renal impairment on www.medicines.org.uk.

- Gabapentin should be reviewed after 4–6 weeks to review benefit, as after this period the initial benefit for neuropathic pain may no longer occur[63].
- If a patient has no response after four weeks of therapeutic medicines for neuropathic pain, they are unlikely to respond. Therefore, the medicine should be tapered and stopped.
- Combinations of gabapentinoids with opioids and/or benzodiazepines can lead to accumulative side-effects such as sedation and ventilator impairment; therefore, use of these combinations should be prioritised for review. Warnings have been issued regarding the risk of respiratory depression with gabapentionoids[64,65].

6.8.2 Tapering guide

Reduction regimes should be individualised, discussed and agreed with the patient and will vary dependent on the patient's response. Dose changes for these drugs should not occur more frequently than weekly[66].

- Pregabalin: reduce the daily dose by 50 mg at each dose change. Dose changes may occur weekly, fortnightly or monthly depending on an agreed reduction regime with the patient[66].
- Gabapentin: reduce the daily dose by 300 mg every dose change. Dose changes may occur weekly, fortnightly or monthly depending on an agreed reduction regime with the patient[66].

If a gabapentinoid has to be discontinued for a medical reason this can be done gradually over a minimum period of one week for any indication[67,68].

6.8.3 Withdrawal effect

Patients may experience withdrawal effects from treatment cessation, therefore it is important to work closely with the patient to monitor their response[69].

Abruptly stopping gabapentin or pregabalin is not recommended. Slow tapering and monitoring of patient is advised to prevent withdrawal[70,71].

Withdrawal symptoms include anxiety, insomnia, nausea, pain and sweating.

For a list of full withdrawal effects please see individual drug on www.medicines.org.uk.

Further information on gabapentinoids can be found on the Live Well with Pain website and in the AWMSG-endorsed *Resources for pharmacological management of pain*.

6.9 Antipsychotics to treat non-cognitive symptoms of dementia (previously known as behavioural and psychological symptoms of dementia [BPSD])

6.9.1 When to consider stopping

The use of antipsychotics to treat non-cognitive symptoms (e.g. agitation, aggression) of dementia should be reviewed.

Antipsychotics are associated with an increased risk of falls and delirium, and long-term use can accelerate cognitive decline. They are also associated with cerebrovascular adverse events and mortality in patients with dementia[72-75].

Patients that are treated with antipsychotics for non-cognitive symptoms of dementia for more than three months should be reviewed, unless:

- the antipsychotic was prescribed for a pre-existing mental health condition;
- the patient is under regular review by a specialist mental health team. This does not include reviews solely planned to assess the on-going benefits of prescribing cholinesterase inhibitors (e.g. donepezil) or memantine;
- the patient has a detailed care plan in place that outlines need for the ongoing treatment for antipsychotic use.

Review and consider reducing or stopping antipsychotic medication after discussion with the patient and/or carer in the following:

- patients who have dementia and who have been on antipsychotics for more than three months and have stable symptoms;
- patients who are palliative or end-of-life;
- patients in whom the harm outweighs the benefit. Review if there is a high risk of adverse effects e.g. patient has comorbidity that places them at high risk of stroke.

Please note, it is important to contact your local mental health team before stopping any antipsychotics.

6.9.2 Tapering guide

- Antipsychotics should be withdrawn slowly with close monitoring in place, especially for re-emergence of target symptoms.
- Engage patients and/or carers in the decision process of tapering and deprescribing including the tapering regime and duration.
- Reduce dose by 25–50% and monitor closely over two weeks.
- If re-emergence of target symptoms occurs, the titration should be slowed over a longer period of time with smaller dose reductions.
- If no re-emergence of target symptoms occurs, review in two weeks to reduce by a further 25–50%, to be followed by step-wise reduction every two weeks dependent on patient’s response.

It is important to note that some patients such as those prescribed antipsychotics longer term (more than three months) may require a slower withdrawal process. In these circumstances it is advised to seek specialist advice from the Mental Health Service within your health board.

6.9.3 Withdrawal effects

Discontinuation of antipsychotics can be associated with the reoccurrence of target symptoms. This may include psychosis, aggression, agitation, delusions and hallucinations.

Low doses of antipsychotics may be discontinued without tapering. However, it is important to closely monitor the patient. Table 5 lists examples of low doses (however, the BNF or Summary of Product Characteristics should always be consulted).

Table 5. Examples of low doses of antipsychotics that may be discontinued without tapering

Medication	Suggested daily "low dose"
Aripiprazole	Less than 5 mg
Olanzapine	Less than 2.5 mg
Quetiapine	Less than 50 mg
Risperidone	Less than 0.5 mg
Amisulpiride	Less than 50 mg

6.9.4 Additional resources

- CEPP National Audit – Antipsychotics in dementia (AWMSG)
    - The aim of this audit is to ensure appropriate prescribing of antipsychotics in patients aged 65 years and over with a diagnosis of dementia.

6.10 Acetylcholine esterase inhibitors and memantine in dementia

Concerns regarding treatment with acetylcholine esterase (AChE) inhibitors and memantine should be highlighted to a specialist for review. Discontinuation of treatment can result in abatement of beneficial effects of treatment. It is important to note that following any treatment breaks re-titration may be required[76-78].

Family/carers should be involved in the process to support the patient.

6.10.1 When to consider stopping

Consider stopping in the following:

- significant cognitive decline over the past six months;
- no benefit of treatment;
- severe or end-stage dementia;
- refusal/inability to take medication that cannot be resolved;
- drug-drug, drug-disease interaction that make treatment a risk;
- severe agitation/restlessness;
- non-dementia terminal illness.

6.10.2 Tapering guide

- It is recommended to slowly taper the dose and monitor response upon withdrawal of AChE and memantine.
- Review at four weeks (shorter follow up may be required in some patients).
- Continue in a step-wise approach until treatment is stopped.

In some cases where risk outweighs benefit, abruptly stopping medication may be necessary.

6.10.3 Treatment breaks

Treatment breaks may require re-titration of drug, contact a specialist to review.
The regimes listed in Table 6 are a suggested guide only[76].

Table 6. Suggested regimes for treatment breaks and suggested actions at the point of resuming treatment

Drug	Treatment break	Action
Memantine	2 days or less	Resume at same dose
	7 days or less	Re-titrate from 10 mg
	More than 7 days	Re-titrate from 5 mg
Rivastigmine (oral)	3 days or less	Resume at same dose
	More than 3 days	Re-titrate from 1.5 mg twice daily
Rivastigmine (patch)	3 days or less	Resume at same dose
	More than 3 days	Re-titrate from 4.5 mg/24 hours
Donepezil	7 days or less	Resume at same dose
	More than 7 days	Re-titrate from 5 mg daily
Galantamine (standard release and XL)	7 days or less	Resume at the same dose
	More than 7 days	Total daily dose of 8 mg

7.0 Antimicrobial stewardship

Please refer to your local health board antimicrobial guidelines.

8.0 Anticholinergic Effect on Cognition (AEC)

The long-term use of anticholinergic drugs in older people is associated with an increased risk of cognitive decline, dementia and all cause mortality[79,80], as well as adverse effects such as constipation, urinary retention, sedation and falls[80].

- The AEC scale assigns a score from 0–3 for each medication, the higher the number the stronger the anticholinergic effect.
- Medications with a score of two or three should be reviewed, especially in older people with cognitive impairment, delirium or dementia.
- Total scores of three or above should be reviewed.
- It is recommended to review medications with the aim to reduce the AEC score.
- Where possible minimise the use of anticholinergics.
- In patients with suspected or diagnosed dementia, NICE recommend minimising anticholinergic use and look for alternative treatments with less anti-cholinergic activity.
- Avoid prescribing anticholinergics with acetylcholinesterase inhibitors (e.g. donepezil, rivastigmine) as this can worsen cognitive impairment.
- Monitor at regular intervals for efficacy and tolerance.
- If concern arises about anticholinergic-induced impaired cognition, conduct a mental state examination and consider switching or stopping medications if clinically appropriate.
- Any changes should be discussed with the patient or carer as well as the risks and benefits.

Table 7. Anticholinergic effect on cognition (AEC) scores of prescribed medications[79]

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	
Ciprofloxacin	Paracetamol	Iloperidone		

Drugs with AEC score of 0		Drugs with AEC score of 1	Drugs with AEC score of 2	Drugs with AEC score of 3
Clopidogrel	Pantoprazole	Lithium	Pimozide	Doxepin
Darifenacin	Pravastatin	Mirtazepine	Prochlorperazine	Hyoscine
Diclofenac	Propranolol	Perphenazine	Promazine	hydrobromide
Diltiazem	Rabeprazole	Prednisolone	Propantheline	Imipramine
Enalapril	Ranitidine	Quinidine	Quetiapine	Lofepramine
Entacapone	Risperidone	Sertindole	Tolterodine	Nortriptyline
Fexofenadine	Rosiglitazone	Sertraline	Trifluoperazine	Orphenadrine
Fluvoxamine	Simvastatin	Solifenacin		Oxybutynin
Furosemide	Theophylline	Temazepam		Procyclidine
Gabapentin	Thyroxine			Promethazine
Gliclazide	(levothyroxine)			Trihexyphenidryl
Haloperidol	Tramadol			(benzhexol)
Ibuprofen	Trazodone			Trimipramine
Ketorolac	Trimethoprim			
Lamotrigine	Trospium			
Levadopa	Venlafaxine			
Lisinopril	Valproate			
Loperamide	Warfarin			
Loratadine	Ziprasidone			
	Zolpidem			

8.1 Additional resources

- National Prescribing Indicators (AWMSG)
    - At the time of publication, one of the included ‘Prescribing Safety Indicators’ allows GP practices to access a list of their patients aged 75 years and over with an AEC score of 3 or more for items on active repeat.

9.0 Falls

There is a significant risk of falls in individuals aged 65 years and over, with at least one fall occurring in 30% of those aged 65 years and over and 50% in those aged 80 years and over. In 2013, falls were estimated to cost the NHS more than £2.3 billion per year and have long-term effects on individuals such as injury, increased mortality, loss of confidence and independence[81]. Those who have already had a fall are at high risk of another and the mortality from a fall at 85 years is 1%[82].

As advised by NICE, individuals who are at risk of falling, have had recurrent falls in the past year or have presented for medical attention due to a fall should have a multifactorial assessment including a medication review[81]. The literature states that patients who take four or more drugs of any pharmacologic classification have a greater risk of falling[83]. It also states that medicines acting on the brain and circulation have the highest propensity to cause falls[84]; for example the risk of falls is estimated to double in those taking psychotropic medication[85]. A large proportion of our older population are encompassed within both of these statements. Hence medication review forms a substantial part of falls prevention.

Medicines can cause falls due to several reasons, including:

- sedation/drowsiness;
- hypogylcaemia;
- confusion;
- vestibular damage;
- impaired postural stability;
- orthostatic hypotension;
- dehydration;
- hypothermia;
- visual impairment;
- drug-induced Parkinsonism.

Recent changes in medicines can cause falls, but long-term medicines that have not been reviewed are often one of the main causes[82].

Table 8. Medicines that can increase the risk of falls which should be taken into consideration when undertaking a medication review and/or when prescribing new medicines[82]

Red (High risk)*	
	Alpha blockers: Alfluzosin, doxazosin, indoramin, prazosin, tamsulosin, terazosin
	Angiotensin converting enzyme inhibitors: Captopril, enalapril, lisinopril, perindopril, rampiril, trandolapril
	Antianginals: Glyceryl trinitrate, isosorbide mononitrate, nicorandil
	Antiepileptics: Carbamazepine, phenobarbitone, phenytoin
	Anti-psychotics: Chlorpromazine, fluphenazine, haloperidol, olanzapine, quetiapine, risperidone
	Benzodiazepines
	Beta blockers: Atenolol, bisoprolol, carvedilol, metoprolol, propranolol, sotalol, timolol eye drops
	Centrally acting alpha 2 receptor agonists: Clonidine, moxonidine
	Dopamine agonists:** Pramipexole, ropinirole
	Monoamine oxidase inhibitors: Isocarboxazid, phenelzine, tranylcypromine
	Monoamine oxidase B inhibitors:** Selegiline
	Opioids
	Sedating antidepressants: Amitriptyline, clomipramine, dosulepin, doxepin, imipramine, lofepramine, mianserin, mirtazapine, nortriptyline, trazodone, trimipramine.
	Serotonin reuptake inhibitors: Duloxetine, venlafaxine
	Thiazide diuretics: Bendroflumethiazide, chlorthalidone, metolazone
	Z drugs: zopiclone/ zolpidem
Orange (Medium risk)*	
	Angiotensin receptor blockers: Candesartan, irbesartan, losartan, olmesartan, telmisartan, valsartan
	Antidysrhythmics: Amiodarone, digoxin, flecanide
	Anti-epileptics: Gabapentin, sodium valproate

	Calcium channel blockers: Amlodipine, diltiazem, felodipine, lercanidipine, nifedipine, verapamil
	Loop diuretics: Bumetanide, furosemide
	Muscle relaxants: Baclofen, dantrolene
	Selective serotonin reuptake inhibitors: Citalopram, fluoxetine, paroxetine, sertraline
Yellow (Possible risk)*	
	Acetylcholinesterase inhibitors: Donepezil, galantamine, rivastigmine
	Antiepileptics: Lamotrigine, levetiracetam, pregabalin, topiramate
	Antipsychotics: Prochlorperazine
	Antihistamines: Cinnarazine, chlorphenamine, hydroxyzine, promethazine, trimeprazine
	Anticholinergics: Oxybutynin, solifenacin, tolterodine
***** This is not a fully comprehensive list. It is intended to raise awareness of the types of drugs that cause falls. Other drugs may cause falls in certain circumstances in certain patients. ****** Do not change these Parkinson's medications without the advice of a specialist	

For further details on how the individual medication groups within the table cause falls, see *Medicines and Falls in Hospital: Guidance Sheet* (Darowski A *et al*. 2011)[82].

Osteoporosis risk should also be assessed as part of the multifactorial assessment, with the relevant treatment commenced as per the NOGG guidance, if appropriate.

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