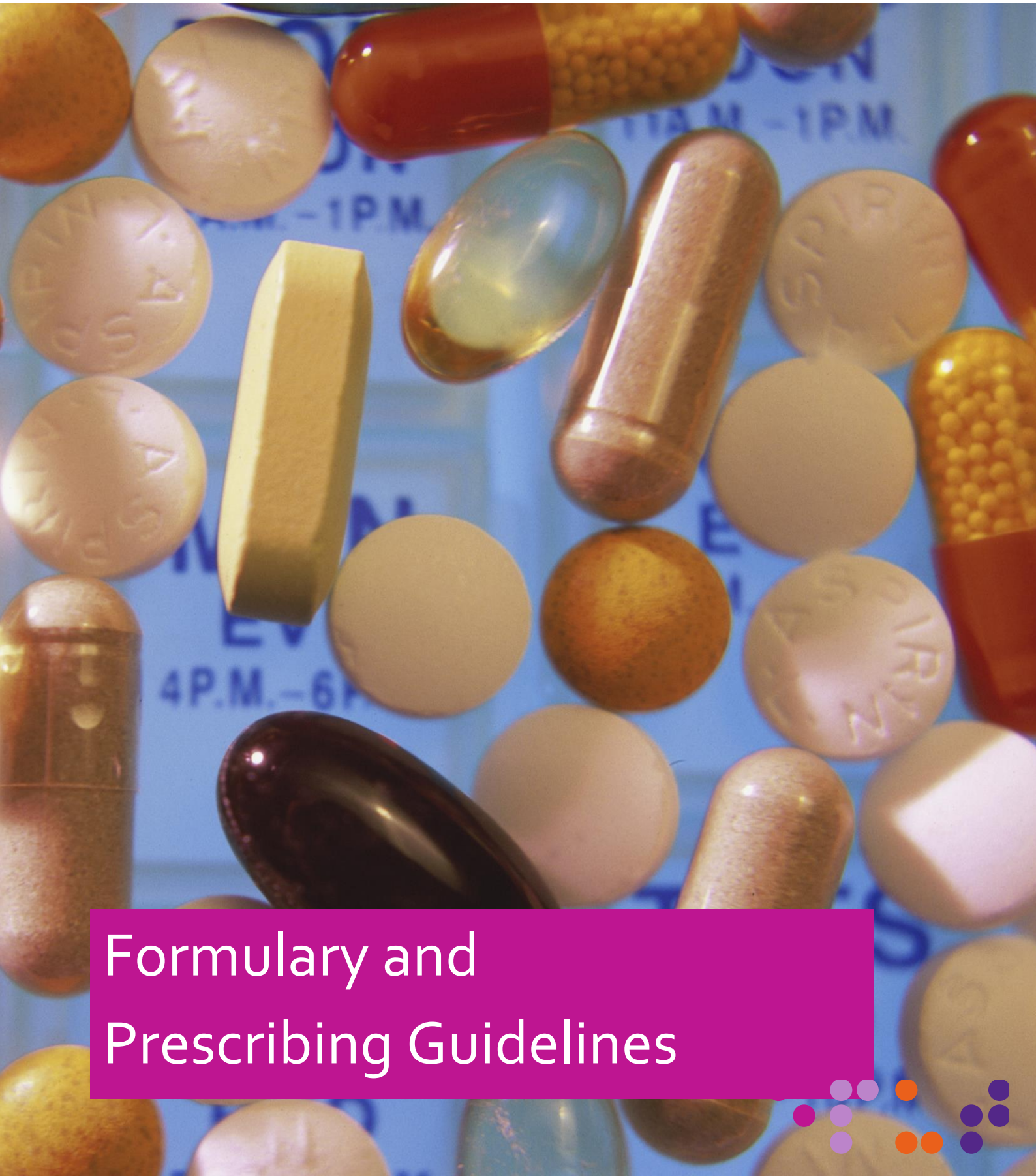
Essex Partnership University
NHS Foundation Trust

SECTION 11: DRUG USE IN OLDER ADULTS



Formulary and Prescribing Guidelines

11.1 Introduction

Older adults have increased sensitivity to medications as a result of age-related pharmacokinetic and pharmacodynamic changes.

11.1.1 Pharmacokinetic changes[1,2,3]

Pharmacokinetic changes include a reduction in the rate of absorption, changes in the volume of distribution, changes in hepatic metabolism, and reductions in urinary excretion.

a) The rate of absorption (albeit, not the extent) of drugs absorbed from the gastro-intestinal tract may be reduced in older adults. An example includes furosemide[4], which when given orally is absorbed at a reduced rate in the elderly, and thus may not effect diuresis as anticipated.

b) As the body ages, the proportions of body water, lean body mass and fat change. The latter increases whilst body water and lean body mass decrease. Continued administration of lipophilic drugs (e.g. nitrazepam and flurazepam) can result in accumulation within fat deposits. Water-soluble medicines (e.g. lithium) however, will now achieve higher concentrations in reduced body water, necessitating lower doses to achieve the same plasma concentration. Consequently, lithium also achieves higher concentrations in older adults due to reduced renal clearance. Albumin concentration usually also decreases with age, and thus, the free and active concentrations of medicines normally highly albumin bound (e.g. phenytoin[5]), can increase. It is therefore essential, to monitor and correct phenytoin levels, commensurate with reduced albumin concentrations (in the young and elderly)

c) Reports of reduced hepatic metabolism in older adults are controversial. Whilst phase II reactions are unchanged, phase I (reduction, oxidation, hydroxylation, and demethylation) are either unchanged or reduced. With increasing age, there is reduced hepatic blood flow (for example, between the ages of 25 – 65, there is a reduction of 45% in blood flow to the liver). Drugs which are subject to significant first pass metabolism by the liver (e.g. propranolol, nitrates and barbiturates) may thus show increased plasma levels in older adults. Changes in cardiac output (e.g. in heart failure) with or without arteriosclerosis, can significantly reduce hepatic metabolism of drugs (most notoriously theophylline, the dose of which should be reduced in acute heart failure). Older adults are also vulnerable (as are younger patients) to changes in drug metabolism induced by changes in smoking behaviour and dosages of drugs (e.g. theophylline, olanzapine and clozapine), and should be reduced when patients terminate smoking or significantly reduce the daily number of cigarettes smoked.

d) Renal changes primarily consist of an age-related decline in the number of nephrons – resulting in a reduced GFR (Glomerular Filtration Rate), reduced urea clearance, and a reduced ability to retain water and sodium. The likelihood of adverse drug events arising with changes in renal function is greatest with medicines that are predominantly renally excreted (e.g. lithium, allopurinol, and fluoroquinolones). See section on acute kidney injury, below.

11.1.2 Pharmacodynamic changes[1,2]

Pharmacodynamic changes include changes in the number of neurones, changes in enzymatic activity and changes in receptor sensitivity.

a) The number of cholinergic neurones decreases with age, rendering the older adult more likely to show confusion and memory impairment. They are also extremely susceptible to heightened confusion and memory loss when administered anticholinergics (e.g. Tricyclic Antidepressants (TCAs), some antipsychotics such as chlorpromazine), and antimuscarinics such as procyclidine). The aforementioned medicines should rarely (at half dose), **if ever**, be used in this population.

b) Monoamine oxidase activity increases with advancing age (resulting in reduced levels of dopamine and noradrenaline) – thus, older patients are more susceptible to dopamine-blocking agents (more likely to show extra-pyramidal side-effects).

c) There is reduced sensitivity of the beta-receptor to beta-blockers (these agents are less likely to be effective in hypertension in the older adults).

The above problems[6] are further compounded in older adults by homoeostatic changes. Such changes include a reduction in baroreceptor responses rendering this population more susceptible to drops in blood pressure without the usual, reflexive auto-regulation of blood flow to maintain BP. Older adults are therefore, in this situation, more prone to syncope.

Additional problems may include:

- Polypharmacy (as older adults are more likely to have co-morbid conditions which require treatment with several drugs)
- Communication problems (due to sensory loss, dementia, mild cognitive impairment, stroke or depression)
- Several healthcare professionals (attending to a single patient) who are frequently located in different trusts and not necessarily aware of the patient's full history or medication list
- Recent discharge from hospital (patient confused as to which drugs to stop and which to continue)
- Atypical presentation of illness (e.g. depression, UTI, or URTI)
- Inappropriate prescribing (occasional prescribing of two drugs from the same therapeutic class, and prescribing of other drugs to counteract side-effects of medicines no longer needed)

In older adults, it is essential to:

1. Check that each drug is still clearly needed and stop (appropriately) any medicines that are no longer necessary
2. If required; are the strengths, frequencies and routes of administration appropriate for the condition being treated
3. Check for drug-drug interactions and drug-disease interactions

4. Actively ascertain if the patient is experiencing drug-related side-effects, and encourage a culture whereby ward staff are invited to enquire about changes which could be drug-related
5. Review recent haematological and biochemical results relevant to a particular drug. Check given indices are not being adversely affected by recent changes in medication or condition.
6. Ascertain what the overall therapeutic plan is and whether it is being achieved
7. Review medication with the aim of reducing the likelihood to fall. For further details of medicines of particular concern refer to CG58 Appendix 7 Falls Drug Guide[12] at the end of this document.
8. What education does the patient need regarding his/her medicines to increase compliance and safety, and how capable are they of self-administering
9. Be aware that older people, especially those with mental health problems are at risk of Acute Kidney injury and that serum creatinine and levels of hydration should be monitored regularly.[11,16] See Acute Kidney Injury, below.
10. Ensure that the pharmaceutical discharge plan is complete, with a final patient interview explaining which medications are required and which have been terminated.

Acute Kidney Injury

NICE have published recommendations[16] for the prevention, detection and management of acute kidney injury.

Identification of acute kidney injury in people with acute illness

It is recommended to investigate for acute kidney injury, by measuring serum creatinine and comparing with baseline, in adults with acute illness if any of the following are likely or present:

- chronic kidney disease (adults with an estimated glomerular filtration rate [eGFR] less than 60 ml/min/1.73 m^2 are at particular risk)
- heart failure
- liver disease
- diabetes
- history of acute kidney injury
- oliguria (urine output less than 0.5 ml/kg/hour)
- neurological or cognitive impairment or disability, which may mean limited access to fluids because of reliance on a carer
- hypovolaemia
- use of drugs that can cause or exacerbate kidney injury (such as non-steroidal anti-inflammatory drugs [NSAIDs], aminoglycosides, angiotensin-converting enzyme [ACE] inhibitors, angiotensin II receptor antagonists [ARBs] and diuretics) within the past week, especially if hypovolaemic
- use of iodine-based contrast media within the past week
- symptoms or history of urological obstruction, or conditions that may lead to obstruction
- sepsis

- deteriorating early warning scores
- age 65 years or over

Identifying acute kidney injury in people with no obvious acute illness

Be aware that in adults with chronic kidney disease and no obvious acute illness, a rise in serum creatinine may indicate acute kidney injury rather than a worsening of their chronic disease.

Ensure that acute kidney injury is considered when a patient presents with an illness with no clear acute component and has any of the following:

- chronic kidney disease, especially stage 3B, 4 or 5, or urological disease
- new onset or significant worsening of urological symptoms
- symptoms suggesting complications of acute kidney injury
- symptoms or signs of a multi-system disease affecting the kidneys and other organ systems (for example, signs or symptoms of acute kidney injury, plus a purpuric rash)

Assessing risk factors in adults having iodine-based contrast media

Before offering iodine-based contrast media to adults for non-emergency imaging, investigate for chronic kidney disease by measuring eGFR or by checking an eGFR result obtained within the past 3 months.

Before offering iodine-based contrast media to adults, assess their risk of acute kidney injury but do not delay emergency imaging. Be aware that increased risk is associated with:

- chronic kidney disease (adults with an eGFR less than 40 ml/min/1.73 m2 are at particular risk)
- diabetes but only with chronic kidney disease (adults with an eGFR less than 40 ml/min/1.73 m2 are at particular risk)
- heart failure
- renal transplant
- age 75 years or over
- hypovolaemia
- increasing volume of contrast agent
- intra-arterial administration of contrast medium with first-pass renal exposure.

Include the risks of developing acute kidney injury in the routine discussion of risks and benefits of the imaging procedure.

Preventing acute kidney injury

Follow the recommendations in the NICE guideline on acutely ill adults in hospital on the use of track and trigger systems (early warning scores) to identify adults who are at risk of acute kidney injury because their clinical condition is deteriorating or is at risk of deteriorating.

When adults are at risk of acute kidney injury, ensure that systems are in place to recognise and respond to oliguria (urine output less than 0.5 ml/kg/hour) if the track and trigger system (early warning score) does not monitor urine output.

Preventing acute kidney injury in adults having iodine-based contrast media

Encourage oral hydration before and after procedures using intravenous iodine-based contrast media in adults at increased risk of contrast-induced acute kidney injury.

For inpatients having iodine-based contrast media, consider intravenous volume expansion with either isotonic sodium bicarbonate or 0.9% sodium chloride if they are at particularly high risk, for example, if:

- they have an eGFR less than 30 ml/min/1.73 m2
- they have had a renal transplant
- a large volume of contrast medium is being used (for example, higher than the standard diagnostic dose or repeat administration within 24 hours)
- intra-arterial administration of contrast medium with first-pass renal exposure is being used.

Consider temporarily stopping ACE inhibitors and ARBs in adults having iodine-based contrast media if they have chronic kidney disease with an eGFR less than 40 ml/min/1.73 m2.

Discuss the person's care with a nephrology team before offering iodine-based contrast media to adults on renal replacement therapy, including people with a renal transplant, but do not delay emergency imaging for this.

Monitoring and preventing deterioration in people with or at high risk of acute kidney injury

Seek advice from a pharmacist about optimising medicines and drug dosing in patients with or at risk of acute kidney injury.

Consider temporarily stopping ACE inhibitors and ARBs in patients with diarrhoea, vomiting or sepsis until their clinical condition has improved and stabilised.

Detecting acute kidney injury

Detect acute kidney injury, in line with the (p)RIFLE, AKIN or KDIGO definitions, by using any of the following criteria:

- a rise in serum creatinine of 26 micromol/litre or greater within 48 hours
- a 50% or greater rise in serum creatinine known or presumed to have occurred within the past 7 days
- a fall in urine output to less than 0.5 ml/kg/hour for more than 6 hours in adults

Identifying the cause(s) of acute kidney injury
Follow the recommendations for urinalysis and ultrasound.

Managing acute kidney injury

Pharmacological management

Do not routinely offer loop diuretics to treat acute kidney injury.
Consider loop diuretics for treating fluid overload or oedema while:

- awaiting renal replacement therapy or,
- renal function is recovering in patient not receiving renal replacement therapy.

Do not offer low-dose dopamine to treat acute kidney injury.

Information and support for patients and carers

Discuss immediate treatment options, monitoring, prognosis and support options as soon as possible with people with acute kidney injury and/or, if appropriate, their carer.

Give information about long-term treatment options, monitoring, self-management and support to people who have had acute kidney injury (and/or their carer, if appropriate) in collaboration with a multidisciplinary team appropriate to the person's individual needs.

Discuss the risk of developing acute kidney injury, particularly the risk associated with conditions leading to dehydration (for example, diarrhoea and vomiting) and drugs that can cause or exacerbate kidney injury (including over-the-counter NSAIDs), with people who are at risk of acute kidney injury, particularly those who have:

- chronic kidney disease with an eGFR less than 60 ml/min/1.73 m2
- neurological or cognitive impairment or disability, which may mean limited access to fluids because of reliance on a carer.

Chronic kidney injury

NICE have published recommendations[17] for the assessment and management of chronic kidney injury.

Monitor GFR at least annually in any patient taking medicines that can adversely affect kidney function, such as calcineurin inhibitors (for example, ciclosporin or tacrolimus), lithium or non-steroidal anti-inflammatory drugs (long-term chronic use of NSAIDs).

Monitor patients for the development or progression of CKD for at least 3 years after acute kidney injury (longer for people with acute kidney injury stage 3) even if eGFR has returned to baseline.

Refer to the recommendations for further guidance about:

- Measuring kidney function
- Who should be tested for CKD
- CKD classification
- Frequency of monitoring
- Risk assessment
- Pharmacotherapy for hypertension, proteinuria
- Pharmacotherapeutic use of Renin–angiotensin system antagonists, statins, oral antiplatelets and anticoagulants.
- Diagnosis, assessment and management of anaemia
- Hyperphosphataemia

- Other complications

Chronic kidney injury and type 2 diabetes

NICE have published specific advice [18] about the use of SGLT2 inhibitor drugs, for patients with type 2 diabetes and chronic kidney disease.

- For adults with chronic kidney disease and type 2 diabetes, offer an angiotensin receptor blocker (ARB) or an angiotensin-converting enzyme (ACE) inhibitor (titrated to the highest licensed dose that the person can tolerate) if albumin-to-creatinine ratio (ACR) is 3 mg/mmol or more, as recommended in the section on pharmacotherapy for CKD in patients with related persistent proteinuria in the NICE guideline on chronic kidney disease [17].

- For adults with type 2 diabetes and CKD who are taking an ARB or an ACE inhibitor (titrated to the highest licensed dose that they can tolerate), offer an SGLT2 inhibitor (in addition to the ARB or ACE inhibitor) if:

    - ACR is over 30 mg/mmol and

    - they meet the criteria in the marketing authorisation (including relevant estimated glomerular filtration rate [eGFR] thresholds).

- For adults with type 2 diabetes and CKD who are taking an ARB or an ACE inhibitor (titrated to the highest licensed dose that they can tolerate), consider an SGLT2 inhibitor (in addition to the ARB or ACE inhibitor) if:

    - ACR is between 3 and 30 mg/mmol and

    - they meet the criteria in the marketing authorisation (including relevant eGFR thresholds).

In November 2021, not all SGLT2 inhibitors were licensed for this indication.

11.2 Choice of psychotropic drugs in the older adult

Where feasible, it is desirable to avoid medications which are hypotensive, anticholinergic, give rise to extra-pyramidal side-effects (EPSE) and cause sedation. Anticholinergic properties in addition to causing mental confusion and memory impairment can also precipitate constipation, difficulties with visual accommodation and urinary retention.

It is essential to ascertain if there is a diagnosis/suspicion of dementia – as this category renders patients treated with antipsychotics particularly vulnerable to ischaemic stroke. Most SPCs for antipsychotics (except risperidone) prohibit the use of such medications in elderly demented subjects. The use of antipsychotics in this population is (with the exception of risperidone and haloperidol) short-term, unlicensed and only where there is significant risk of harm to the patient and/or others. See section 7 for further details.

Consider tests for thyroid dysfunction for patients with depression or unexplained anxiety.[15]

11.2.1 Antipsychotics

"The use of antipsychotic medication for people with dementia: a time for action" (known as the Banerjee Report[7]) was published in 2009 having been commissioned by the DH. The report identifies that antipsychotics are being over-prescribed, when alternative, non pharmacological approaches to dealing with anxiety and behavioural problems are available. This report contains 11 recommendations that will, if implemented, reduce the use of these drugs to the level where benefit will outweigh risk and assure us that patients are being managed safely and effectively. As the report points out, behavioural problems in people with dementia can be distressing and dangerous, so in some cases antipsychotic medication may be the best option. Further information about treatment of dementia can be found in section 7.

Hypotensive, sedative and anticholinergic effects are particularly noticeable in with First Generation Antipsychotics (FGAs), especially chlorpromazine. The FGA antipsychotic, haloperidol is especially likely to generate EPSEs in this population. Where possible they should be avoided.

Haloperidol is licensed for the treatment of persistent aggression and psychotic symptoms in patients with moderate to severe Alzheimer's dementia and vascular dementia when non-pharmacological treatments have failed and when there is a risk of harm to self or others.

The newer atypical antipsychotics such as olanzapine and risperidone, are better-tolerated, but must also be dosed cautiously to ameliorate hypotensive effects (especially with quetiapine), EPSEs (especially with risperidone) and sedation (especially with olanzapine). Their starting doses and incremental dose increases are lower, and incremental intervals are longer –endorsing the old age saying: 'start low, go slow'.

Risperidone is the only atypical antipsychotic licensed for the short-term treatment (up to 6 weeks) of persistent aggression in patients with moderate to severe Alzheimer's dementia (only where there is a significant risk of harm to patient and/or to others). Although not specified in the SPC, baseline and regular BP and HR monitoring is recommended as risperidone has alpha-blocker properties.

Postural hypotension has been infrequently observed in the elderly within **Olanzapine** clinical trials. As with other antipsychotics, it is recommended that blood pressure is measured periodically in patients over 65 years. Olanzapine does have anticholinergic activity, and patients on this medication should be monitored for constipation.

The SPC for **Quetiapine** specifies that the effective dose in the older adult group is likely to be lower than in younger patients. The common side effects quoted are somnolence and orthostatic hypotension. Therefore regular BP and HR monitoring are advisable.

Clozapine is considered safe, effective and reasonably well-tolerated (if dosed carefully) in the elderly. There may be an increased incidence of agranulocytosis

so extra care (that is, follow-up for increased temperature/signs of infection) is warranted.

Delirium and antipsychotics

NICE[13] reviewed the drug treatment of delirium. Olanzapine is no longer recommended as the clinical need can now be met by a licensed product, haloperidol. If a person with delirium is distressed or considered a risk to themselves or others and verbal and non-verbal de-escalation techniques are ineffective or inappropriate, consider giving short-term (usually for 1 week or less) haloperidol. Start at the lowest clinically appropriate dose and titrate cautiously according to symptoms.

Older patients are at an increased risk of adverse neurological and cardiac effects when being treated with haloperidol for delirium. The lowest possible dose of haloperidol should be used for the shortest possible time, and cardiac and extrapyramidal adverse effects should be closely monitored.

When prescribing haloperidol for the acute treatment of delirium, consider the advice shown below (MHRA[19]):

- special caution is required when using haloperidol for the acute treatment of delirium in frail, elderly patients
- only consider haloperidol for delirium when non-pharmacological interventions are ineffective and no contraindications are present (including Parkinson's disease and dementia with Lewy bodies)
- before initiating treatment, a baseline electrocardiogram (ECG) and correction of any electrolyte disturbances is recommended; cardiac and electrolyte monitoring should be repeated during treatment (see below)
- prescribe the lowest possible dose for the shortest possible time, ensuring that any dose up-titration is gradual and reviewed frequently
- monitor for and investigate early any extrapyramidal adverse effects, such as acute dystonia, parkinsonism, tardive dyskinesia, akathisia, hypersalivation, and dysphagia
- report suspected adverse reactions associated with haloperidol on a Yellow Card

11.2.2 Antidepressants

As above, consideration must be given to the possibility of anticholinergic, hypotensive, sedative (for example with the Tricyclic antidepressants) and dyskinetic (for example with paroxetine) side-effects. Additionally, there should be monitoring, especially in older adults, for antidepressant-induced hyponatraemia.

SSRIs are generally used first-line. They offer considerable advantages over Tricyclic antidepressants including potentially fewer side-effects, safety in overdose, less dosage titration, once a day administration and greater patient adherence.

Tricyclic antidepressants (TCAs) can cause orthostatic hypotension, anticholinergic side effects (constipation, urinary retention, changes in visual accommodation), intracardiac conduction changes (such as slowing down conduction through the His-Purkinje system), weight gain, and are significantly more dangerous in overdose than SSRIs. All but lofepramine should rarely be used in older adults

The **irreversible MAOIs** (such as phenelzine and tranylcypromine) are associated with serious drug-drug and drug-food interactions. Additionally, they can cause orthostatic hypotension, weight gain, oedema and sexual dysfunction. Although not known as anticholinergic medicines, patients have claimed to experience blurred vision and urinary retention with these agents. They are considered more toxic in the older population as a result of the increased potential for falls in this group, but can, in cases of highly resistant depression, be very effective.

The **reversible MAOI**, moclobemide, is considered to be less toxic in older adults (relative to phenelzine, or tranylcypromine) with an SPC claiming that no dose reductions are required in this age group[8].

No dosage reduction is required (relative to younger patients) when **mirtazapine** is used in older adults albeit the SPC cites that dosage increments should be implemented with care. It can, usefully, increase appetite and sleep.

Trazodone is not considered an effective antidepressant. Most people cannot tolerate the attendant sedative effects associated with antidepressant-effective doses of 300-600mg per day. It is however, a very useful adjunct in insomnia in older patients but caution is warranted with drowsiness, dizziness (can cause blood pressure drops) and a dry mouth.

11.2.3 Anxiolytics and Hypnotics

Benzodiazepines should always be used with care in the older adults – there is potential for daytime drowsiness, cognitive impairment, hypotension, and reduced muscle tone (the latter contributing to an increased frequency of falls). Temazepam is used in older adults, but at a reduced dose relative to younger adults. Half the normal dose is recommended, that is, 5-15 mg at night. As indicated in Section 5 (Insomnia in Adults), long-term administration is not recommended.

The FDA has warned of a serious risk of death when benzodiazepines are used in combination with Opioid analgesic or cough preparations.[10]

Zopiclone can be used in the older adult group. Although the manufacturer claims lack of accumulation in this population, a lower initial dose of 3.75mg zopiclone is recommended. Subsequently, depending on effectiveness and acceptability, the dosage may be increased.

Melatonin (now available as the licensed product, Circadin®) is indicated for the short-term treatment (thirteen weeks) of primary insomnia (characterised by poor quality of sleep) specifically in patients over 55. Melatonin is naturally produced by the pineal gland, but only in relative darkness and during the nocturnal phase of the circadian cycle. There is an age-related reduction in endogenous melatonin production. Thus, administration of exogenous melatonin is believed (and has

been shown) to improve sleep quality in older adults with primary insomnia. Melatonin is currently non-formulary in older adults

11.2.4 Mood stabilizers

Lithium, carbamazepine, valproate and atypical antipsychotics are advocated for use in older adults with bipolar affective disorder.

The older require **lithium** levels which are considerably lower than those used in younger patients. Specifically, the maintenance levels in the older patients should be kept within the range of 0.4mmol/L – 0.8mmol/L (12 hours post dose). Lithium can cause mild tremor, polyuria, and hypothyroidism. Avoidance of toxicity depends on regular monitoring of levels along with patient and/or carer education regarding symptoms of said impending toxicity (e.g. slurred speech and change in tremor presentation from mild to coarse). Lithium is a renally excreted drug and thus, is subject to drug interactions with NSAIDs and ACE-inhibitors (both classes can increase Lithium levels).

Carbamazepine is associated with blood dyscrasias, hyponatraemia and dose-related unsteadiness and dizziness (monitor carbamazepine levels). It is involved in a multitude of drug-related interactions (such as reduction of the effect of warfarin, some analgesics and antibiotics). The starting dose is lower in the elderly at 100 mg twice a day.[9]

Valproic acid, as Depakote is effective as a mood stabilizer but can cause gastric irritation, weight gain (especially with olanzapine), sedation, and blood dyscrasias (specifically thrombocytopenia). Recommended starting dose is 250mg daily.

11.3 Choice of non-psychotropic drugs in the older adult

11.3.1 Physical health

The geography of EPUT is covered by several CCGs and several Sustainability and Transformation Partnerships (STPs), each with their own formulary and prescribing guidelines for the management of medical conditions. Prescribers should follow the local formulary, wherever possible, for the management of non-psychiatric conditions. However it should be noted that some medicines and products have been agreed for inpatient treatment Trust-wide, so anomalies may exist. In such instances reference should be made to the pharmacy team to resolve any issues.

Reference should be made to the Community Health Services Formulary and Prescribing Guidelines, where this covers treatments for specific physical conditions, for example food supplements.

Links to local formularies can be found on the Trust intranet, in the section for Formulary & Prescribing Guidelines in Community Health Services. Local formularies can also be accessed at each CCG public website.

11.3.2 End of life care

Community health services (non-psychiatry) support care delivery to all patients at end of life, irrespective of diagnosis. End of life care guidelines are available on the intranet, in the section, “End of Life Care”. This contains useful documents and links, including guideline CG88, “End of Life Clinical Guideline”.

EPUT MH&LD and EPUT CHS do not maintain their own formulary and prescribing guidelines for end of life / palliative care. Instead, reference should be made to documents from the local CCGs, hospices and STPs, who in each area have different guidance.

Prescribers are recommended to access the guidance from the CCG websites, as they will contain the most up to date versions, and describe the best practice as delivered by local teams.

The latest recommendations from NICE are published in guideline NG142: End of life care for adults: service delivery, October 2019 [14].

References

1. Kim J et al. ‘Geriatric Drug Use’. In ‘Applied Therapeutics: the clinical use of drugs 2008’ edited by Koda-Kimble M et al.
2. Hughes S. Prescribing for the elderly patient: why do we need to exercise caution? Br J Clin Pharmacol 1998; 46: 531-533
3. Mayersohn M. Pharmacokinetics in the elderly. Environmental Health Perspectives 1994; 102 (S11):
4. Sica D. Drug absorption in the management of congestive heart failure: loop diuretics. Congestive Heart Failure 2003; 9: 287-292
5. Patterson M et al. Plasma protein binding of phenytoin in the ages in vivo studies. Br J Clin Pharmac 1982; 13: 423-425
6. Mangoni A et al. Age-related changes in pharmacokinetics and pharmacodynamics: basic principles and practical applications. Br J Clin Pharmacol 2004; 57(1): 6-14
7. Banerjee S. The Use of Antipsychotic medication for people with dementia. Department of Health; 2009
8. NICE Clinical Guideline CG161- Falls June 13 (Reviewed January 2016)
9. Summary of Product Characteristics for Individual Drugs [accessed October 2017, Haloperidol June 2019] http://www.medicines.org.uk/EMC/
10. http://www.fda.gov/Drugs/DrugSafety/default.htm Accessed September 2016
11. Guidance for Mental Health Professionals on the management of Acute Kidney Injury https://www.thinkkidneys.nhs.uk/aki/wp-content/uploads/sites/2/2016/06/Guidance-for-mental-health-patients-version-v18.pdf
12. CG58 Appendix 7 Falls Drug Guide

13. NICE clinical guideline CG103. Delirium: prevention, diagnosis and management. Published date: July 2010 Last updated: March 2019
14. NICE guideline NG142: End of life care for adults: service delivery. Published date: 16 October 2019. Accessed 5/5/2020.
15. NICE guideline NG145: Thyroid disease: assessment and management. Published date: 20 November 2019. Accessed 6/5/2020.
16. NICE guideline NG148: Acute kidney injury: prevention, detection and management. Published date: 18 December 2019. Accessed 6/5/2020.
17. NICE guideline NG203: Chronic kidney disease: assessment and management. Published: 25 August 2021. Last updated: 24 November 2021. Accessed 25.11.2021.
18. NICE guideline NG28: Type 2 diabetes in adults: management. Published: 02 December 2015 Last updated: 24 November 2021. Accessed 13.4.2022.
19. MHRA Drug Safety Update. Volume 15 Issue 5 December 2021. Haloperidol (Haldol): reminder of risks when used in elderly patients for the acute treatment of delirium.