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NHS
Cumbria
Clinical Commissioning Group

STOPP START Toolkit Supporting Medication Review

STOPP:

Screening Tool of Older People's potentially inappropriate Prescriptions.

START:

Screening Tool to Alert doctors to Right i.e. appropriate, indicated Treatments.[1]

STOPP: Screening Tool of Older People's potentially inappropriate Prescriptions.[1]

Prescriptions that are potentially inappropriate in persons aged ≥ 65 years of age

START: Screening Tool to Alert doctors to Right i.e. appropriate, indicated Treatments.[1]

Medication that should be considered for people ≥ 65 years of age where no contraindication exists

An evidence based approach to prescribing in the elderly.

Introduction

A definition of medication review is "a structured, critical examination of a patient's medicines with the objective of reaching an agreement with the patient about treatment, optimising the impact of medicines, minimising the number of medication-related problems and reducing waste".[2]

It is commonly agreed that older people are at greater risk of adverse effects from their medicines due to age related changes in their major organs which in turn alter pharmacokinetics and pharmacodynamics. They also often have multiple co-morbidities leading to drug-drug interactions or cautions and contraindications to preferred treatments.

These patients however are often excluded from drug trials making it difficult for the clinician to weigh up the benefits versus risks, let alone explain them to the patient. Furthermore, although with increasing age a patient can move from benefiting from a treatment to being at significant risk from it, there can be difficulty in stopping medication for the fear of being accused of ageism.

This document is based on the STOPP START Tool a medication review tool designed to identify medication where the risks out weigh the benefits in the elderly and vice versa.

Eighteen experts in geriatric pharmacotherapy initially contributed to suggesting and then rating the criteria. The STOPP criteria were evaluated (along with Beer's criteria[3]) against hospital admissions — one third of the patients with "potentially inappropriate prescriptions"

according to STOPP criteria presented with an associated adverse drug event.

All recommendations from the STOPP START Tool are included here, and where space allows, local and national guidance (in blue-edged boxes) these can only be considered correct at time of publication.

The tool was validated in patients aged 65 and over but there is still a place for clinical judgement in deciding whether a person is "elderly" in terms of the potential effects of medication.

The recommendations are grouped according to the main British National Formulary chapters[4] with the STOPP items on the left (coloured red) and the START items (coloured green) on the right of the double page. The rationale for the intervention is given in italics.

The process of medication review is covered in the practice guide to clinical medication review.[5] As well as using the list of drugs here to decide which might need to be stopped in the frail elderly it should also be considered if the drug gives daily symptomatic benefit, prevents rapid worsening of symptoms or replaces a hormone vital for normal function e.g. thyroxine. If so it should normally be continued.

A study of prescribing in general practice in Scotland[6] used a panel of GPs and pharmacists to develop "prescribing safety indicators" (PSI) to judge the prescribing against. These were mostly either high risk drug combinations (drug interactions) or drug-disease combinations (contraindications). The indicators not already covered by STOPP are given in the blue supporting information boxes however it is the clinicians responsibility to consider other drug interactions or contra-indications not listed here.

The following drugs or drug classes were most often implicated in a UK study[7] looking at cause of admission in two hospitals over a six month period (result given as percentage of adverse drug reaction—ADR—related admissions which in turn were 6.5% of all admissions).

1.	NSAIDs including aspirin	29.6%
2.	Diuretics	27.3%
3.	Warfarin	10.5%
4.	ACEI/A2RAS	7.7%
5.	Antidepressants including lithium	7.1%
6.	Betablockers	6.8%
7.	Opiates	6.0%
8.	Digoxin	2.9%
9.	Prednisolone	2.5%
10.	Clopidogrel	2.4%

This study was in patients over the age of 16, but clinicians will recognise that these drugs are commonly prescribed in older people.

The authors suggested that over 70% of the ADRs were avoidable. These findings are supported by a 2006 systematic review[8] which found the four most common drug groups associated with preventable drug-related admissions to be antiplatelets (16%), diuretics (15.9%), NSAIDs (11%) and anticoagulants (8.3%). In addition to those listed above, they found drugs used in diabetes (3.5%), positive inotropes (3.2%), calcium channel blockers (2.8%) and antiepileptics (2.3%) were also implicated. (This review was not confined to the UK population and not all studies were specific to older people).

If wanting to reduce the burden of polypharmacy in gradual steps it might be prudent to tackle the above drugs as a priority after removing ineffective or unnecessary treatment.

Many anticholinergic (antimuscarinic) drugs are included in the STOPP sections already but as combining anticholinergic drugs increases the risk of side effects (including confusion, falls and death) the Anticholinergic Cognitive Burden scale[9] for some commonly prescribed drugs is given on page 27 and in more detail in the appendices of the practice guide to clinical medication review.[5]

Particular caution should be taken if considering stopping the following drugs (continue treatment, gradual withdrawal or specialist advice before stopping):[10]

- ACEI and diuretics used in heartfailure.
- Amiodarone, CCBs, betablockers or digoxin used to control heart rate or rhythm.
- Anticonvulsants used in epilepsy.
- Antidepressant, antipsychotic or mood stabilizing drugs.
- Antimuscarinic or other drugs used in Parkinson's disease.
- Steroids, DMARDs or immunosuppressant drugs.

Further information to aid the assessment of benefits versus risks including number needed to treat and number needed to harm can be found in the appendices of the practice guide.[5]

Colour Key.

Medication to consider stopping in patients over 65 from the STOPP Tool[1]

Medication to consider starting in patients over 65 from the START Tool [1]

National and local guidance e.g. NICE Guidelines[11] or other supporting/useful information e.g. prescribing safety indicators (PSI).

STOPP: Screening Tool of Older People's potentially inappropriate Prescriptions.[1]

The following STOPP prescriptions are potentially inappropriate in persons aged ≥65 years of age

Gastrointestinal System BNF Chapter 1

Diphenoxylate, loperamide or codeine phosphate

- for treatment of diarrhoea of unknown cause* *(risk of delayed diagnosis, may exacerbate constipation with overflow diarrhoea, may precipitate toxic megacolon in inflammatory bowel disease, may delay recovery in unrecognised gastroenteritis).*
- for treatment of severe infective gastroenteritis i.e. bloody diarrhoea, high fever or severe systemic toxicity *(risk of exacerbation or protraction of infection).*
- **Prochlorperazine** or **metoclopramide** with Parkinsonism *(risk of exacerbating Parkinsonism).*
- **Proton pump inhibitor** at **treatment dose** for peptic ulcer disease at full therapeutic dosage for > 8 weeks *(earlier discontinuation or dose reduction for maintenance/ prophylactic treatment of peptic ulcer disease, oesophagitis or GORD indicated).*
- **Anticholinergic antispasmodic drugs** with chronic constipation *(risk of exacerbation of constipation).*

Review enteral nutrition: **NICE CG32** (Nutrition support in adults) recommends assessment using a tool such as MUST:
www.bapen.org.uk/pdfs/must/must_full.pdf

START: Screening Tool to Alert doctors to Right i.e. appropriate, indicated Treatments.[1]

These START medications should be considered for people ≥ 65 years of age with the following conditions, where no contraindication exists.

Gastrointestinal System BNF Chapter 1

- **Proton Pump Inhibitor** with severe gastro-oesophageal acid reflux disease or peptic stricture requiring dilatation.
- **Fibre supplement** for chronic, symptomatic diverticular disease with constipation.

NICE CG59 Osteoarthritis

"Offer a standard NSAID...Co-prescribe with a **proton pump inhibitor**"

Local dyspepsia and gastric ulcer prescribing guidelines are available from the **Medicines Management** intranet pages.[5]

* For diarrhoea of unknown cause consider the possibility of Clostridium difficile infection (CDI) if there is a history of antibiotic use or recent hospital discharge.

Stop antimotility agents and PPIs

Stop antibiotics

Cardiovascular System BNF Chapter 2

STOPP

- **Digoxin** at a long-term dose > 125µg/day with impaired renal function — estimated GFR <50ml/min *(increased risk of toxicity).*

Loop diuretic

- for dependent ankle oedema only i.e. no clinical signs of heart failure *(no evidence of efficacy, compression hosiery usually more appropriate).*
- as first-line monotherapy for hypertension *(safer, more effective alternatives available).*
- **Thiazide diuretic** with a history of gout *(may exacerbate gout).*

Beta-blocker

- in combination with verapamil *(risk of symptomatic heart block).*
- **Non-cardioselective beta-blocker** with Chronic Obstructive Pulmonary Disease (COPD) *(risk of bronchospasm)*.

Calcium channel blockers

- with chronic constipation *(may exacerbate constipation).*
- Use of **diltiazem or verapamil** with NYHA Class III or IV heart failure *(may worsen heart failure).*
- **Vasodilator drugs** known to cause hypotension in those with persistent postural hypotension i.e. recurrent > 20mmHg drop in systolic blood pressure *(risk of syncope, falls). Stop if patient has fallen in past 3 months.*

Aspirin

- with a past history of peptic ulcer disease without histamine H2 receptor antagonist or Proton Pump Inhibitor *(risk of bleeding).*
- at dose > 150mg day *(increased bleeding risk, no evidence for increased efficacy).*
- with no history of coronary, cerebral or peripheral arterial symptoms or occlusive arterial event *(not indicated).*
- to treat dizziness not clearly attributable to cerebrovascular disease *(not indicated).*
- with concurrent bleeding disorder *(high risk of bleeding).*

Warfarin

- for first, uncomplicated deep venous thrombosis for longer than 6 months duration *(no proven added benefit).*
- for first uncomplicated pulmonary embolus for longer than 12 months duration *(no proven benefit).*
- with concurrent bleeding disorder *(high risk of bleeding).*
- Use of aspirin and warfarin in combination without gastroprotection (avoid cimetidine because of interaction with warfarin)(*high risk of gastrointestinal bleeding).*

Clopidogrel

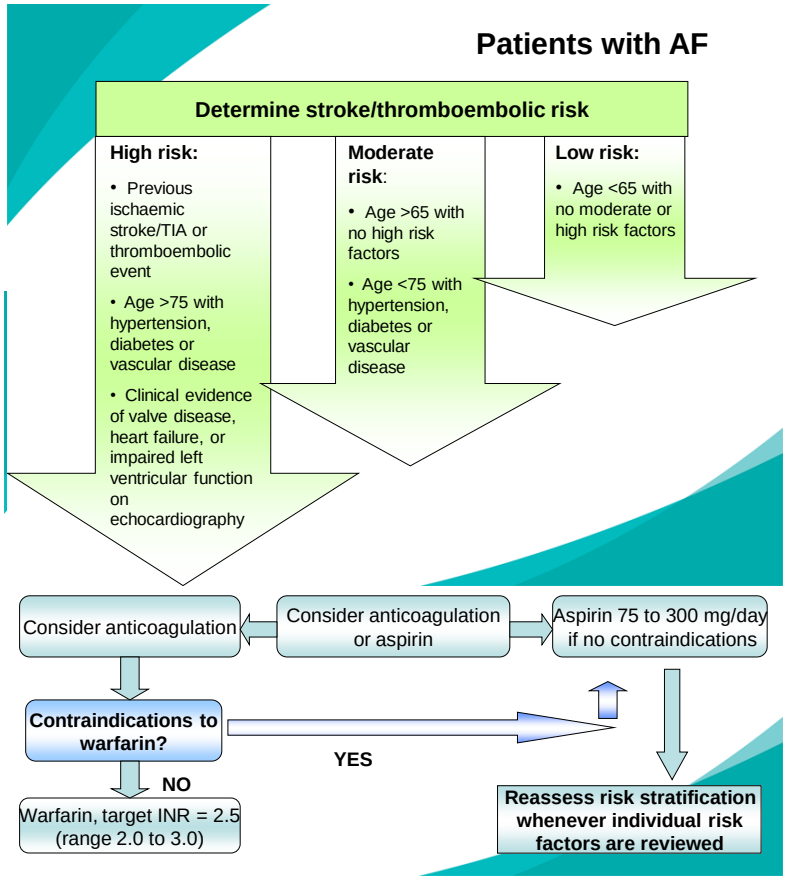
- with concurrent bleeding disorder *(high risk of bleeding).*

Dipyridamole

- as monotherapy for cardiovascular secondary prevention *(no evidence for efficacy except in ischaemic stroke).*
- with concurrent bleeding disorder *(high risk of bleeding*).

Prescribing safety indicators: The combination of NSAIDs, ACEI/A2RA and diuretic is considered particularly risky. Antiplatelets should not be combined with warfarin—even if indicated the benefits are unlikely to outweigh the harms in the frail elderly.

NICE CG36 Atrial Fibrillation (AF)
When to start warfarin or aspirin in AF:



NICE TA 210 covers which antiplatelet to use to prevent occlusive vascular events e.g. **MI** use aspirin first line; **ischaemic stroke** use clopidogrel first line and **TIA** use MR dipyridamole AND aspirin.

Cardiovascular System BNF Chapter 2

START

- **Warfarin** in the presence of chronic atrial fibrillation (see NICE guidance on page 12).
- **Aspirin** in the presence of chronic atrial fibrillation, where warfarin is contraindicated, but not aspirin.
- **Aspirin** with a documented history of atherosclerotic coronary disease in patients with sinus rhythm.
- **Clopidogrel** with a documented history of ischaemic stroke or peripheral vascular disease
- **Antihypertensive** therapy where systolic blood pressure consistently >160 mmHg.
- **Statin** therapy with a documented history of coronary, cerebral or peripheral vascular disease, where the patient's functional status remains independent for activities of daily living and life expectancy is > 5 years.*
- **Angiotensin Converting Enzyme (ACE) inhibitor** with chronic heart failure.
- **ACE inhibitor** following acute myocardial infarction.
- **Beta-blocker** with chronic stable angina.

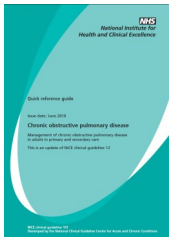
*NICE CG 67 Lipid Modification Prescribing Guidelines do not specify a degree of independence or life expectancy for secondary prevention (offer to all adults with clinical evidence of CVD); in primary prevention they suggest systematic strategies are used to identify people aged 40-74 likely to be at high risk— statins *can* be started in older people but risk calculators are inaccurate, they may be at greater risk from the treatment and benefit is unlikely to be gained until after five years of therapy.

Respiratory System BNF Chapter 3

STOPP

- **Theophylline** as monotherapy for COPD *(safer, more effective alternatives; risk of adverse effects due to narrow therapeutic index).*
- **Systemic corticosteroids** instead of inhaled corticosteroids for maintenance therapy in moderate-severe COPD *(unnecessary exposure to long-term side-effects of systemic steroids).*
- **Nebulised ipratropium** with glaucoma *(may exacerbate glaucoma).*
- **First generation antihistamines** *(sedative, may impair sensorium). Stop if patient has fallen in past 3 months*.

NICE CG 101 COPD



Theophylline

Only offer theophylline after trials of short- and long-acting bronchodilators or to people who cannot use inhaled therapy.

Oral Corticosteroids

Maintenance use of oral corticosteroid therapy in COPD is not normally recommended.

Some people with advanced COPD may need maintenance oral corticosteroids if treatment cannot be stopped after an exacerbation. Keep the dose as low as possible, monitor for osteoporosis and offer prophylaxis.

Respiratory System BNF Chapter 3

START

- Regular inhaled **beta 2 agonist** or **anticholinergic (antimuscarinic)** agent for mild to moderate asthma or COPD.

- Review patients with mild or moderate COPD at least once a year and severe or very severe COPD (FEV1 <50% predicted) at least twice a year. Follow NICE guidance regarding treatment selection for COPD. (Use BTS/SIGN guidelines for asthma).

NICE CG 101 COPD

Assess the need for **oxygen** therapy in people with any of the following:

-very severe airflow obstruction (FEV1 <30% predicted)
-cyanosis
-polycythaemia
-peripheral oedema
-raised jugular venous pressure
-oxygen saturations less than or equal to 92% breathing air.

Give people with FEV1 < 30% a course of **antibiotic** and **oral corticosteroid** tablets to keep at home.

Central Nervous System

BNF Chapter 4

STOPP

Tricyclic antidepressants (TCAs)

- with dementia *(risk of worsening cognitive impairment).*
- with glaucoma *(likely to exacerbate glaucoma).*
- with cardiac conductive abnormalities *(pro-arrhythmic effects).*
- with constipation *(likely to worsen constipation).*
- with an opiate or calcium channel blocker *(risk of severe constipation).*
- with prostatism or prior history of urinary retention *(risk of urinary retention).*

Benzodiazepines

- if long-term (i.e. > 1 month) and long-acting
  e.g. chlordiazepoxide, flurazepam, nitrazepam and benzodiazepines with long-acting metabolites e.g. diazepam *(risk of prolonged sedation, confusion, impaired balance, falls).*
- if fallen in past 3 months

Antipsychotics*

- long-term (i.e. > 1 month) as hypnotics *(risk of confusion, hypotension, extra-pyramidal side effects, falls).*
- long-term (> 1 month) in those with parkinsonism *(likely to worsen extra-pyramidal symptoms).*
- if fallen in past 3 months (may cause gait dyspraxia, Parkinsonism).
- **Phenothiazines** in patients with epilepsy *(may lower seizure threshold).*
- **Anticholinergics** to treat extra-pyramidal side-effects of antipsychotic medications *(risk of anticholinergic toxicity).*

- **Selective serotonin re-uptake inhibitors** (SSRI's) with a history of clinically significant hyponatraemia *(<130mmol/l within the previous 2 months).*
- **First generation antihistamines** if prolonged use (> 1 week) i.e. chlorphenamine, cyclizine, promethazine (risk of sedation and anti-cholinergic side effects).

Opiates

- Use of long-term strong opiates as first line therapy for mild-moderate pain
  (WHO analgesic ladder not observed—more details page 16).
- Regular opiates for more than 2 weeks in those with chronic constipation without concurrent use of laxatives *(risk of severe constipation).*
- long-term in those with dementia unless for palliative care or management of chronic pain syndrome *(exacerbation of cognitive impairment).*
- long-term in those with recurrent falls *(risk of drowsiness, postural hypotension, vertigo).*

NICE CG90 Depression in Adults:

The first step in mild depression is not routinely to prescribe e.g. offer cognitive behavioural therapy (CBT).

Prescribing safety indicators: The combination of tricyclic antidepressants and heart failure is considered risky (reduced contractility and pro-arrhythmic).[12]

*When reviewing antipsychotics the original diagnosis must be carefully considered—if for psychosis then benefit may well outweigh risks. See also page 19—dementia.

Central Nervous System
BNF Chapter 4
Further information:

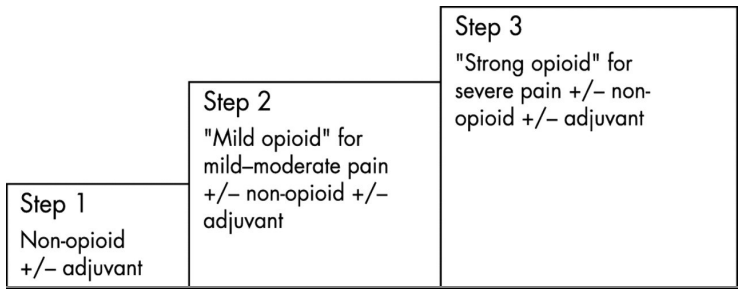
Welsh MeReC gives guidance on stopping benzodiazepines, antidepressants and antipsychotics available at **www.wemerec.org**.

Patient.co.uk has both patient information and professional resources on stopping benzodiazepines.

For **palliative care** the website **www.gp-palliativecare.co.uk** contains local information e.g. NHS Cumbria End of Life Strategy and national guidance.

WHO analgesic ladder:

Mild Opioid: codeine, dihydrocodeine, tramadol.
Strong opioid: morphine, diamorphine, buprenorphine, oxycodone, pethidine, tramadol—at high doses.



Central Nervous System
BNF Chapter 4

START

- **Levodopa** in idiopathic Parkinson's disease with definite functional impairment and resultant disability.

- **Antidepressant** drug in the presence of moderate-severe depressive symptoms lasting at least three months.

NICE CG42 Dementia covers the use of **acetylcholinesterase inhibitors (AChEIs) and memantine** in dementia. They should be started by a specialist and reviewed by a specialist team to ascertain if it is worthwhile continuing them.

Acetylcholinesterase inhibitors are indicated in mild to moderate Alzheimer's Disease (AD).

Memantine is indicated in moderate AD if AChEIs are contraindicated or not tolerated and is indicated in severe AD.

In elderly patients with dementia, **antipsychotic drugs** are associated with a small increased risk of mortality and an increased risk of stroke or transient ischaemic attack. Furthermore, elderly patients are particularly susceptible to postural hypotension and to hyper- and hypothermia in hot or cold weather.[5]

Cumbria Partnership Trust guidance on treating BPSD (behavioural and psychological symptoms in patients with dementia) are available from the **Medicines Management** intranet pages.[5]

Endocrine System BNF Chapter 6

STOPP

- **Glibenclamide or chlorpropamide** with type 2 diabetes mellitus *(risk of prolonged hypoglycaemia).*

- **Beta-blockers** in those with diabetes mellitus and frequent hypoglycaemic episodes i.e. > 1 episode per month *(risk of masking hypoglycaemic symptoms).*

Oestrogens

- with a history of breast cancer or venous thromboembolism *(increased risk of recurrence)*
- without progestogen in patients with intact uterus *(risk of endometrial cancer).*

NICE CG87 Type 2 Diabetes covers:
-offering lifestyle advice as well as medication to achieve individually set HbA1c levels (and not to pursue highly intensive management to levels of less than 6.5%)

-self monitoring of blood glucose only when it can be used as part of the overall management

-which medication to use

Prescribing safety indicators: Glitazones should not be used in heart failure. The BNF advises caution prescribing glitazones in the elderly because of increased risk of fracture, bladder cancer and heart failure.

Endocrine System BNF Chapter 6

START

- **Metformin** with type 2 diabetes +/- metabolic syndrome (in the absence of renal impairment—estimated GFR <50ml/min).

- **ACE inhibitor** or Angiotensin Receptor Blocker in diabetes with nephropathy i.e. overt urinalysis proteinuria or micoralbuminuria (>30mg/24 hours) +/- serum biochemical renal impairment—estimated GFR <50ml/min.

- **Antiplatelet** therapy in diabetes mellitus if one or more co-existing major cardiovascular risk factor present (hypertension, hypercholesterolaemia, smoking history).*

- **Statin** therapy in diabetes mellitus if one or more co-existing major cardiovascular risk factor present.*

*In 2009 The MHRA issued advice that aspirin is not licensed for primary prevention and recent studies supported its use only in secondary prevention. However they did state that the benefits and risks have to be considered for individual patients particularly the benefits with vascular disease including diabetes (but also the risks of gastrointestinal harms).[13]
NICE CG 67 Lipid Modification Prescribing Guidelines re primary prevention say that diabetics should be considered at high risk.
NICE CG 66 Type 2 Diabetes says that patients over 40 years should be offered a statin irrespective of CVD status (based on the cost effectiveness of simvastatin).

Urogenital System BNF Chapter 7

STOPP

Bladder antimuscarinic drugs*

- with dementia *(risk of increased confusion, agitation).*
- with chronic glaucoma *(risk of acute exacerbation of glaucoma).*
- with chronic constipation *(risk of exacerbation of constipation).*
- with chronic prostatism *(risk of urinary retention).*

Alpha-blockers

- in males with frequent incontinence i.e. one or more episodes of incontinence daily *(risk of urinary frequency and worsening of incontinence).*
- with long-term urinary catheter *in situ* i.e. more than 2 months *(drug not indicated).*

*__Fesoterodine__ is a "black drug" locally i.e. unsuitable for prescribing as other drugs are preferred. The traffic light prescribing guidelines are available from the **Medicines Management** intranet pages.[5]

Improvement with antimuscarinic drugs is generally small (less than 20% compared to placebo) so patients may have been tried on several brands. Even if on a formulary drug consider a drug holiday to reassess efficacy. There is no reason to expect patches or slow release versions to be more effective.[5]

Urogenital System BNF Chapter 7

START

NICE CG40 Urinary incontinence in women

There is evidence to support the use of pelvic floor muscle training and bladder training ahead of medication (see table below).

Immediate release oxybutinin should be offered to women with OAB or mixed UI if bladder training has been ineffective. There is no evidence of clinically significant differences between the antimuscarinic drugs.

OAB: overactive bladder syndrome
UI: urinary incontinence

Manage conservatively

	Stress UI	Mixed UI	Urge UI or OAB	First pregnancy
Pelvic floor muscle training	*	*		*
Bladder training		*	*	
Antimuscarinic treatment		*	*	

Musculoskeletal System

BNF Chapter 10

STOPP

Non-steroidal anti-inflammatory drug (NSAID)

- with history of peptic ulcer disease or gastrointestinal bleeding, unless with concurrent histamine H2 receptor antagonist, PPI or misoprostol *(risk of peptic ulcer relapse).*
- with moderate-severe hypertension (moderate: 160/100mmHg – 179/109mmHg; severe: ≥180/110mmHg) *(risk of exacerbation of hypertension).*
- with heart failure *(risk of exacerbation of heart failure).*
- with warfarin *(risk of gastrointestinal bleeding).*
- with chronic renal failure - estimated GFR 20-50ml/min. *(risk of deterioration in renal function).*
- Long-term use of NSAID (>3 months) for relief of mild joint pain in osteoarthritis *(simple analgesics preferable and usually as effective for pain relief).*
- Long-term **NSAID** or **colchicine** for chronic treatment of gout where there is no contraindication to allopurinol *(allopurinol first choice prophylactic drug in gout).*
- Long-term **corticosteroids** (>3 months) as monotherapy for rheumatoid arthritis or osteoarthritis (*risk of major systemic corticosteroid side-effects*).

Prescribing safety indicators: NSAIDs should not be prescribed in patients with peptic ulcer disease or in patients aged 75 or over without gastroprotection.

NSAIDs should not be prescribed in patients aged 65+ with eGFR <60 or to patients with heart failure.

Musculoskeletal System

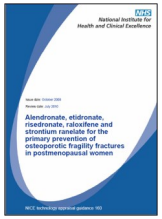
BNF Chapter 10

START

- **Disease-modifying anti-rheumatic drug (DMARD)** with active moderate-severe rheumatoid disease lasting > 12 weeks.
- **Bisphosphonates** in patients taking maintenance oral corticosteroid therapy.
- **Calcium and Vitamin D** supplement in patients with known osteoporosis (radiological evidence or previous fragility fracture or acquired dorsal kyphosis).

NICE TA160 and TA161 cover **prevention of osteoporosis.**

In primary prevention, women aged 75 and over do not require a DEXA scan before starting alendronic acid if they have two or more clinical risk factors or indicators of low BMD; for secondary prevention this is reduced to one or more.



For treatments other than alendronic acid a DEXA scan is required because the treatments are only indicated at certain T scores; unless, in *secondary prevention*, the clinician considers it inappropriate or unfeasible.

In 2011 concerns were raised about cardiovascular risks of calcium and vitamin D supplements. The MHRA[13] issued guidance that the data limitations meant that there should be no change to current practice.

There were also reports of atypical fractures with long term bisphosphonate therapy. The MHRA advice was to periodically review the benefits and risks, particularly after 5 years therapy.

Wound Management

Local Wound Management Prescribing Guidelines are available from the **Medicines Management** intranet pages.[5]

If after using a silver product for 1-2 weeks, no improvement in the wound is seen, then a full reassessment of the wound and patient should be undertaken.

Anticholinergic Burden Scale (ACB)[9]

A total score of three or more is considered clinically relevant. More scores are given in appendices of the practice guide to clinical medication review.[5]

Score 1	Score 2	Score 3
Alverine	Amantadine	Amitriptyline & most TCAs
Atenolol & most beta-blockers	Belladonna alkaloids not otherwise listed	Atropine
Bupropion	Carbamazepine	Chlorphenamine and sedating antihista-mines
Chlorthalidone	Cyproheptadine	Dicylomine
Cimetidine & H2RAs	Methotrimeprazine (Levomepromazine)	Doxepin and others related to TCAs
Codeine & other opiates	Oxcarbazepine	Hyoscine (scopolamine)
Diazepam & BZDs	Pethidine	Olanzapine and most atypicals
Digoxin	Pimozide	Orphenadrine
Furosemide & other diu-retics	Cetirizine & non-sedating antihista-mines*	Oxybutynin and most incontinence drugs
Haloperidol	Loperamide*	Paroxetine and most SSRIs

*From NHS Scotland Polypharmacy Guidance Oct 2012

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12. SIGN Guideline 95 Heart failure, annex 5

*13. MHRA Drug Safety Updates and alerts available at **www.mhra.gov.uk***

Every effort has been made to ensure the information in this document is current and correct at the time of publication, however errors may have occurred and data for individual drugs, national or local guidance may have changed. Where there is any doubt, information should be checked against manufacturers' recommendations, published literature or other specialist sources.

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