

Electronic supplementary material 2 (ESM2): GheOP³S-tool version 2

Article title: Ghent Older People's Prescriptions community Pharmacy Screening (GheOP³S)-tool version 2: update of a tool to detect drug-related problems in older people in primary care

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Authors: Katrien Foubert, Andreas Capiou, Els Mehuys, Leen De Bolle, Annemie Somers, Mirko Petrovic, Koen Boussery

Author affiliation: Katrien Foubert, Pharmaceutical Care Unit, Faculty of Pharmaceutical Sciences, Ghent University, Ottergemsesteenweg 460, 9000 Ghent, Belgium, Tel. +32 9 264 80 73, katrien.foubert@ugent.be, ORCID: 0000-0001-8406-2951

Ghent Older People's Prescriptions community Pharmacy Screening (GheOP³S)-tool version 2

General disclaimer: This tool supports the detection of potential drug-related problems and it is not a substitute for a thorough clinical evaluation.

List 1: Potentially inappropriate medication for older people

This list contains potentially inappropriate medication for older people, **independent** of their comorbidities.

No.	Criterion	Rationale	Alternative
1	Centrally-acting antihypertensives (e.g. clonidine, guanfacine, methyldopa, moxonidine, rilmenidine)	High risk of adverse central nervous system effects; May cause bradycardia and orthostatic hypotension; Not recommended as routine therapy for hypertension	Consider other safer antihypertensive, unless clear intolerance or lack of efficacy with other classes of antihypertensives
2	Digoxin > 0.125 mg/day	Unfavourable risk/benefit ratio (safer alternatives available); Risk of overdose in renal insufficiency: nausea, vomiting, drowsiness, visual disturbances, cardiac rhythm disturbances	1st Re-evaluate whether indication is still present, if not: discontinue therapy; 2nd If therapy is necessary: reduce daily dose of digoxin to ≤ 0.125mg/day and advise to monitor digoxin serum level
3	Acetylsalicylic acid > 100 mg/day	No evidence for increased efficacy; Increased risk of bleeding and gastrointestinal adverse effects (e.g. ulcer, bleeding, perforation) in high-risk groups (e.g. > 75 years or taking systemic corticosteroids, anticoagulants, or antiplatelet agents)	1st Re-evaluate whether indication is still present, if not: discontinue therapy; 2nd If used as antiplatelet: reduce dose to 80-100 mg/day; If used for fever or pain: prefer paracetamol; If used for inflammation: prefer lowest possible dose of (topical) NSAID with(out) PPI and limit duration of use (<i>see criterion 15 ' Systemic NSAIDs'</i>)
4	Dipyridamole	Safer alternatives available (more evidence for acetylsalicylic acid); Risk of vasodilatation and orthostatic hypotension	Substitute dipyridamole with acetylsalicylic acid in low dose or other antithrombotic drug according to indication
5	PPIs > 8 weeks	Potential increased risk for adverse effects: pneumonia, vitamin B12 deficiency, hypomagnesemia, fractures, gastrointestinal infections, renal disease	1st Re-evaluate whether indication is still present, if not: gradually withdraw therapy; 2nd If therapy is necessary: identify potential drug-related cause and consider stopping or dose reduction of causative medication; 3rd Consider non-pharmacological approach with withdrawal plan to stop or to reduce to lowest possible dose
6	Alizapride	Can cause extrapyramidal effects, including tardive dyskinesia; Risk may be higher in frail older people and with prolonged exposure	1st Re-evaluate indication. If not used for nausea/vomiting caused by anesthesia/surgical procedure or chemotherapy/radiotherapy: discuss non-pharmacological approach; 2nd If therapy is necessary: switch to safer alternative (e.g. domperidone in lowest possible dose for max. 7 days)
7	Metoclopramide	Can cause extrapyramidal effects, including tardive dyskinesia; Risk may be higher in frail older people and with prolonged exposure	1st Re-evaluate whether indication is still present, if not: discontinue therapy; 2nd If therapy is necessary: consider non-pharmacological approach and consider safer alternative (e.g. domperidone in lowest possible dose for max. 7 days) or reduce metoclopramide dose to 3 x 5 mg/day and use for max. 5 days
8	Liquid paraffin	Can lead to hypocalcaemia and hypokalaemia, can lead to lipid pneumonia in case of aspiration	1st Discontinue therapy; 2nd In case of constipation: identify potential drug-related cause of constipation and consider stopping or dose reduction of causative medication; 3rd Propose non-pharmacological approach (e.g. lifestyle modification) and/or macrogol (first choice)/lactulose
9	Contact laxatives (e.g. bisacodyl, picosulfate, senna) for daily use > 2 weeks	Increased risk of adverse effects (nausea, abdominal cramps, electrolyte disturbance, diarrhoea with risk for dehydration) when used chronically in older people; Long-term safety in older people is unknown	1st Re-evaluate whether indication is still present, if not: discontinue therapy; 2nd If therapy is necessary: identify potential drug-related cause of constipation and consider stopping or dose reduction of causative medication; 3rd Propose non-pharmacological approach (e.g. lifestyle modification) and/or macrogol (first choice)/lactulose
10	Theophylline	Safer alternative available; Risk of adverse effects due to narrow therapeutic index; Questionable evidence	Re-evaluate and consider safer alternative according to global initiative for asthma (GINA) or global initiative for chronic obstructive lung disease (GOLD) guidelines
11	Narcotic antitussives (e.g. codeine, ethylmorphine, dihydrocodeine, dextromethorphan, noscapine, pholcodine)	Older people are more sensitive to adverse effects (e.g. constipation and sedation)	Consider non-pharmacological approach and/or safer alternative

12	Long-acting sulphonylurea derivatives (e.g. glibenclamide, glimepiride)	Higher risk of severe prolonged hypoglycaemia	Discontinue or switch to other antidiabetic agent (e.g. metformin or other sulphonylurea derivative (gliclazide, gliquidone))
13	Desmopressin	Avoid for treatment of nocturia or nocturnal polyuria: high risk of hyponatremia	1st Check potential drug-related cause; 2nd Consider stopping and switching to non-pharmacological approach
14	Opioids	Increased risk of adverse effects in older people (e.g. central nervous system adverse effects such as confusion/delirium and nausea, constipation, falls) and risk of opioid dependence/tolerance; Metabolisation of codeine/tramadol depends on CYP2D6 genotype leading to different clinical responses; Poor long-term effects; <i>Specific for tramadol</i> : Increased risk of hypoglycaemia, serotonin syndrome due to drug-drug interactions, may exacerbate or cause hyponatremia; <i>For combination of paracetamol with codeine or tramadol</i> : dose adjustment of individual drugs is not possible, different pharmacokinetic properties of both drugs	1st Check if safer options were used: non-pharmacological approach, max. dose of paracetamol, short-term use of topical or systemic NSAID with(out) PPI; 2nd If opioid is necessary: avoid codeine/tramadol/fixed combinations and start with lowest possible dose of immediate-release opioid ("Start low - go slow"); 3rd Consider to continue nonopioid analgesics (i.e. max. dose of paracetamol); 4th Limit duration of use and consider adding osmotic laxative; 5th Check for other fall risk increasing drugs and re-evaluate regularly
15	Systemic* NSAIDs	Increased risk of gastrointestinal adverse effects (e.g. ulcer, bleeding, perforation) in high-risk groups (incl. >75 years or taking corticosteroids, anticoagulants, or antiplatelet agents); Increased cardiovascular risk (e.g. increased blood pressure, heart failure); Increased risk of renal injury	1st Re-evaluate whether indication is still present, if not: discontinue therapy; 2nd Switch to paracetamol and/or topical NSAID; 3rd If NSAID (depending on patient characteristics e.g. cardiovascular and gastrointestinal risks) is necessary, prefer lowest possible dose and limit duration of use; 4th Add PPI in standard dose in patients with increased gastrointestinal risk; 5th Advise to closely monitor renal function or blood pressure depending on diagnoses
16	Bisphosphonates for > 5 years	Fracture prevention for long-term use of bisphosphonates is not proven, with increasing risks of rare adverse effects (osteonecrosis of the jaw and atypical femur fractures)	1st Consider stopping therapy; 2nd Discuss non-pharmacological approach to reduce risk of falls and fractures
17	Benzodiazepines or Z-drugs	In older people, benzodiazepines/Z-drugs increase the risk of sedation, confusion, impaired cognition, delirium, falls, fractures, and car accidents	1st Re-evaluate whether indication is still present, if not: gradually withdraw therapy; 2nd In case of insomnia: check for potential sleep disturbing medication; 3rd If therapy is necessary: consider non-pharmacological approach with withdrawal plan to stop or to reduce to lowest possible dose and/or switch to safer alternative
18	Antipsychotics > 1 month	Increased risk of adverse effects (e.g. anticholinergic, metabolic, parkinsonism); Increased risk of cerebrovascular accident, cognitive decline and mortality in patients with dementia	1st Avoid antipsychotics for behavioural and psychological symptoms in dementia (BPSD) unless non-pharmacological options have failed or are not possible and the patient is threatening harm to self or others, if not: gradually withdraw therapy; 2nd If therapy is necessary: check potential causes (e.g. pain, urinary tract infection, constipation) and consider non-pharmacological approach; 3rd Consider lowest possible dose of antipsychotic and limit duration of use
19	Antidepressants > 1 year	Potential anticholinergic and sedative effects (especially tricyclic antidepressants); Can cause orthostatic hypotension	1st Re-evaluate whether indication is still present, if not: gradually withdraw therapy; 2nd If therapy is necessary: consider non-pharmacological approach and/or a less anticholinergic/sedative alternative
20	Barbiturates (e.g. phenobarbital, primidone)	High rate of physical dependence, tolerance to sleep benefits, greater risk of overdose at low dosages	Consider safer alternative depending on indication, unless for epilepsy in specialised care
21	Nitrofurantoin > 6 months	Potential for pulmonary toxicity, hepatotoxicity, and peripheral neuropathy, especially with long-term use; Safer alternatives available; Prophylactic (daily) antibiotic therapy for recurrent lower urinary tract infections is not recommended, especially in older people with renal insufficiency. Avoid in people with creatinine clearance < 30 ml/min	1st Discontinue therapy: prophylactic (daily) antibiotic therapy in recurrent lower urinary tract infections is not recommended, especially not with nitrofurantoin in older people with renal insufficiency; 2nd If therapy is necessary: consider non-pharmacological approach

22	Sedating antihistaminic drugs (e.g. chlorphenamine = chlorpheniramine, cinnarizine, diphenhydramine, dimenhydrinate, dimetindene, doxylamine, hydroxyzine, ketotifen, pheniramine)	Highly anticholinergic: risk for sedation and anticholinergic effects; Clearance reduced with advanced age; Tolerance develops when used as hypnotic	1st Re-evaluate whether indication is still present, if not: discontinue therapy; 2nd Prefer switching to local therapy or less sedating antihistaminic drug (e.g. bilastine, (levo)cetirizine, (des)loratadine, ebastine, fexofenadine, mizolastine, rupatadine)
23	Oral elemental iron > 200 mg/day	No evidence of enhanced iron absorption above these doses; Increased risk of gastrointestinal adverse effects	1st Re-evaluate whether indication is still present, if not: discontinue therapy; 2nd If therapy is necessary: prefer elemental iron < 200 mg/day (or according to national guidelines) of an immediate release form. To avoid gastrointestinal problems: start with lowest possible dose and increase dose if necessary according to gastrointestinal tolerance. Consider alternate-day dosing in case of gastrointestinal problems
24	Oral decongestants (e.g. phenylephrine, pseudoephedrine)	Higher risk of adverse effects e.g. hypertension, arrhythmias, convulsions, psychoses/hallucinations, insomnia, urinary retention	Discontinue therapy and prefer intranasal therapy (hypertonic saline solution, vasoconstrictor < 10 days or corticosteroid)
25	Intranasal decongestants > 10 days	Risk of rebound nasal congestion (rhinitis medicamentosa), higher blood pressure	Discontinue therapy and prefer hypertonic saline solution and/or intranasal corticosteroid
<p><i>DOAC: direct oral anticoagulant; NSAID: nonsteroidal anti-inflammatory drug; PPI: proton pump inhibitor</i> <i>*Systemic e.g. oral, parenteral (e.g. intravenous, intramuscular, subcutaneous), rectal suppository, certain transdermal patches</i></p>			

List 2: Potentially inappropriate medication for older people, dependent on comorbidities

This list contains potentially inappropriate medication for older people, **dependent** on their comorbidities (= contraindications). Only comorbidities that can be unambiguously derived from the actual medication use (e.g. medication history) were retained, as Belgian community pharmacists do not have access to medication indications (diagnoses) or other clinical information (e.g. laboratory results).

No.	Criterion	Comorbidity	Rationale	Alternative
26	Thiazide and loop diuretics	Regular gout flares	May precipitate or worsen gout	1st If diuretic is necessary: consider dose reduction of thiazide/loop diuretic and (only if necessary) consider to add potassium sparing diuretic or angiotensin inhibitor; 2nd If not possible: start urate-lowering drug while continuing original diuretic. Maintain adequate hydration and monitor uric acid levels; 3rd Only in case of persistent gout flares: prefer other class of suitable drugs (e.g. dihydropyridine calcium channel blocker or angiotensin inhibitor)
27	Non-selective β blockers	Asthma or COPD	May exacerbate respiratory disease	Consider cardioselective β blocker (e.g. acebutolol, atenolol, betaxolol, bisoprolol, celiprolol, esmolol, metoprolol, nebivolol) in lowest possible dose or other suitable drug
28	Antiemetics inhibiting dopamine receptor (e.g. alizapride, metoclopramide)	Parkinson's disease	Dopamine receptor antagonists with potential to worsen parkinsonian symptoms	1st Re-evaluate whether indication is still present, if not: discontinue therapy; 2nd If therapy is necessary: discuss non-pharmacological approach and consider domperidone in lowest possible dose and limit duration (max. 7 days)
29	Drugs likely to cause constipation: opioids, diltiazem, verapamil, drugs with anticholinergic properties (e.g. antihistamines, antidepressants, antiepileptics, antiparkinson drugs, antipsychotics, spasmolytics; see Table A), calcium, aluminium antacids	Known constipation	May worsen constipation	1st Re-evaluate whether indication is still present, if not: discontinue therapy; 2nd If therapy is necessary: prefer switching to safer alternative with the same indication (e.g. with no or less anticholinergic activity, see Table A); 3rd If not possible: consider dose reduction and limit duration of use; 4th Discuss non-pharmacological approach for constipation and add osmotic laxative if necessary
30	Systemic predniso(lo)ne-equivalents > 7.5 mg/day	Diabetes	May worsen diabetes mellitus	1st Warn patient about possible glycaemia dysregulation and advise to increase monitoring of glycaemia and blood pressure; 2nd If possible: consider dose reduction of corticosteroid and limit duration of use
31	Antipsychotics other than clozapine or quetiapine	Parkinson's disease	Dopamine receptor antagonists with potential to worsen parkinsonian symptoms	1st Discuss switching Parkinson's disease medication that might have triggered psychotic symptoms or dose reduction of antipsychotic with specialist; 2nd Reconsider need for antipsychotic therapy; 3rd If therapy is necessary: discuss prescribing clozapine or quetiapine with specialist, preferably in a lower dose for patients with Parkinson's disease
32	Drugs with anticholinergic properties (e.g. antihistamines, antidepressants, antipsychotics, spasmolytics) (see Table A)	Known benign prostatic hyperplasia	Increased risk of anticholinergic adverse effects may decrease urinary flow and cause urinary retention	1st Re-evaluate whether indication is still present, if not: discontinue therapy; 2nd If therapy is necessary: consider non-pharmacological approach and/or prefer switching to safer drug with the same indication with no or less anticholinergic activity (see Table A); 3rd If not possible: consider dose reduction and limit duration of use
33	Drugs with anticholinergic properties (e.g. antihistamines, antidepressants, antipsychotics, spasmolytics) (see Table A)	Known dementia/Cognitive impairment	Increased anticholinergic medication burden may worsen cognitive and behavioural function; Increased risk of adverse central nervous system effects	1st Re-evaluate whether indication is still present, if not: discontinue therapy; 2nd If therapy is necessary: discuss non-pharmacological approach. Prefer switching to safer alternative with the same indication with no or less anticholinergic activity (see Table A); 3rd If not possible: consider dose reduction and limit duration of use

COPD: chronic obstructive pulmonary disease

List 3: Potentially omitted medication in older people

This list contains potentially omitted medications (or potential prescribing omissions) in older people for which an indication exists.

No.	Criterion	Rationale	Alternative
34	Predniso(lo)ne-equivalent of ≥ 7.5 mg for ≥ 3 months without calcium/vitamin D supplementation and bisphosphonate	Long-term use of corticosteroids is associated with increased risk of bone loss and fractures	1st If long-term corticosteroid therapy is necessary: discuss non-pharmacological approach to reduce risk of falls and fractures; 2nd Start calcium/vitamin D and consider starting a bisphosphonate (e.g. alendronate) according to local guidelines
35	Opioids without laxative	Opioids adversely impact the sensorimotor function of the gastrointestinal tract which can lead to bowel dysfunction encompassing a spectrum of symptoms including nausea, vomiting, bloating, gastro-oesophageal reflux-related symptoms and constipation	1st Re-evaluate whether indication for opioid is still present, if not: discontinue therapy (<i>see criterion 14 'Opioids'</i>); 2nd If therapy is necessary: discuss non-pharmacological approach of constipation and consider starting an osmotic laxative (especially in case of chronic use)
36	Methotrexate without folic acid supplement	Methotrexate (an antimetabolite) has an antagonistic effect on folic acid metabolism, which can cause mucosal, gastrointestinal, hepatic or haematologic adverse effects; Supplementation with folic or folinic acid may ameliorate these adverse effects	Consider a folic acid supplement (e.g. 5 to 10 mg once a week (one day after methotrexate intake) or 1 mg/day)
37	Osteoporotic therapy (e.g. bisphosphonates, denosumab, selective estrogen receptor modulators, teriparatide) without adequate calcium/vitamin D	Combined calcium and vitamin D supplements in a daily dose of 0.5–1.2 g and 400–800 IU, respectively, are generally recommended in people receiving bone protective therapy, since most evidence for the efficacy of interventions is based on co-administration of the agent with calcium and vitamin D supplements	1st Re-evaluate whether osteoporotic therapy is still necessary (< 5 years or 5 to 10 years for high risk patients), if not (> 5 years and no high risk patient): discontinue therapy; 2nd If therapy is still necessary: start calcium (dose depending on dietary intake) and vitamin D
38	Older person without yearly influenza vaccination	Influenza in older people can cause respiratory complications (e.g. pneumonia, exacerbation of chronic respiratory disease, hospitalisations, and death)	Discuss need for influenza vaccination with physician and patient
39	Older person with high risk of pneumococcal infection (e.g. important comorbidity or immunosuppression) without pneumococcal vaccination (double vaccination with pneumococcal conjugate vaccine (PCV)13 and pneumococcal polysaccharide vaccine (PPV)23 according to national guidelines) at least once after age 65	<i>Streptococcus pneumoniae</i> is responsible for a considerable burden of illness and death in adults worldwide, usually from pneumonia and less often from invasive pneumococcal disease; Vaccination might reduce such illness and death	Discuss the need for pneumococcal vaccination with physician and patient; In addition, high risk patients should repeat vaccination with pneumococcal polysaccharide vaccine (PPV)23 every 5 years

List 4: Drug-Drug interactions especially relevant in older people

Disclaimer list 4: This list contains interactions deemed relevant (for older people) by the expert panel and is not a substitute for a thorough drug interaction screening in daily practice. Interactions not mentioned on this list could be equally important.

General alternative: "Check national guidelines or drug interaction checkers for specific recommendations".

No.	Criterion	Rationale
40	Combination of drugs leading to increased risk of digoxin toxicity: (1) Digoxin + Macrolide (2) Digoxin + Verapamil/diltiazem	↑ risk of digoxin toxicity (e.g. anorexia, nausea, vomiting, abdominal pain, confusion, weakness, lethargy, fatigue, delirium, confusion, disorientation, changes in vision, irregular heartbeat, palpitations)
41	β blocker (including eye drops) + Verapamil/diltiazem	↑ risk of hypotension, sinus bradycardia, disturbances in the atrioventricular conduction and reduced left ventricular function
42	Calcium channel blocker + Strong CYP3A4 inhibitor (e.g. clarithromycin, erythromycin, grapefruit juice, itraconazole, ketoconazole, posaconazole, ritonavir, saquinavir, voriconazole)	↑ risk of hypotension or shock
43	RAAS inhibitor + Potassium sparing diuretic/potassium supplement/potassium containing drug	↑ risk of hyperkalaemia
44	RAAS inhibitor + Trimethoprim/sulfamethoxazole	↑ risk for hyperkalaemia
45	Combination of QT prolonging drugs or combination of QT prolonging drug and drug that inhibits metabolism of this drug	↑ risk of QT prolongation, torsade de pointes
46	Combination of drugs leading to increased bleeding risk: (1) Antiplatelet drug (esp. acetylsalicylic acid) + VKA/DOAC (2) DOAC + LMWH (3) Systemic* NSAID + Antiplatelet drug (4) Systemic* NSAID + Systemic* corticosteroid (5) Systemic* NSAID + SSRI/SNRI (6) Systemic* NSAID + VKA/DOAC (7) VKA + Amiodarone (8) VKA + Azole (9) VKA + SSRI/SNRI (10) VKA + Trimethoprim/sulfamethoxazole (11) VKA + Macrolide (excluding azithromycin) (12) VKA + Quinolone	↑ risk of bleeding
47	Theophylline + Quinolone/macrolide	↑ risk of theophylline toxicity
48	Oral antidiabetics with risk of hypoglycaemia/insulin + Non-selective β blocker	↑ risk of masking first symptoms of hypoglycaemia (tachycardia, tremor) and reducing response to hypoglycaemia
49	Phosphodiesterase type-5 inhibitors (e.g. sildenafil, tadalafil, vardenafil) + Nitrate	↑ risk of potentially serious hypotension or even myocardial infarction
50	Systemic* NSAID + Diuretic	↓ antihypertensive/diuretic effect, ↑ risk of worsening heart failure or oedema and renal failure
51	Systemic* NSAID + RAAS inhibitor	↓ of antihypertensive effect, in heart failure: ↓ in renal function + hyperkalaemia
52	Combination of fall-risk increasing drugs (see Table B)	Fall-risk increasing drugs can increase the prevalence of falls, which can lead to a higher morbidity and mortality rate, higher healthcare needs and costs (e.g. due to fractures)
53	Alprazolam/triazolam/zolpidem/zopiclone + Strong CYP3A4 inhibitor (e.g. clarithromycin, erythromycin, grapefruit juice, itraconazole, ketoconazole, posaconazole, ritonavir, saquinavir, voriconazole)	↑ risk of increasing effects of hypnotics leading to a higher risk of sedation, fall incidents and hip fractures

54	Combination of drugs leading to increased risk of lithium toxicity: (1) Lithium + RAAS inhibitor (2) Lithium + Systemic* NSAID (3) Lithium + Diuretic	↑ risk of lithium toxicity (e.g. diarrhoea, nausea/vomiting, ataxia, drowsiness, confusion, muscular weakness, tremor)
55	Combination of drugs with anticholinergic properties (see Table A)	↑ risk for anticholinergic adverse effects
56	Phenytoin + Trimethoprim/sulfamethoxazole	↑ risk of phenytoin toxicity (e.g. headache, dizziness, nausea/vomiting, ataxia, nystagmus, loss of balance)
57	Tamoxifen + Strong CYP2D6 inhibitor (e.g. paroxetine/fluoxetine)	↑ risk of decreased efficacy of tamoxifen, increasing the risk of breast cancer recurrence
<p><i>DOAC: direct oral anticoagulant; LMWH: low molecular weight heparin; NSAID: nonsteroidal anti-inflammatory drug; RAAS: renin-angiotensin-aldosterone system; SNRI: serotonin and noradrenalin reuptake inhibitor; SSRI: selective serotonin reuptake inhibitor; VKA: vitamin K antagonist</i></p> <p><i>*Systemic e.g. oral, parenteral (e.g. intravenous, intramuscular, subcutaneous), rectal suppository, certain transdermal patches</i></p>		

List 5: Pharmaceutical care-related criteria for older people to be addressed in the community pharmacy

This list contains general pharmaceutical care-related criteria, especially relevant for older people, that should be addressed by the community pharmacist while assessing the appropriateness of the patient's medication use (e.g. by performing a patient interview).

No.	Criterion	Rationale	Alternative
58	The electronic patient record or medication list is incomplete or inaccurate	A complete and accurate medication record is necessary to perform a medication review	Perform medication reconciliation: add missing medication such as inhalers, injections, patches, drops, over-the-counter drugs (e.g. NSAID, acetylsalicylic acid, dietary supplements, herbal medications) and delete medication that the patient is no longer taking; Provide patient with an updated medication list
59	Contraindications -that can be unambiguously derived from the patient's medication history (e.g. diabetes, Parkinson's disease)- are missing in the electronic patient record	Contraindications are necessary to perform a medication review	Add known contraindications to the electronic patient record
60	The patient is taking medication with a questionable efficacy and/or unfavourable safety profile <u>e.g.</u> :	Drugs with a questionable efficacy and/or unfavourable safety profile increase the risk of adverse effects, potential interactions and drug burden in older people	
60a	- venotropic or vasodilatory drugs (e.g. cinnarizine, naftidrofuryl, pentoxifylline, piracetam)	Questionable efficacy; Increased risk of adverse effects (e.g. orthostatic hypotension and falls) and interactions	1st Re-evaluate whether indication is still present and prefer stopping therapy; 2nd Prefer non-pharmacological approach, a drug with a favourable risk/benefit ratio for a specified time, or refer to physician
60b	- Ginkgo biloba or Panax Ginseng, red yeast rice, glucosamine, chondroitin	Questionable efficacy; Increased risk of adverse effects and interactions	1st Prefer stopping therapy; 2nd Consider non-pharmacological approach, a drug with a favourable risk/benefit ratio for a specified time or refer to physician
60c	- vitamins, minerals and trace elements without documented deficiency	Increased risk of adverse effects and interactions; Unnecessary increasing drug burden for older people	1st Re-evaluate whether patient has a documented deficiency, if not: discontinue therapy; 2nd If therapy is necessary: consider to limit duration of use
61	Medication is being prescribed to treat an adverse effect of another medication (i.e. prescribing cascade)	Prescribing cascades can lead to adverse outcomes and unnecessary costs for patients and the healthcare system; Contributing factors include advanced age and the associated polypharmacy	Contact the prescriber and discuss stopping the medication (or reducing the dose) that is causing the adverse effect. Discuss potential non-pharmacological approach or safer alternative
62	The patient's renal function has not been taken into account during the use of renally cleared medications (see Addendum "Medications that should be avoided or used with caution in older people with a reduced renal function")	In people with a reduced renal function, dose adjustments should be considered for renally cleared medications in order to ensure medication safety	Check SmPC, national formulary and/or Renal Drug Handbook for specific recommendations and contact prescriber to adapt the medication dose or frequency
63	The frail patient or patient with impaired cognition/vision has unaddressed difficulties with medication management or has unaddressed healthcare needs	Managing medication is complex for people with impaired cognition/vision. This can increase the risk of medication errors, medication-related hospital admissions, and dependence on others to assist or adhere with medication management tasks; The risk is even greater with medication requiring a strict dosage regimen	Discuss the need for additional assistance from formal (e.g. nurse) or informal caregiver (e.g. partner, family, neighbour)
64	Certain pharmaceutical care aspects are insufficiently managed for or by the patient (especially important for patients with polypharmacy):	Providing general pharmaceutical care to older patients can increase medication knowledge, adherence, medication appropriateness,	

	medication effectiveness, medication safety etc. Older people often do not comprehend their medication list	
64a	- The patient is insufficiently informed about his/her medication, condition or diagnosis and possible non-pharmacological alternatives	Provide additional information (e.g. counselling, patient information leaflet) or refer to physician
64b	- The patient's medication use is incorrect or suboptimal (e.g. incorrect inhaler or eye drop technique, suboptimal medication intake in relation to food)	Improve the patient's medication use by discussing the need for correct medication intake and by providing additional help (e.g. demonstration of inhaler or eye drop technique, patient information leaflet, using an ointment jar instead of a tube, providing compliance aids such as a spacer or a multidose drug dispensing box, providing help from a home care nurse)
64c	- The dosage form is suboptimal for the patient (e.g. large tablets in case of swallowing difficulties, dry powder inhaler in case of respiratory insufficiency, systemic therapy where topical therapy is sufficient)	Discuss an alternative dosage form or additional help for the patient (e.g. liquid in case of swallowing difficulties, pressurized metered dose inhaler (preferably with spacer) in case of respiratory insufficiency, local therapy (ointment) in case of adverse effects of systemic therapy such as a tablet)
64d	- Medication is splitted or crushed improperly	Discuss which medications can be splitted or crushed, provide a splitting or crushing device and demonstrate the use of this device
64e	- The medication regimen could be simplified or optimised according to patient's preferences	Discuss possible improvements with the patient and/or physician e.g. reducing dosing frequency by administering medications at the same time, standardising routes of administration, providing long-acting formulations, providing combination formulations
64f	- The medication regimen or medication list is unclear for the patient	Discuss the drug regimen or medication list with the patient and clarify (both verbal and written) difficulties e.g. indications, route of administration, dosage and timing, intake in relation to food/other medications, duration of use and provide a medication list in a form that the patient understands (e.g. table versus written text per moment of intake)
64g	- The patient's medication adherence is suboptimal	Interventions to improve adherence can improve morbidity, healthcare utilities and patient satisfaction Discuss and optimise the patient's medication adherence
NSAID: nonsteroidal anti-inflammatory drug; SmPC: summary of product characteristics		

Addendum containing medications that should be avoided or used with caution (need for reduction in dose or dosing frequency) in older people with a reduced renal function

Disclaimer Addendum: This non-limitative list contains medications for which the expert panel strongly advises to avoid their use or to apply extra caution in older people with a reduced renal function. The use of this list is no substitute for a thorough clinical evaluation. Medications not listed could also be potentially inappropriate for a patient with a reduced renal function.

General alternative: "Check SmPC, national formulary and/or Renal Drug Handbook for specific recommendations and contact prescriber to adapt the medication dose or frequency".

Criterion
Allopurinol
Antibiotics: amoxicillin with clavulanic acid, ciprofloxacin, nitrofurantoin, norfloxacin, trimethoprim-sulfamethoxazole
Antiepileptics: gabapentin, levetiracetam, pregabalin
Chlortalidon and thiazides
Colchicine
Digoxin
DOACs: apixaban, dabigatran, edoxaban, rivaroxaban
Duloxetine
Fondaparinux
H ₂ -receptor antagonists: cimetidine, famotidine, nizatidine, ranitidine
LMWH
Metformin
Potassium sparing diuretics (e.g. amiloride, spironolactone, triamterene)
RAAS inhibitors
Sotalol
Systemic* NSAIDs
Tramadol
<i>DOAC: direct oral anticoagulant; LMWH: low molecular weight heparin; NSAID: nonsteroidal anti-inflammatory drug; RAAS: renin-angiotensin-aldosterone system; SmPC: summary of product characteristics</i>
<i>*Systemic e.g. oral, parenteral (e.g. intravenous, intramuscular, subcutaneous), rectal suppository, certain transdermal patches</i>

Table A: Medications with high risk for anticholinergic adverse effects

This table contains medications with (high and low) anticholinergic properties present on the Duran list (2013) [1], anticholinergic medications cited by the Belgian Commented Drugs Repertory (2020) [2] and the 2019 updated AGS Beers criteria® [3].

General alternative: "Switch to safer medication with the same indication with no or less anticholinergic activity (e.g. check [https:// www.anticholinergicscales.es/](https://www.anticholinergicscales.es/), Medichec® <https://www.medichec.com/>, <http://www.acbcalc.com/>)".

Potency	Criterion
H	Acepromazine*
	Aclidinium†
L	Alimemazine*
L	Amantadine*
H	Amitriptyline
H	Amoxapine*
H	Atropine
L	Baclofen
H	Benztropine = benztropine*
	Biperiden†
L	Bromocriptine
H	Brompheniramine*
H	Butylhyoscinebromide (= butylscopolaminebromide)
L	Carbamazepine
H	Carbinoxamine*
L	Cetirizine
L	Chlordiazepoxide*
H	Chlorphenamine (= chlorpheniramine)
H	Chlorpromazine*
L	Cimetidine*
L	Citalopram
H	Clemastine*
H	Clidinium-chlordiazepoxide*
H	Clomipramine
L	Clonazepam
H	Clozapine
L	Codeine
L	Cyclobenzaprine*
H	Cyproheptadine*
H	Darifenacin
H	Desipramine*
H	Dexchlorpheniramine*
L	Diazepam
H	Dicyclomine*
L	Digitoxin*
H	Dimenhydrinate
H	Diphenhydramine
L	Disopyramide
L	Domperidone
L	Dosulepin
H	Doxepine*
H	Doxylamine
L	Entacapon
L	Fentanyl
	Fesoterodine†
L	Fexofenadine
H	Flavoxate*
L	Fluoxetine
H	Fluphenazine*
L	Fluvoxamine
	Glycopyrronium†
L	Haloperidol
H	Homatropine*
L	Hydrocodone*
H	Hydroxyzine

H	Hyoscyamine*
H	Imipramine
H	Ipratropium
L	Ketorolac
H	Levomepromazine
L	Lithium
L	Loperamide
L	Loratadine
L	Loxapine*
	Maprotiline†
H	Meclozine
L	Meperidine (=pethidine)
L	Methadone
L	Methocarbamol*
L	Mirtazapine
L	Morphine
	Nefopam†
H	Nortriptyline
L	Olanzapine
H	Orphenadine*
L	Oxcarbazepine
H	Oxybutynin
L	Oxycodone
L	Paroxetine
H	Perphenazine*
L	Phenelzine*
L	Pimozide
L	Prochlorperazine*
H	Procyclidine
L	Promazine*
H	Promethazine*
H	Propantheline*
	Propiverine†
	Prothipendyl†
H	Protriptyline*
H	Pyrilamine*
L	Quetiapine
L	Ranitidine*
L	Risperidone
H	Scopolamine (= hyoscine)
	Solifenacin†
L	Temazepam*
L	Theophylline
H	Thioridazine*
	Tiotropium†
H	Tizanidine
H	Tolterodine
L	Tramadol
L	Trazodone
L	Triazolam
H	Trifluoperazine*
H	Trihexyphenidyl
H	Trimipramine*
H	Tropatepine*
H	Trospium*
	Umeclidinium†
<i>H: Drugs with high anticholinergic potency</i>	
<i>L: Drugs with low(er) anticholinergic potency</i>	
<i>*Not on Belgian market according to the Belgian Commented Drugs Repertory (2021)</i>	
<i>† Additional anticholinergic medication cited by the Belgian Center for Pharmacotherapeutic Information (Belgian Commented Drugs Repertory, 2020), no specification of anticholinergic potency</i>	

Table B: Fall-risk increasing drugs

This table contains 14 medication classes of fall-risk increasing drugs (FRIDs) according to according to the European Screening Tool of Older Persons Prescriptions in older adults with high fall risk (STOPPFall) [4].

Criterion
Alpha-blockers for prostate hyperplasia
Alpha-blockers used as antihypertensives
Anticholinergics
Antidepressants
Antiepileptics
Antihistamines
Antipsychotics
Benzodiazepines
Benzodiazepine-related drugs
Centrally-acting antihypertensives
Diuretics
Opioids
Overactive bladder and urge incontinence medications
Vasodilators used in cardiac diseases

References

1. Duran, C.E., M. Azermai, and R.H. Vander Stichele, *Systematic review of anticholinergic risk scales in older adults*. Eur J Clin Pharmacol, 2013. **69**(7): p. 1485-96.
2. Belgian Center for Pharmacotherapeutic Information (BCFI). *Belgian Commented Drugs Repertory*. 2020; Available from: <http://www.bcfi.be/>.
3. The 2019 American Geriatrics Society Beers Criteria® Update Expert Panel, *American Geriatrics Society 2019 Updated AGS Beers Criteria(R) for Potentially Inappropriate Medication Use in Older Adults*. Journal of the American Geriatrics Society, 2019. **67**(4): p. 674-694.
4. Seppala, L.J., et al., *STOPPFall (Screening Tool of Older Persons Prescriptions in older adults with high fall risk): a Delphi study by the EuGMS Task and Finish Group on Fall-Risk-Increasing Drugs*. Age and ageing, 2020.