# Deprescribing/ Appropriate Prescribing

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## **Disclosures**

• The activity speaker does not have any financial relationships with commercial entities to disclose.

## **Learning Objectives**

- Describe the purpose of Beers Criteria
- Describe the problems resulting from polypharmacy (e.g. prescribing cascade)
- Identify medications that can be considered for deprescribing
- Identify medications that can may be underutilized in the elderly
- Describe adverse drug effects affecting elderly patients associated from inappropriately prescribed medications

## **Abbreviations**

- American Geriatrics Society (AGS)
- Potentially Inappropriate Medication (PIM)
- Adverse drug event (ADE)
- Albumin to creatinine ratio (ACR)
- Sulfonylureas (SU)

- Thiazolidinediones (TZDs)
- Heart failure with reduced ejection fraction (HFrEF)
- Trimethoprim-Sulfamethoxazole (TMP-SMX)
- Venous thromboembolism (VTE)
- Contraindicated (CI)

## **Epidemiology**

- In 2015, 617.1 million (9%) of the 7.3 billion people estimated worldwide were ≥ 65 years of age
- By 2030, this will increase to approximately 1 billion (12% of the projected total worldwide population)
- By 2050, this will increase to 1.6 billion (17% of the projected total worldwide population)

## Pharmacodynamic and Pharmacokinetic Changes in the Elderly

- Pharmacodynamic
  - Increased sensitivity to medications
- Pharmacokinetic
  - Reduction in renal and hepatic clearance
  - Increased volume of distribution
  - Drug absorption

## **Renal Considerations**

- Decreased renal elimination
- SCr may be under-estimated in the elderly
- Remember the importance of GFR and CrCl
- CKD Staging (ACR consideration-A1, A2, A3)
  - Stage 1: GFR: > or equal to 90 ml/min
  - Stage 2: GFR: 60 to 89 ml/min
  - Stage 3: GFR: 30 to 59 ml/min
    - 3a vs. 3b
  - Stage 4: GFR: 15 to 29 ml/min
  - Stage 5: GFR: < 15 ml/min (or dialysis patients)</li>

Vassalotti JA, Centor R, Turner BJ, Greer RC, Choi M, Sequist TD; National Kidney Foundation Kidney Disease Outcomes Quality Initiative. Am J Med. 2016 Feb;129(2):153-162.e7. doi: 10.1016/j.amjmed.2015.08.025. Epub 2015 Sep 25.

## **Polypharmacy**

- Use of more medications than is clinically necessary
- "Prescribing cascade"
- Increased risk for adverse drug events and drug-drug interactions
  - Adults >65 years of age are twice as likely to go the ED (177,000 visits annually) for ADE and almost seven times more likely to be hospitalized as a result of that ED visit.

## **Medications to Target for Deprescribing**

- Antihypertensives
- Antihyperglycemic medications
- NSAIDs
- CNS medications
- Proton pump inhibitors
- Statins
- Bisphosphonates

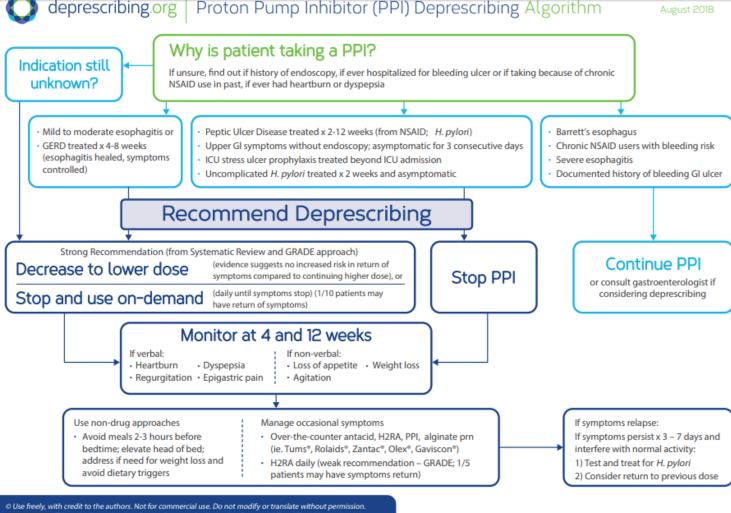
American Geriatrics Society 2019 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. *J Am Geriatr Soc.* 2019; 00:1-21.

O'Mahony D, O'Sullivan D, Byrne S, O'Connor M N, Ryan C, Gallagher P; STOPP/START criteria for potentially inappropriate prescribing in older people: version 2. *Age Ageing* 2015; 44 (2): 213-218. doi: 10.1093/ageing/afu145

Bemben, N. Deprescribing: An application to medication management in older adults. *Pharmacother*. 2016; 36 (7):774-780.

## **Steps to Deprescribing**

- Thorough medication history/medication reconciliation
- Medication assessment
  - Quantity and type of medications
  - Multiple prescribers
- Determine if a medication should be discontinued
  - Life expectancy
  - Patient preference
  - Symptom control, quality of life, cure, prevention
- Develop a plan for medication discontinuation
- Monitor effects of discontinued medication



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#### PPI Availability

| PPI  | Standard dose<br>(healing) (once daily)* | Low dose (maintenance)<br>(once daily) |
|--|--|--|
| Omeprazole<br>(Losec*) - Capsule               | 20 mg <sup>+</sup>                       | 10 mg <sup>+</sup>                     |
| Esomeprazole<br>(Nexium* ) - Tablet            | 20 <sup>a</sup> or 40 <sup>b</sup> mg    | 20 mg                                  |
| Lansoprazole<br>(Prevacid*) - Capsule          | 30 mg <sup>+</sup>                       | 15 mg <sup>†</sup>                     |
| Dexlansoprazole<br>(Dexilant*) - Tablet        | 30 <sup>c</sup> or 60 <sup>d</sup> mg    | 30 mg                                  |
| Pantoprazole<br>(Tecta* , Pantoloc* ) - Tablet | 40 mg                                    | 20 mg                                  |
| Rabeprazole<br>(Pariet*) - Tablet              | 20 mg                                    | 10 mg                                  |

#### Legend

| a Non-erosive reflux disease |
|------------------------------|
| b Reflux esophagitis         |

- c Symptomatic non-erosive gastroesophageal reflux disease
- d Healing of erosive esophagitis
- + Can be sprinkled on food

\* Standard dose PPI taken BID only indicated in treatment of peptic ulcer caused by H. pylori; PPI should generally be stopped once eradication therapy is complete unless risk factors warrant continuing PPI (see guideline for details)

#### Key

GERD = gastroesophageal reflux disease

SR = systematic review

NSAID = nonsteroidal anti-inflammatory druas

GRADE = Grading of Recommendations Assessment, Development and Evaluation

H2RA = H2 receptor antagonist

#### Engaging patients and caregivers

Patients and/or caregivers may be more likely to engage if they understand the rationale for deprescribing (risks of continued PPI use; long-term therapy may not be necessary), and the deprescribing process

#### PPI side effects

- When an ongoing indication is unclear, the risk of side effects may outweigh the chance of benefit
- PPIs are associated with higher risk of fractures, C. difficile infections and diarrhea, community-acquired pneumonia, vitamin B12 deficiency and hypomagnesemia
- Common side effects include headache, nausea, diarrhea and rash

#### Tapering doses

- No evidence that one tapering approach is better than another
- Lowering the PPI dose (for example, from twice daily to once daily, or halving the dose, or taking every second day) OR stopping the PPI and using it on-demand are equally recommended strong options
- Choose what is most convenient and acceptable to the patient

#### On-demand definition

Daily intake of a PPI for a period sufficient to achieve resolution of the individual's reflux-related symptoms; following symptom resolution, the medication is discontinued until the individual's symptoms recur, at which point, medication is again taken daily until the symptoms resolve





## **But What About Underutilization?**

- Underutilization is the omission of drug therapy which is indicated for the treatment or prevention of a disease
- Reasons for underutilization
  - Increased risk for adverse drug events
  - Current complex medication regimen
  - Life expectancy/comorbid conditions
  - Omission
  - Limited evidence in elderly population

## Resources

- American Geriatrics Society (AGS) Beers Criteria For Potentially Inappropriate Medication (PIM)
  - Medications to avoid in older adults
    - Increase risk of confusion, falls, and mortality
  - 2015 update gave consideration to renal dose adjustments and drug-drug interactions
- Screening Tool of Older People's Prescriptions (STOPP)/Screening Tool to Alert to Right Treatment (START)
  - Identifies potential errors in medication use in the elderly
  - Identifies potential omissions in prescribing

## **Beers Criteria**

- Medications prescribed that are found on Beers are associated with poor health outcomes
  - Confusion
  - Falls
  - Mortality
- Avoiding PIMs can decrease ADE risk

## **2019 Beers Specific Updates**

- Aspirin: use in caution for adults ≥70 years of age in primary prevention
- TMP-SMX: Use with caution in reduced kidney function and taking an ACEi/ARB
- Caution expanded from dabigatran to include rivaroxaban in treating VTE or Afib in adults >75 years old
- Tramadol added to the list of medications that may cause hyponatremia
- Vasodilators were removed from Beers since syncope is a common side effect
- Chemotherapeutic medications were removed from Beers

## 2019 Beers Specific Updates

- H2 Blockers removed from the avoid list for dementia or cognitive impairment but remain for delirium
- Glimepiride was added to the list so that glipizide is the best SU option.
- SNRIs should be avoided in individuals with a history of falls/fractures
- Pimavanserin was deemed the preferred agent over aripiprazole in the treatment of psychosis in patients with Parkinsons
  - Quetiapine, pimavanserin, and clozapine are considered acceptable options in the above patients but not as a general rule
- Non DHP CCBs should be avoided in HFrEF
- NSAIDs, COX2 inhibitors, TZDs, and dronedarone should be used with caution in older adults with HF who are asymptomatic and avoided in older adults who are symptomatic

## 2019 Beers Specific Updates

- Drug-Drug Interactions
  - TMP-SMX + phenytoin can increase the risk of phenytoin toxicity
  - TMP-SMX or Macrolides (excluding azithromycin), or ciprofloxacin + warfarin can increase the risk of bleeding
  - o 3 or more CNS agents can increase the risk of falls
- Kidney Function
  - Ciprofloxacin and TMP-SMX have an increase risk of CNS effects, tendon rupture, and worsening renal function
  - o TMP-SMX has an increased risk of hyperkalemia and worsening renal function
  - o Dofetilide can cause QT prolongation and torsades de pointes
  - Edoxaban should be avoided in CrCL <15 ml/min</li>

## **Utilizing Beers Criteria**

**Therapeutic Category, Drugs** 

| Anticholinergics (eg: meclizine, diphenhydramine, hydroxyzine)  | Increased risk of confusion, dry mouth, constipation Diphenhydramine appropriate for allergic reactions  |
|---|--|
| Anti-infective (Nitrofurantoin)                                 | Avoid if CrCl is <30 ml/min or for long term use: Inc. risk of pulmonary toxicity, hepatotoxicity, peripheral neuropathy   |
| Alpha blockers (e.g. doxazosin)                                 | Avoid use as antihypertensive due to orthostatic hypotension   |
| Central acting alpha 2 agonist (example: clonidine, methyldopa) | Avoid as first line antihypertensive due to bradycardia and orthostatic hypotension  |
| Digoxin   | Atrial Fibrillation: Avoid as first line; more effective medications available; may increase mortality  Heart Failure: Possible benefit in HFrEF (conflicting evidence); however, other medications have stronger data. Consider low dose as side effects are dose dependent and greater benefits are not seen with higher doses |

Rationale

Renal: Avoid doses >0.125 mg/day if CKD Stage 4 or 5

## **Utilizing Beers Criteria**

Thorangutic Category Drugs | Pationalo

| Therapeutic Gategory, Drugs | Nationale   |
|-----------------------------|---|
| Antidepressants             | Some are highly anticholinergic: sedating, orthostatic hypotension  |
| Antipsychotics              | Increased risk of stroke, cognitive decline, mortality, (Avoid in behavioral complications of dementia or delirium unless other options failed)-use acceptable in schizophrenia and bipolar |

Benzodiazepines
Short-intermediate: alprazolam, lorazepam, temazepam
Long: diazepam, clonazepam

benavioral complications of dementia or delirium unless other options failed)-use acceptable in schizophrenia and bipolar

Increased risk of cognitive impairment, falls, factures

Long acting may be appropriate for seizure disorder, alcohol withdrawal

Long: diazepam, clonazepam

Barbiturates (example, pentobarbital, secobarbital, phenobarbital)

Eszopiclone, Zolpidem, Avoid use: Increase in delirium, falls, fractures, ED visits, little improvement in sleep

#### Why is patient taking an antipsychotic?

- · Psychosis, aggression, agitation (behavioural and psychological symptoms of dementia - BPSD) treated ≥ 3 months (symptoms controlled, or no response to therapy).
- · Primary insomnia treated for any duration or secondary insomnia where underlying comorbidities are managed
- Schizophrenia
- · Schizo-affective disorder
- Bipolar disorder
- Acute delirium
- · Tourette's syndrome
- Tic disorders
- Autism
- . Less than 3 months duration of psychosis in dementia

- Intellectual disability
- Developmental delay Obsessive-compulsive
- disorder Alcoholism
- Cocaine abuse
- Parkinson's disease psychosis
- · Adjunct for treatment of Major Depressive Disorder

### Recommend Deprescribing

Strong Recommendation (from Systematic Review and GRADE approach)

Taper and stop AP (slowly in collaboration with patient and/or caregiver; e.g. 25%-50% dose reduction every 1-2 weeks)

#### Stop AP

Good practice recommendation

#### Monitor every 1-2 weeks for duration of tapering

#### **Expected benefits:**

· May improve alertness, gait, reduce falls, or extrapyramidal symptoms

Adverse drug withdrawal events (closer monitoring for those with more severe baseline symptoms):

· Psychosis, aggression, agitation, delusions, hallucinations

#### Continue AP

or consult psychiatrist if considering deprescribing

#### If BPSD relapses:

#### Consider:

· Non-drug approaches (e.g. music therapy, behavioural management strategies)

#### Restart AP drug:

- · Restart AP at lowest dose possible if resurgence of BPSD with re-trial of deprescribing in 3 months
- At least 2 attempts to stop should be made

#### Alternate drugs:

· Consider change to risperidone, olanzapine, or aripiprazole

#### If insomnia relapses:

#### Consider

- · Minimize use of substances that worsen insomnia (e.g. caffeine, alcohol)
- · Non-drug behavioural approaches (see reverse)

#### Alternate drugs

Other medications have been used to manage insomnia. Assessment of their safety and effectiveness is beyond the scope of this deprescribing algorithm. See AP deprescribing guideline for details.

INSTRUCTOR RECHIRCHS

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#### Commonly Prescribed Antipsychotics

| Antipsychotic               | Form                          | Strength   |
|-----------------------------|-------------------------------|--|
| Chlorpromazine              | T<br>IM, IV                   | 25, 50, 100 mg<br>l25 mg/mL  |
| Haloperidol (Haldol®)       | T<br>L<br>IR, IM, IV<br>LA IM | 0.5, 1, 2, 5, 10, 20 mg<br>2 mg/mL<br>5 mg/mL<br>50, 100 mg/mL                     |
| Loxapine (Xylac®, Loxapac®) | T<br>L<br>IM                  | 2.5, 5, 10, 25, 50 mg<br>25 mg/L<br>25, 50 mg/mL                                   |
| Aripiprazole (Abilify®)     | T<br>IM                       | 2, 5, 10, 15, 20, 30 mg<br>300, 400 mg   |
| Clozapine (Clozaril®)       | T                             | 25, 100 mg   |
| Olanzapine (Zyprexa®)       | T<br>D<br>IM                  | 2.5, 5, 7.5, 10, 15, 20 mg<br>5, 10, 15, 20 mg<br>10mg per vial                    |
| Paliperidone (Invega®)      | ER T<br>PR IM                 | 3, 6, 9 mg<br>50mg/0.5mL, 75mg/0.75mL,<br>100mg/1mL, 150mg/1.5mL                   |
| Quetiapine (Seroquel®)      | IRT<br>ERT                    | 25, 100, 200, 300 mg<br>50, 150, 200, 300, 400 mg                                  |
| Risperidone (Risperdal®)    | T<br>S<br>D<br>PR IM          | 0.25, 0.5, 1, 2, 3, 4 mg<br>1 mg/mL<br>0.5, 1, 2, 3, 4 mg<br>12.5, 25, 37.5, 50 mg |

IM = intramuscular, IV = intravenous, L = liquid, S = suppository, SL = sublingual, T = tablet, D = disintegrating tablet, ER = extended release, IR = immediate release, LA = long-acting, PR = prolonged release

#### Antipsychotic side effects

- · APs associated with increased risk of:
  - Metabolic disturbances, weight gain, dry mouth, dizziness
  - · Somnolence, drowsiness, injury or falls, hip fractures, EPS, abnormal gait, urinary tract infections, cardiovascular adverse events, death
- · Risk factors: higher dose, older age, Parkinsons', Lewy Body Dementia

#### Engaging patients and caregivers

#### Patients and caregivers should understand:

- The rationale for deprescribing (risk of side effects of continued AP use)
- · Withdrawal symptoms, including BPSD symptom relapse, may occur
- They are part of the tapering plan, and can control tapering rate and duration

#### Tapering doses

- . No evidence that one tapering approach is better than another
- Consider:
  - Reduce to 75%, 50%, 25% of original dose on a weekly or bi-weekly basis and then stop; or
- . Consider slower tapering and frequent monitoring in those with severe baseline BPSD Tapering may not be needed if low dose for insomnia only

#### Sleep management

#### Primary care:

- 1. Go to bed only when sleepy
- 2. Do not use your bed or bedroom for anything but sleep (or intimacy)
- 3. If you do not fall asleep within about 20-30 min at the beginning of the night or after an awakening, exit the bedroom
- 4. If you do not fall asleep within 20-30 min on returning to bed, repeat #3
- 5. Use your alarm to awaken at the same time every morning
- 6. Do not nap
- 7. Avoid caffeine after noon
- 8. Avoid exercise, nicotine, alcohol, and big meals within a hrs of hedtime

#### Institutional care:

- 1. Pull up curtains during the day to obtain bright light exposure
- 2. Keep alarm noises to a minimum
- 3. Increase daytime activity and discourage daytime sleeping
- 4. Reduce number of naps (no more than 30 mins and no naps after 2pm)
- 5. Offer warm decaf drink, warm milk at night
- 6. Restrict food, caffeine, smoking before hedtime
- 7. Have the resident toilet before going to bed
- 8. Encourage regular bedtime and rising times
- 9. Avoid waking at night to provide direct care
- 10. Offer backrub, gentle massage

#### **BPSD** management

- Consider interventions such as: relaxation, social contact, sensory (music or aroma-therapy), structured activities and behavioural therapy
- Address physical and other disease factors: e.g. pain, infection, constipation, depression
- Consider environment: e.g. light, noise
- Review medications that might be worsening symptoms









#### Why is patient taking a BZRA?

If unsure, find out if history of anxiety, past psychiatrist consult, whether may have been started in hospital for sleep, or for grief reaction.

Insomnia on its own OR insomnia where underlying comorbidities managed For those 65 years of age: taking BZRA regardless of duration (avoid as first line therapy in older people) For those 18-64 years of age: taking BZRA > 4 weeks

Engage patients (discuss potential risks, benefits, withdrawal plan, symptoms and duration)

#### Recommend Deprescribing

#### Taper and then stop BZRA

(taper slowly in collaboration with patient, for example ~25% every two weeks, and if possible, 12.5% reductions near end and/or planned drug-free days)

- For those > 65 years of age (strong recommendation from systematic review and GRADE approach)
- · For those 18-64 years of age (weak recommendation from systematic review and GRADE approach)
- Offer behavioural sleeping advice; consider CBT if available (see reverse)

#### Monitor every 1-2 weeks for duration of tapering

Expected benefits:

· May improve alertness, cognition, daytime sedation and reduce falls

Withdrawal symptoms:

Insomnia, anxiety, irritability, sweating, gastrointestinal symptoms (all usually mild and last for days to a few weeks)

- Other sleeping disorders (e.g. restless legs)
- · Unmanaged anxiety, depression, physical or mental condition that may be causing or aggravating insomnia
- Benzodiazepine effective specifically for anxiety Alcohol withdrawal

#### Continue BZRA

- Minimize use of drugs that worsen insomnia (e.g. caffeine, alcohol etc.)
- Treat underlying condition
- Consider consulting psychologist or psychiatrist or sleep specialist

#### If symptoms relapse: Consider

This algorithm and accompanying advice support recommendations in the NICE guidance on the use of

zaleplon, zolpidem and zopiclone for the short-term management of insomnia, and medicines optimisation, National Institute for Health and Care Excellence, February 2019

 Maintaining current BZRA dose for 1-2 weeks. then continue to taper at slow rate

#### Alternate drugs

Other medications have been used to manage insomnia. Assessment of their safety and effectiveness is beyond the cope of this algorithm. See BZRA deprescribing guideline for details.

Use non-drug approaches to manage insomnia

Use behavioral approaches and/or CBT (see reverse)

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#### **BZRA Availability**

| BZRA                               | Strength                    |
|------------------------------------|-----------------------------|
| Alprazolam (Xanax®) <sup>T</sup>   | 0.25 mg, 0.5 mg, 1 mg, 2 mg |
| Bromazepam (Lectopam®) T           | 1.5 mg, 3 mg, 6 mg          |
| Chlordiazepoxide <sup>c</sup>      | 5 mg, 10 mg, 25 mg          |
| Clonazepam (Rivotril®) T           | 0.25 mg, 0.5 mg, 1 mg, 2 mg |
| Clorazepate (Tranxene®) C          | 3.75 mg, 7.5 mg, 15 mg      |
| Diazepam (Valium®) <sup>T</sup>    | 2 mg, 5 mg, 10 mg           |
| Flurazepam (Dalmane®) <sup>c</sup> | 15 mg, 30 mg                |
| Lorazepam (Ativan®) T, S           | 0.5 mg, 1 mg, 2 mg          |
| Nitrazepam (Mogadon®) <sup>T</sup> | 5 mg, 10 mg                 |
| Oxazepam (Serax®) <sup>T</sup>     | 10 mg, 15 mg, 30 mg         |
| Temazepam (Restoril®) <sup>C</sup> | 15 mg, 30 mg                |
| Triazolam (Halcion®) T             | 0.125 mg, 0.25 mg           |
| Zopiclone (Imovane*, Rhovane*) T   | 5 mg, 7.5 mg                |
| Zolpidem (Sublinox®) S             | 5 mg, 10 mg                 |

T = tablet, C = capsule, S = sublingual tablet

#### BZRA Side Effects

- BZRAs have been associated with:
  - physical dependence, falls, memory disorder, dementia, functional impairment, daytime sedation and motor vehicle accidents
- Risks increase in older persons

#### Engaging patients and caregivers

#### Patients should understand:

- The rationale for deprescribing (associated risks of continued BZRA use, reduced long-term efficacy)
- Withdrawal symptoms (insomnia, anxiety) may occur but are usually mild, transient and short-
- term (days to a few weeks) They are part of the tapering plan, and can control tapering rate and duration

#### Tapering doses

- No published evidence exists to suggest switching to long-acting BZRAs reduces incidence of withdrawal symptoms or is more eff-ective than tapering shorter-acting BZRAs
- If dosage forms do not allow 25% reduction, consider 50% reduction initially using drug-free days during latter part of tapering, or switch to lorazepam or oxazepam for final taper steps

#### Behavioural Management

#### Primary care:

- Go to bed only when sleepy
- 2. Do not use bed or bedroom for anything but sleep
- If not asleep within about 20-30 min at the beginning of the night or after an awakening, exit the bedroom
- 4. If not asleep within 20-30 min on returning to bed.
- Use alarm to awaken at the same time every morning.
- 6. Do not nap
- 7. Avoid caffeine after noon
- 8. Avoid exercise, nicotine, alcohol, and big meals within 2 hrs of bedtime

#### Institutional care:

- Pull up curtains during the day to obtain bright light exposure
- Keep alarm noises to a minimum
- Increase daytime activity & discourage daytime sleeping
- 4. Reduce number of naps (no more than 30 mins and no naps after 2 pm)
- Offer warm decaf drink, warm milk at night
- 6. Restrict food, caffeine, smoking before bedtime
- 7. Have the resident toilet before going to bed
- Encourage regular bedtime and rising times
- Avoid waking at night to provide direct care Offer backrub, gentle massage

#### Using CB1

#### What is cognitive behavioural therapy (CBT)?

CBT includes 5-6 educational sessions about sleep/insomnia, stimulus control, sleep restriction, sleep hygiene, relaxation training and support

#### Does it work?

- CBT has been shown in trials to improve sleep outcomes with sustained long-term benefits
- Clinical psychologists usually deliver CBT, however, others can be trained or can provide aspects of CBT education; self-help programs are available

How can providers and patients find out about it?

Some resources can be found here: http://sleepwellns.ca/

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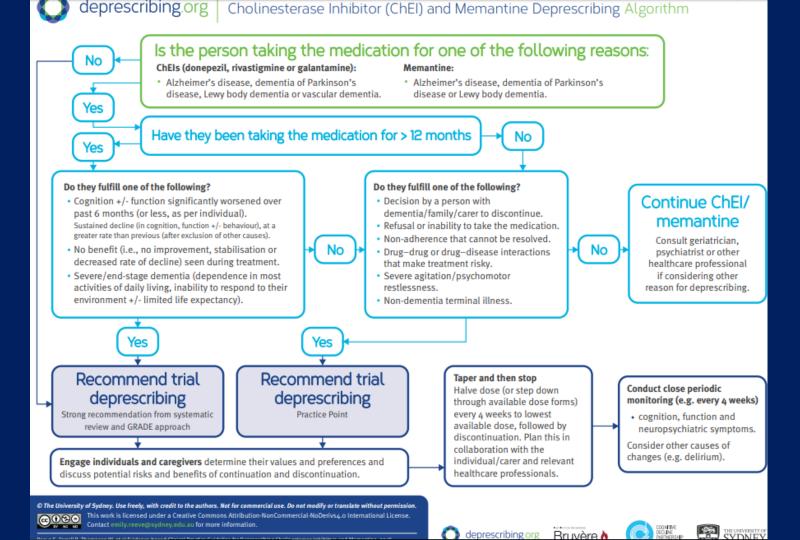


This algorithm and accompanying advice support recommendations in the NICE guidance on the use of

zaleplon, zolpidem and zopiclone for the short-term management of insomnia, and medicines

optimisation. National Institute for Health and Care Excellence, February 2019







#### deprescribing.org | Cholinesterase Inhibitor (ChEI) and Memantine Deprescribing Notes

#### Monitoring during tapering and after discontinuation

| Timing of symptoms<br>after dose reduction/<br>discontinuation | Types of symptoms  | Action to be taken<br>by family/nurses/<br>care staff  | Possible cause*  |
|--|--|--|--|
| Less than 1 week   | Severe symptoms,<br>including agitation,<br>aggression,<br>hallucina-<br>tions or reduced<br>consciousness | Restart previous<br>dose immediately<br>and contact<br>responsible<br>healthcare<br>professional as soon<br>as possible  | Adverse drug<br>withdrawal reaction  |
| 2 to 6 weeks   | Worsening of<br>cognition,<br>behavioural or<br>psychological<br>symptoms or<br>function                   | Contact responsible healthcare professional and consider restarting previous dose and/or make an appointment to see responsible healthcare professional at the next available time | Re-emergence of<br>symptoms that<br>were being treated<br>by ChEI/<br>memantine  |
| 6 weeks to<br>3 months   | Worsening of cognition, behavioural or psychological symptoms or function                                  | Contact responsible<br>healthcare<br>professional at the<br>next available time<br>to make an<br>appointment   | Likely progression<br>of condition or<br>possible<br>re-emergence of<br>symptoms that<br>were being treated<br>by ChEI/memantine |
| > 3 months   | Any  | As per usual care  | Progression of condition   |

- · \*Exclude other causes of change in condition (e.g. infection or dehydration) first.
- Discuss monitoring plan with the individual/family/carer and write it down for them (e.g. frequency and type of follow-up). Ensure they have a way to contact a clinician if needed.

#### Engaging individuals and family/carers

#### Determining suitability for deprescribing

- Discuss treatment goals what do they value the most (cognition, quality of life, remaining independent)?
- Ask about experience with dementia symptoms when treatment started and over last 6 months.
- Ask about side effects.

#### Helping the individual and family/carers to make an informed decision

- Deprescribing is a trial medication can be restarted if appropriate.
- There are uncertain benefits and harms to both continuing and discontinuing the medication.
- · Tailor discussion about benefits and harms to the individual.
- · Explore fears and concerns about deprescribing.
- Consider medication costs and local reimbursement/subsidisation criteria.
- If the recommendation to deprescribe is being made due to progression of dementia, remind family/ carers that the person with dementia may continue to decline after deprescribing, and explain why.

#### Non-pharmacological management and ongoing care after deprescribing

See (http://sydney.edu.au/medicine/cdpc/resources/dementia-guidelines.php) for Australian guidelines on care of people with dementia, including behavioural and psychological symptoms.

#### ChEI and memantine availability (Australia)

|   | ,   |
|---|---|
| Drug  | Strength  |
| Donepezil (Aricept®, Aridon®, Arazil®)        | Tablet – 5mg, 10mg                                      |
| Galantamine (Galantyl®, Gamine XR®, Reminyl®) | Controlled release capsule – 8mg, 16mg, 24mg            |
| Rivastigmine (Exelon®)                        | Capsule - 1.5mg, 3mg, 4.5mg, 6mg                        |
|   | Patch - 4.6mg/24 hours, 9.5mg/24 hours, 13.3mg/24 hours |
| Memantine (Ebixa®, Memanxa®)                  | Tablet - 10mg, 20mg                                     |

#### ChEI and memantine side effects.

- · Common: include gastrointestinal effects, dizziness, confusion, headache, insomnia, agitation, weight loss and falls.
- Rare (ChEI): may include urinary, cardiovascular (e.g., bradycardia), pulmonary and dermatological (e.g. Stevens-Johnson syndrome) complications, Pisa syndrome, seizures, gastrointestinal haemorrhage and rhabdomyolysis.
- · Lack of evidence of potential harms in complex older adults.









## **Utilizing Beers Criteria**

Sulfonylureas

Proton-pump inhibitors

**TZDs** 

| Therapeutic Category   | Rationale  |
|------------------------|--|
| Estrogen +/- Progestin | Carcinogenic, lack of cardio or cognitive protection (Avoid oral and transdermal) Vaginal formulations can be used for GU symptoms |
| Testosterone           | Avoid unless confirmed hypogonadism with symptoms: May increase risk for cardiac issues- CI in hx of prostate cancer               |

increase risk for cardiac issues- CI in hx of prostate cancer

Insulin sliding scale

Increase hypoglycemia without improvement in hyperglycemia

Hypoglycemia: Avoid glyburide, glimepiride, chlorpropamide

Risk of C. diff and bone fractures. Avoid for >8 weeks unless

in HF

Avoid in HF

high risk patient

H2 Blockers

Safe to use except in those with delirium

No



Does your elderly (>65 years of age) patient with type 2 diabetes meet one or more of the following criteria:

- At risk of hypoglycemia (e.g. due to advancing age, tight glycemic control, multiple comorbidities, drug interactions, hypoglycemia history or unawareness, impaired renal function, or on sulfonylurea or insulin)
- · Experiencing, or at risk of, adverse effects from antihyperglycemic
- Uncertainty of clinical benefit (due to: frailty, dementia or limited life-expectancy)

- Set individualized A1C and blood glucose (BG) targets (otherwise healthy with 10+ years life expectancy, A1C < 7% appropriate; considering advancing age, frailty, comorbidities and time-to-benefit, A1C < 8.5% and BG < 12mmol/L may be acceptable; at end-of life, BG < 15mmol/L may be acceptable) (good practice recommendation)</li>
- Address potential contributors to hypoglycemia (e.g. not eating, drug interactions such as trimethoprim/sulfamethoxazole and sulfonylurea, recent cessation of drugs causing hyperglycemia – see reverse)

# Continue Antihyperglycemic(s) Still at risk? No

### Recommend Deprescribing

- Reduce dose(s) or stop agent(s)
  - most likely to contribute to hypoglycemia (e.g. sulfonylurea, insulin; strong recommendation from systematic review and GRADE approach) or other adverse effects (good practice recommendation)
- Switch to an agent
  - with lower risk of hypoglycemia (e.g. switch from glyburide to gliclazide or non-sulfonylurea; change NPH or mixed insulin to detemir or glargine insulin to reduce nocturnal hypoglycemia; strong recommendation from systematic review and GRADE approach)
- Reduce doses
  - · of renally eliminated antihyperglycemics (e.g. metformin, sitagliptin; good practice recommendation) See guideline for recommended dosing

#### Monitor daily for 1-2 weeks after each change (TZD - up to 12 weeks):

- · For signs of hyperglycemia (excessive thirst or urination, fatigue)
- For signs of hypoglycemia and/or resolution of adverse effects related to antihyperglycemic(s)

Increase frequency of blood glucose monitoring if needed

A1C changes may not be seen for several months

If hypoglycemia continues and/or adverse effects do not resolve:

Reduce dose further or try another deprescribing strategy

If symptomatic hyperglycemia or blood glucose exceeds individual target:

 Return to previous dose or consider alternate drug with lower risk of hypoglycemia

300



#### Antihyperglycemics and Hypoglycemia Risk

| Drug   | Causes hypoglycemia?   |
|--|--|
| Alpha-glucosidase inhibitor                            | No   |
| Dipeptidyl peptidase-4 (DPP-4) inhibitors              | No   |
| Glucagon-like peptide-1 (GLP-1) agonists               | No   |
| Insulin  | Yes (highest risk with<br>regular insulin and NPH<br>insulin)          |
| Meglitinides   | Yes (low risk)   |
| Metformin  | No   |
| Sodium-glucose linked transporter 2 (SGLT2) inhibitors | No   |
| Sulfonylureas  | Yes (highest risk with<br>glyburide and lower risk<br>with gliclazide) |
| Thiazolidinediones (TZDs)                              | No   |

#### Drugs affecting glycemic control

- Drugs reported to cause hyperglycemia (when these drugs stopped, can result in hypoglycemia from antihyperglycemic drugs) e.g. quinolones (especially gatifloxacin), beta-blockers (except carvedilol), thiazides, atypical antipsychotics (especially olanzapine and clozapine), corticosteroids, calcineurin inhibitors (such as cyclosprine, sirolimus, tacrolimus), protease inhibitors
- Drugs that interact with antihyperglycemics (e.g. trimethoprim/sulfamethoxazole with sulfonylureas)
- Drugs reported to cause hypoglycemia (e.g. alcohol, MAOIs, salicylates, guinolones, guinine, beta-blockers, ACEIs, pentamidine)

#### Engaging patients and caregivers

- Some older adults prefer less intensive therapy, especially if burdensome or increases risk of
- Patients and/or caregivers may be more likely to engage in discussion about changing targets or considering deprescribing if they understand the rationale:
  - Risks of hypoglycemia and other side effects
  - Risks of tight glucose control (no benefit and possible harm with A1C < 6%)
  - Time to benefit of tight glucose control
  - Reduced certainty about benefit of treatment with frailty, dementia or at end-of-life
- Goals of care: avoid hyperglycemic symptoms (thirst, dehydration, frequency, falls, fatique, renal insufficiency) and prevent complications (5-10 years of treatment needed)
- Many countries agree on less aggressive treatment of diabetes in older persons
- Reviewing options for deprescribing, as well as the planned process for monitoring and thresholds for returning to previous doses will help engage patients and caregivers

#### Hypoglycemia information for patients and caregivers

- Older frail adults are at higher risk of hypoglycemia
- There is a greater risk of hypoglycemia with tight control
- Symptoms of hypoglycemia include: sweating, tachycardia, tremor BUT older patients may not typically have these
- Cognitive or physical impairments may limit older patient's ability to respond to hypoglycemia symptoms
- Some drugs can mask the symptoms of hypoglycemia (e.g. beta blockers)
- Harms of hypoglycemia may be severe and include: impaired cognitive and physical function, falls and fractures, seizures, emergency room visits and hospitalizations

#### Tapering advice

- Set blood glucose & A1C targets, plus thresholds for returning to previous dose, restarting a drug or
- Develop tapering plan with patient/caregiver (no evidence for one best tapering approach; can stop oral antihyperglycemics, switch drugs, or lower doses gradually e.g. changes every 1-4 weeks, to the minimum dose available prior to discontinuation, or simply deplete patient's supply)
- Doses may be increased or medication restarted any time if blood glucose persists above individual target (12-15 mmol/L) or symptomatic hyperglycemia returns







## **Utilizing Beers Criteria**

| Therapeutic Category, Drugs  | Rationale   |
|--|---|
| Nonselective NSAIDs (example, aspirin >325 mg/day, ibuprofen, meloxicam, naproxen) | Increased risk of GI bleeding, peptic ulcer; avoid chronic use unless patient cannot tolerate alternatives and patient can take a GI protective agents (PPI, misoprostol) |
| Muscle relaxants: (example carisoprodol, methocarbamol)                            | Poorly tolerated (anticholinergic effects), increase in fractures   |

## Medication Appropriateness Index: Questions to Consider

- Is there an indication for the drug?
- Is the medication effective for the condition?
- Is the dosage correct?
- Are the directions correct?
- Are the directions practical?
- Are there drug-drug interactions?
- Are there drug-disease interactions?
- Is there unnecessary duplication?
- Is the duration of therapy acceptable?
- Is this drug the least expensive alternative?

## Resources

- Primary literature
- Guidelines
- Drug information resources
- Stay current

## **In summary**

- Prioritize appropriately
- Streamline medications
- Consider cost
- Adjust doses appropriately
- Make monitoring parameters clear to patient
- Monitor for ADEs
- Utilize adherence tools
- Assess health literacy and numeracy
- Understand cultural differences

## Thank you for completing the following:

You may open the survey in your web browser by clicking the link below:

https://redcap.nova.edu/redcap/surveys/?s=CHETXK48Y4

If the link above does not work, try scanning the QR code:



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