UNIT 1 PRESCRIBING IN THE ELDERLY

Structure:

1.0 OBJECTIVES

After undertaking the activities in this unit, you should be able to:

- Recognise the features unique to prescribing in the elderly
- Prescribe age-appropriate drugs in the elderly
- Perform un-prescribing in the elderly
- Prescribe drugs at proper dose, considering renal and hepatic functions
- Prescribe drugs avoiding drug-drug and drug-disease interactions
- Identify common and rare adverse events due to drugs in elderly

1.1 INTRODUCTION

You have been taught in the theory module on drug prescribing in the elderly, that rational therapeutics is of utmost importance in older patients. The theory module covered age-related physiological changes and how they affect pharmacokinetics and pharmacodynamics. Polypharmacy or the simultaneous use of 5 or more medications is a common problem in the elderly. This has

also been emphasized upon in the theory module. This creates several possibilities of adverse drug reactions, drug-drug, and drug-disease interactions. This also necessitates un-prescribing or reducing prescription load in elderly, at times. The modification of doses of drugs based on comorbidities in the elderly is also of utmost importance. In this practical module, you will learn the practical translations of these topics, and how to rationally prescribe in the elderly.

1.2 AGE-APPROPRIATE DRUG PRESCRIBING TOOLS

There are several internationally accepted guidelines which deal with relevant safe prescribing issues in the elderly. Two important ones are the Beers criteria and the STOPP/START criteria.

Did You Know?

Polypharmacy is a common problem in the elderly and makes geriatric prescribing difficult.

1.2.1 Beers Criteria

The Beers criteria or in full, the Beers criteria for potentially inappropriate medication use in older adults is a set of guidelines generated intermittently on a 3-year cycle by the American Geriatrics Society since 2011. The latest version of the criteria was published in 2019.

The Beers criteria mainly provides a list of medications which are inappropriate in the elderly and should be avoided either always or under specific situations.

- For example, peripheral alpha-1 blockers should be avoided as routine anti-hypertensives in the elderly due to the risk of causing orthostatic hypotension.
- The anti-Parkinsonian medications of the central anti-cholinergic drugs class, such as benztropine and trihexyphenidyl should be also avoided in the elderly due to their anti-cholinergic effect. A common practice is to use these as add-ons in younger patients receiving anti-psychotic medications. However, these are not recommended in the elderly.
- Non-steroidal anti-inflammatory drugs should be avoided in elderly patients with chronic kidney disease due to increased risk of aggravated renal damage.

The criteria also mentions drugs which should be used with caution in the elderly.

- One common notable example is that of the direct oral anticoagulants dabigatran and rivaroxaban (for treatment of venous thromboembolism and in atrial fibrillation) which should be used with

caution in those ≥ 75 years of age due to a high risk of gastrointestinal bleeding.

The Beers criteria also has sections on drug-disease, drug-syndrome, and drug-drug interactions, and a list of drugs whose doses need to be reduced in the face of reduced renal function. An exhaustive discussion is beyond this module, but examples are mentioned in the theory module, and the Beers criteria is available online. All practitioners of Geriatrics are strongly advised to make themselves familiar with the same and refer to the same while prescribing medications in elderly.

1.2.2 STOPP/START Criteria

Potentially inappropriate prescribing in elderly includes:

- Drugs prescribed with a risk>benefit element
- Drugs prescribed in excessive doses or for excessive duration
- An unfavourable choice of medication for any ailment
- Not prescribing a clinically indicated medicine despite there being no contraindications

To reduce the prevalence of potentially inappropriate prescribing in the elderly, and to provide improvement over the existing Beers criteria, the STOPP/START criteria was developed by Gallagher, O'Mahony and others in 2008. As per the authors' group, they significantly reduce adverse drug reactions if applied as a single-point intervention within 72 hours of admission. Further, the STOPP criteria medications are associated with adverse drug events significantly as compared to Beers criteria medications. **Prudent advice would be to keep both the *Beers* and *STOPP/START* criteria in mind while prescribing in the elderly.** Again, detailed listing of all the criteria is not possible in this module and the same are available freely on the internet for easy referral of all readers. Some examples are mentioned below.

- STOPP stands for Screening Tool of Older People's Prescriptions
  - Aspirin with a past history of peptic ulcer disease without concomitant proton pump inhibitor (risk of recurrent peptic ulcer)- should be stopped
  - Verapamil or diltiazem with NYHA Class III or IV heart failure (may worsen heart failure)- should be stopped
- START stands for Screening Tool to Alert to Right Treatment

Points to Ponder

What is the drawback of adding central anticholinergics in prescriptions for elderly with Parkinsonism?

Answer

These drugs predispose the elderly to delirium due to their central nervous system effects. Hence, their use is better avoided as per the Beers criteria.

- Vitamin K antagonists or direct thrombin inhibitors or factor Xa inhibitors in the presence of chronic atrial fibrillation- should be started
- Proton Pump Inhibitor with severe gastro-oesophageal reflux disease or peptic stricture requiring dilatation- should be started

Check Your Progress 1

1. Name two established tools for prescribing in the elderly.

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2. What additional medication should be prescribed in order to reduce adverse effects, while prescribing aspirin to an elderly patient?

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1.3 THERAPEUTIC CASCADE, POLYPHARMACY, UN-PRESCRIBING, AND FILTERS

Therapeutic cascade or prescribing cascade refers to the phenomenon of one prescribed drug causing an adverse event (commonly called side effect) which is mis-diagnosed as a new symptom or disease entity and another medication added to control this. This gradually results in multiple medications being used in elderly patients, where reducing original prescription numbers would suffice. Often the prescribing cascade results in polypharmacy. Sometimes elderly patients visiting multiple specialists and general practitioners, and in the Indian setting also visiting quacks and neighbourhood drug stores for over-the-counter medications, also results in polypharmacy. Polypharmacy may result in several complications in the elderly, some innocuous such as nausea or anorexia and some severe such as cardiac toxicity, seizures, or delirium. Hence, practitioners of geriatrics often have to resort to un-prescribing or reducing the number of medications prescribed. Un-prescribing or de-prescribing remains one of the major planks of the geriatric practice. Drug safety is of greater importance in elderly healthcare than drug efficacy, and a classic teaching remains that 'any new symptom in an elderly patient on medications should be considered an adverse event of a drug unless proved otherwise'.

Think and Reflect

Can you think of some strategies to reduce wrong prescribing practices in the elderly, at the peripheral health center level?

Here you will learn how to practically perform un-prescribing in elderly patients and the various filters (sequential steps) used for the same (**Fig. 1.1**).

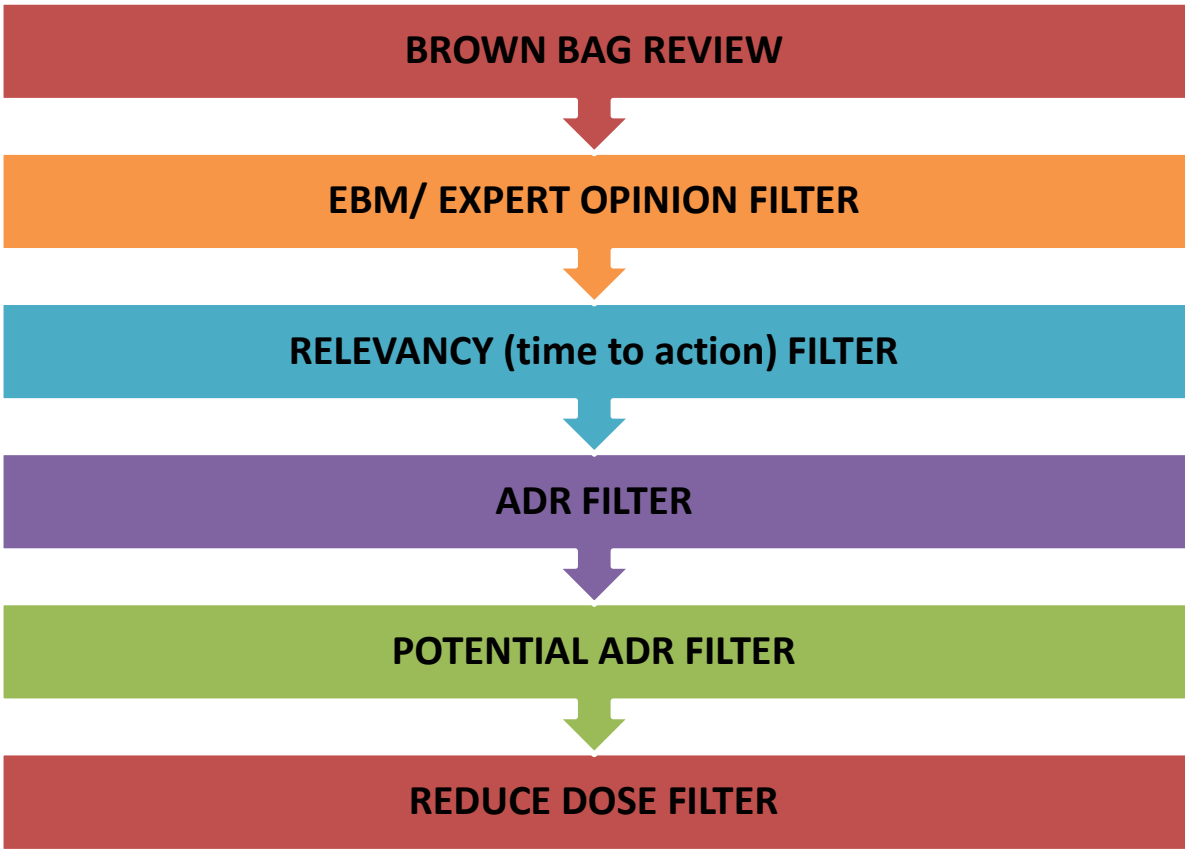

Fig. 1.1. The steps of reducing prescription load in elderly (Un-prescribing)

*Based on protocol described in Current Diagnosis and Treatment- Geriatrics (2nd edition; Lange)

Steps of Un-prescribing

1. **Brown bag review-** The first step is to always advise elderly patients coming to the out-patient setup to bring all medications being currently taken by them, including over-the-counter ones and those prescribed by other doctors. The geriatrician should carefully go through the medications and confirm that the patient is taking the appropriate prescribed dose of each (compliance), and there is no duplication from different doctors, or medication errors as per previously described Beers and STOPP-START criteria.

2. **Evidence based medicine or Expert opinion-**The next step involves eliminating those medications which have poor clinical trial or expert opinion evidence for benefits in the elderly. For example, the benefits of statins have not been demonstrated in those more than 70 years of age for primary prevention of atherosclerotic cardiovascular disease. Thus, statins may be removed from the prescriptions of the very old if recently added for this indication.Another similar example includes

aspirin for primary prophylaxis against cardiovascular events in elderly with diabetes.

3. **Relevancy or time to action-** Some medications such as statins need a long period to result in benefits as evidenced from cardiovascular protection trials. So, it would be meaningless to initiate these drugs in elderly patients with advanced disease states such as chronic kidney disease or congestive heart failure or malignancies where the life expectancy is less than 2.5 years.

4. **Adverse drug reaction (ADR)-** Any drug which results in an adverse drug reaction in an elderly patient should be replaced by safer alternatives unless the benefits are significant if the same is continued, and the adverse events are tolerable. For example, an elderly patient on multiple neuropsychiatric medications which cause somnolence may need reduction of the ones least likely to cause any benefit. Similarly, if an elderly patient with diabetes on glimepiride monotherapy has episodes of hypoglycaemia, the drug may be replaced by safer choices such as shorter acting sulfonylureas or metformin or DPP4 inhibitors. A common practice among neurology sub-specialists who mainly deal with younger patients is to initiate anti-Parkinsonian therapy in elderly with multiple medications which include levodopa-carbidopa, amantadine, pramipexole, trihexyphenidyl, etc. Usually, patients in such cases present with neuropsychiatric disturbances, and prescription reduction is needed. A switch to isolated levodopa-carbidopa therapy often suffices.

5. **Potential adverse drug reactions-** Besides reducing medicines which are causing adverse drug reactions, an effort should be made to not prescribe those which are likely to result in ADRs, in the first place. The Beers criteria and the STOPP criteria may be referred to for the same.

6. **Dose Reduction-** The final step in un-prescribing involves prescribing lower than classically described doses of medications in the elderly. Despite absence of trial evidence for these low doses in many cases, they are commonly observed to work in the elderly. They also cause a lesser burden of adverse events. Some examples include-

   a. The anti-psychotic medication olanzapine is usually started at a dose of 5 mg once daily, but even 2.5 mg may work well in the elderly.

Did You Know?

Un-prescribing is routinely practised in geriatric services, and contrary to misconception among doctors, patients do not mind a doctor reducing their prescription burdens.

b. Pregabalin is a common neuropathic pain medication which may be useful in the elderly at doses as low as 75 mg once daily, which is much less than the recommended adult dose.

Check your Progress 2

1. What do you mean by a brown bag review?

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2. Which is the drug of choice for an elderly patient with Parkinson's disease?

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1.4 RENAL AND HEPATIC MODIFICATIONS OF DRUG DOSAGES

While medications in all age groups need to be prescribed at appropriate dosages with modifications based on renal and hepatic function, this attains even more significance in the elderly. This is because of the higher prevalence of chronic kidney and liver disease in the elderly. Further, normal renal function also declines with age, and the elderly have a lower creatinine clearance (Cr.Cl.) or glomerular filtration rate as compared to gender and weight matched younger people. Renal dose modifications are usually decided based on the calculated creatinine clearance values, which are slightly higher than the actual glomerular filtration rates. The most commonly used formula for Cr.Cl. calculation is the Cockcroft-Gault equation which is depicted below. The calculation is straightforward and can be done manually even in an out-patient setting.

Cockcroft-Gault equation

Cr.Cl. in mL/min = [(140-Age in years) X Body weight in kgs] / [72 X Serum creatinine concentration in mg/dL]

The value obtained is further multiplied by 0.85 for females

The Beers criteria provides a list of drugs to be avoided or used with caution in elderly with reduced Cr.Cl. values. For example, dabigatran should be avoided if Cr.Cl. is < 30 mL/min. Levetiracetam dose needs to be reduced if Cr.Cl. ≤ 80 mL/min due to the increased risk of central nervous system adverse events. The exhaustive list can be obtained from the detailed Beers criteria itself. Another option that is easy to follow is to refer to online medical information sites such as Medscape which are reliable, with the

facility to create a free account. Detailed drug dose modification by Cr.Cl. for most commonly used drugs can be found in Medscape and other online resources. Fewer number of medications need hepatic dose modification- the guidelines are less clear. Usually, chronic liver disease is staged using the Child Pugh's staging system which is a determinant to predict mortality in patients with cirrhosis. Most drugs metabolized in the liver need to be avoided in advanced stages of liver cirrhosis, that is Child Pugh's class C. It is better to prefer renal-metabolized drugs instead of hepatic metabolized drugs in acute hepatic failure cases (caused by toxins, drugs themselves, hepatotropic viruses, heart failure, and shock), but again guidelines are less clear. The Medscape is again a ready reference for common hepatic modifications of drug dosages. The essence of writing a geriatric prescription is to double-check (double-think) while writing each medicine, weighing the pros and cons, probable contraindications and adverse events, and necessary dose modifications. After completing the prescription, the geriatrician must go over the same in entirety to look for potential errors of omission and commission.

Points to Ponder

Which are the common organ dysfunctions which require an alteration of drug doses?

Answer

Renal and hepatic diseases necessitate alteration in doses of prescribed drugs.

Check Your Progress 3

1. What is the creatinine clearance of an elderly man of age 80 years who has a body weight of 65 kg and a serum creatinine level of 3.5 mg/dL?

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2. Which staging system is used for chronic liver disease, while deciding on dose-modifications of drugs?

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1.5 DRUG-DRUG AND DRUG-DISEASE INTERACTIONS

The Beers criteria provides examples of conditions where drugs interact with other drugs and can result in prescribing issues, and also examples of how individual health conditions may affect the prescribing of certain medications. Here, some representative examples are provided but the readers are advised to go through detailed listings.

1.5.1 Drug-disease Interactions

Some common examples from the Beers criteria include:

- Cilostazol used in peripheral vascular disease has a potential to increase mortality in patients with heart failure, and hence should be avoided in such patients.
- Benzodiazepines and anticholinergics should be avoided in patients with dementia or cognitive impairment.
- High dose aspirin or COX-2 non-selective inhibitors should be avoided in those with a history of peptic ulcer disease unless alternatives are not effective or gastroprotective agents may be given.

1.5.2 Drug-drug Interactions

Some common examples include:

- Using Angiotensin converting enzyme inhibitors and spironolactone together should be avoided especially in patients with chronic kidney disease, as the additive risk of potentially life-threatening hyperkalaemia is quite high
- Using corticosteroids and NSAIDs together should be avoided due to a higher risk of peptic ulcer disease or gastrointestinal bleeding

Think and Reflect

What may be the commonly prescribed drugs in an elderly patient with diabetes, hypertension, and chronic kidney disease?

Check Your Progress 4

1. Name one contraindication to using cilostazol.

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2. Which organization publishes the Beers criteria?

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1.6 OTHER CONSIDERATIONS WHILE PRESCRIBING IN THE ELDERLY

While prescribing in the elderly, doctors need to be aware of certain other useful information. These are summarised in **Table 1.1**.

Table 1.1. Relevant to know while prescribing in the Elderly

Loading dose	Certain drugs such as major anti-epileptics in cases of status epilepticus need to be administered in higher-than-normal doses called loading doses. This helps in achieving therapeutic effect faster based on pharmacokinetic properties of the drug.
Change of formulation	Drugs such as thyroxine, anti-epileptics such as phenytoin, have batch to batch variability and also depending on manufacturers. Hence, doctors must be careful while prescribing these. A patient well-controlled on one brand may not show same response to another brand/preparation.
Abrupt withdrawal	Abrupt withdrawal of certain medications can result in serious adverse events. These should be avoided in prescriptions. Examples include: i. Beta-blockers such as metoprolol when withdrawn abruptly may result in reflex hypertension ii. Anti-epileptic drugs if withdrawn abruptly may result in new seizures iii. Abrupt withdrawal of corticosteroids after prolonged use can precipitate an adrenal crisis, resulting in shock
Drug-food interactions	Certain medications such as warfarin, calcium supplements, anti-Parkinsonian drugs, thyroxine, etc interact with food if consumed together. Geriatricians need to be aware of these interactions and advise accordingly
Improving medication adherence	Practitioners of geriatric medicine should pay special attention to the following while prescribing: i. social and financial issues such as

	caregiver support, resources to purchase medications etc. ii. ease of administration (consumption) of medications including handling of packaging and bottles iii. need for monitoring of blood parameters such as blood glucose levels while taking certain medications iv. avoiding complex prescriptions
Special considerations while prescribing anti-microbials	Anti-microbial resistance is a major concern due to indiscriminate antimicrobial use. Hence, prescription of these drugs should be as per strict local protocols or based on specific disease diagnosis or culture reports. The use of high-end, broad-spectrum antibiotics should be avoided as far as possible unless other options are unavailable. Anti-microbials are also notorious for causing hypersensitivity reactions and it is prudent to always make note of past allergies while prescribing them. In case of parenteral administration, cutaneous sensitivity testing should be done.
Clarity of prescription	The practitioner should ensure clarity in writing prescriptions. The patient-details, brief note of complaints, working diagnoses, advised, and reported investigation results should be clearly documented. Any reason for change of previous medication or addition of new drug should be clearly mentioned. The prescribed medications should be clearly written in legible handwriting, preferably with local-language instructions for usage in addition to standard pharmacy abbreviations. Timing of use and dosage should be clearly mentioned.

	The practitioner should sign legibly at the end of the prescription, with clear mention of registration number and date if mandated by the setting of practice. The doctor should not only be particular in maintaining the paper-record but should explain the directions to the patient or caregiver clearly, and empathetically. The patient or caregiver must be allowed to ask relevant questions and gain clarifications.

1.7 REPORTING ADVERSE DRUG REACTIONS

It is the responsibility of every clinician to report adverse drug reactions to appropriate regulatory agencies. Types of adverse drug reactions are mentioned in **Table 1.2**. In India, the Pharmacovigilance Programme of India (PvPI) encourages practitioners to report any known or new adverse drug reactions to the nearest Adverse Drug Reaction (ADR) monitoring center (AMC) which is a part of medical colleges. They can fill up a detailed ADR form with the assistance of technical associates. They can also make use of a toll-free helpline number or simply email the details of the adverse drug reaction to pvpi.ipcindia@gmail.com,while maintaining patient confidentiality. There is no hassle associated with reporting ADRs and the doctor is in no way penalized for ADRs developing due to prescribed medications, within the limits of fair medical practice.

Did You Know?

Antimicrobial resistance is a looming danger in India due to unregulated use of antibiotics by both trained and untrained medical practitioners.

Table 1.2. Types of Adverse Drug Reactions

Type A	Dose-related adverse drug reactions. E.g., oral anti-diabetic drug induced hypoglycaemia (predictable)
Type B	Idiosyncratic adverse drug reactions. E.g., hyper-sensitivity to penicillin group of drugs (unpredictable)
Type C	Chronic adverse drug reactions. E.g., steroid induced osteoporosis (occurs after months of use of drug which accumulates)
Type D	Delayed adverse drug reactions.

	E.g., tardive dyskinesias with anti-psychotic agents (occur after years of use of drug which does not accumulate)
Type E	Withdrawal reactions E.g., opioid and benzodiazepine withdrawal reactions
Type F	Drug failure E.g., antibiotic resistance

Check Your Progress 5

1. What are type E adverse drug reactions?

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2. Name the programme which is responsible for collecting data of adverse drug reactions in India.

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1.8 CASE STUDIES

1. A 75-year-old man with tremors in one hand and slowness of gait visits a neurosurgeon for consultation. He is prescribed piracetam 800 mg thrice daily, amantadine 100 mg twice daily and trihexyphenidyl 2 mg thrice daily. He is also prescribed risperidone 0.5 mg daily for insomnia. What are the possible serious issues with this case?

   The patient presents with delirium to you after 10 days. What will be the approach to managing the patient?

2. A 65-year-old lady visits a local physician for dizziness and is prescribed hydrochlorothiazide 12.5 mg daily for hypertension (150/90 mm Hg recorded blood pressure). On the next visit the patient complains of increased dizziness/ vertigo. The doctor adds betahistine to the prescription. The patient is brought to you in a drowsy state after 2 days. You take a background history and find that she was on carbamazepine 150 mg twice daily for 3 years for seizure disorder. Discuss the approach and possibilities of this case.

   The local physician adding betahistine is an example of which common problem in geriatric prescribing?

3. An elderly man of 70 years with newly diagnosed diabetes (fasting blood sugar 250 mg/dL, post glucose challenge blood sugar 350 mg/dL and

Points to Ponder

If an elderly patient has never had hypersensitivity (allergic) reactions to antibiotics in the past, can it be confirmed that they will never have the same in the future?

Answer

No. This is because hypersensitivity reactions to antibiotics are usually Type B adverse drug reactions which are idiosyncratic (unpredictable).

HbA1c of 7.5%) comes to you. He has no complaints except dryness of mouth. You find the only abnormality on examination is a blood pressure of 170/95 mm Hg. In investigations, renal and liver function tests come out normal. Urine has 3+ protein and electrocardiogram shows T-wave inversion on chest leads V3-V6. There is no history of prior cardiac disease or current chest pain or breathing trouble. Write a sample prescription for this patient.

1.9 LET US SUM UP

In this practical module, you have been made familiar with standard tools available to the geriatric practitioner in the rational prescription of medicines in the elderly. Further, the stepwise technique of un-prescribing has also been highlighted. Some representative examples have been provided for drug-drug and drug-disease interactions, and practical means of renal and hepatic drug dose modifications have been discussed. Using knowledge gained from this module, peripheral geriatric practitioners may make their practice sounder and elderly-friendly.

1.10 ANSWERS TO CHECK YOUR PROGRESS

Check Your Progress 1

1. The Beers criteria and the STOPP/START criteria
2. Proton pump inhibitors (rabeprazole etc) or histamine H2 receptor blockers (famotidine etc)

Check Your Progress 2

1. Checking all medications being taken by the patient during his/her visit to the geriatrician, including medications prescribed by the geriatrician as well as other doctors, and over the counter medications, is called a brown bag review. It aims to confirm compliance, rule out duplications and inappropriate prescribing.
2. Levodopa-carbidopa combination

Check Your Progress 3

1. 15.5 mL/min
2. Child-Pugh score

Check Your Progress 4

1. Heart failure
2. American Geriatrics Society

Check Your Progress 5

1. Withdrawal reactions e.g., opioid and benzodiazepine withdrawal reactions
2. Pharmacovigilance Programme of India

1.11 REFERENCES AND FURTHER READINGS

1. By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. “American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults.” Journal of the American Geriatrics Society vol. 67,4 (2019): 674-694. doi:10.1111/jgs.15767
2. O'Mahony, Denis. “STOPP/START criteria for potentially inappropriate medications/potential prescribing omissions in older people: origin and progress.” Expert review of clinical pharmacology vol. 13,1 (2020): 15-22. doi:10.1080/17512433.2020.1697676
3. ICMR NvCCPPrescribing Skills Course-2020, for Indian Medical Graduates