

# Best Practices for Appropriate Prescribing

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# Beers Criteria: History and Utilization

- › **Original 1991** – Nursing home patients
- › **1997** For all elderly; adopted by Centers for Medicare & Medicaid Services (CMS) in 1999 for nursing home regulation
- › **2003** Adopted by Medicare Part D, National Committee for Quality Assurance (NCQA), Healthcare Effectiveness Data and Information Set (HEDIS)
- › **2012** Adopted by American Geriatrics Society (AGS); Further adoption into quality measures
- › **2015** Introduction of drug-drug interactions (DDI), renal dosage tables
- › **2018** Updated and published in 2019. Grading the strength and quality of each potentially inappropriate medications (PIMs) statement based on the level of evidence and strength of recommendation.



# Quality and Strength of Evidence

## Quality of Evidence

- › **High-quality evidence:** “Evidence...obtained from 1 or more welldesigned and well-executed randomized, controlled trials (RCTs) that yield consistent and directly applicable results.”
- › **Moderate-quality evidence:** “Evidence...obtained from RCTs with important limitations.... evidence from welldesigned controlled trials without randomization, well-designed cohort.”
- › **Low-quality evidence:** “Evidence obtained from observational studies would typically be rated as low quality because of the risk for bias.”

## Strength of Evidence

- › **Strong:** Harms, adverse events, and risks clearly outweigh benefits.
- › **Weak:** Harms, adverse events, and risks may not outweigh benefits.





Table 2 (Contd.)

Organ System, Therapeutic Category, Drug(s)	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation
<b>Endocrine</b>				
Androgens Methyltestosterone Testosterone	Potential for cardiac problems; contraindicated in men with prostate cancer	Avoid unless indicated for confirmed hypogonadism with clinical symptoms	Moderate	Weak
Desiccated thyroid	Concerns about cardiac effects; safer alternatives available	Avoid	Low	Strong
Estrogens with or without progestins	Evidence of carcinogenic potential (breast and endometrium); lack of cardioprotective effect and cognitive protection in older women	Avoid systemic estrogen (eg, oral and topical patch)	Oral and patch: high	Oral and patch: strong
	Evidence indicates that vaginal estrogens for the treatment of vaginal dryness are safe and effective; women with a history of breast cancer who do not respond to nonhormonal therapies are advised to discuss the risks and benefits of low-dose vaginal estrogen (dosages of estradiol <25 µg twice weekly) with their healthcare provider	Vaginal cream or vaginal tablets: acceptable to use low-dose intravaginal estrogen for management of dyspareunia, recurrent lower urinary tract infections, and other vaginal symptoms	Vaginal cream or vaginal tablets: moderate	Topical vaginal cream or tablets: weak
Growth hormone	Impact on body composition is small and associated with edema, arthralgia, carpal tunnel syndrome, gynecomastia, impaired fasting glucose	Avoid, except for patients rigorously diagnosed by evidence-based criteria with growth hormone deficiency due to an established etiology	High	Strong
Insulin, sliding scale (insulin regimens containing only short- or rapid-acting insulin dosed according to current blood glucose levels without concurrent use of basal or long-acting insulin)	Higher risk of hypoglycemia without improvement in hyperglycemia management regardless of care setting. Avoid insulin regimens that include only short- or rapid-acting insulin dosed according to current blood glucose levels without concurrent use of basal or long-acting insulin. This recommendation does not apply to regimens that contain basal insulin or long-acting insulin.	Avoid	Moderate	Strong
Megestrol	Minimal effect on weight; increases risk of thrombotic events and possibly death in older adults	Avoid	Moderate	Strong
Sulfonylureas, long acting Chlorpropamide Glimepiride Glyburide (also known as glibenclamide)	Chlorpropamide: prolonged half-life in older adults; can cause prolonged hypoglycemia; causes SIADH Glimepiride and glyburide: higher risk of severe prolonged hypoglycemia in older adults	Avoid	High	Strong
<b>Gastrointestinal</b>				
Metoclopramide	Can cause extrapyramidal effects, including tardive dyskinesia; risk may be greater in frail older adults and with prolonged exposure	Avoid, unless for gastroparesis with duration of use not to exceed 12 weeks except in rare cases	Moderate	Strong
Mineral oil, given orally	Potential for aspiration and adverse effects; safer alternatives available	Avoid	Moderate	Strong
Proton-pump inhibitors	Risk of <i>Clostridium difficile</i> infection and bone loss and fractures	Avoid scheduled use for >8 weeks unless for high-risk patients (eg, oral corticosteroids or chronic NSAID use), erosive esophagitis, Barrett esophagitis, pathological hypersecretory condition, or demonstrated need for maintenance treatment (eg, because of failure of drug discontinuation trial or H2-receptor antagonists)	High	Strong



# Goal of AGS 2019 Beers Criteria

## Goals:

- › Improve care by decreasing exposure to POTENTIALLY inappropriate medications (PIMs)
- › Educational tool
- › Quality measure
- › Research tool

Prescribing Assessment vs. Quality Measure



# AGS 2019 Beers Criteria

- › **First-generation antihistamines:** Highly anticholinergic
  - Diphenhydramine (oral), Doxylamine, Hydroxyzine, Meclizine, Promethazine, etc.
  - Diphenhydramine is still appropriate for acute allergic reaction
- › **Antiparkinsonian agents:** Benztropine (oral), Trihexyphenidyl
  - Highly anticholinergic. More effective agents available for PD
  - Not recommended for prevention or treatment of extrapyramidal symptoms with antipsychotics
- › **Antispasmodics:** Highly anticholinergic
  - Dicyclomine (excludes ophthalmic), Hyoscyamine, Scopolamine, etc.
- › **Antithrombotics:** May cause orthostatic hypotension; more effective alternatives available
  - Dipyridamole, oral short acting
  - Extended-Release combination with aspirin (Aggrenox) is ok
- › **Nitrofurantoin:** Potential for pulmonary toxicity, hepatotoxicity, and peripheral neuropathy, especially with long-term use; safer alternatives available
  - Avoid if creatinine clearance  $<30$  mL/min or for long-term suppression
  - Quality of Evidence: Low
  - Strength of Evidence: Strong



## AGS 2019 Beers Criteria

- › **Peripheral alpha-1 blockers for HTN treatment:** High risk of orthostatic hypotension and associated harms, especially in older adults. Still ok for treatment of BPH.
  - Doxazosin, Prazosin, Terazosin
- › **Disopyramide** (antiarrhythmic): May induce heart failure in older adults because of potent negative inotropic action; strongly anticholinergic; other antiarrhythmic drugs preferred
- › **Dronedarone:** Worse outcomes have been reported in patients taking dronedarone who have permanent atrial fibrillation or severe or recently decompensated heart failure.
- › **Digoxin:** In HF, higher dosages are not associated with additional benefit and may increase risk of toxicity. Decreased renal clearance of digoxin may lead to digoxin toxicities.
  - If used for atrial fibrillation or HF failure, **avoid dosages >0.125 mg/day**
- › **Nifedipine (immediate release):** Risk for hypotension; risk of precipitating MI
- › **Amiodarone:** Effective for maintaining sinus rhythm but has greater toxicities. Avoid as first-line therapy for A Fib unless patient has HF or substantial left ventricular hypertrophy



# AGS 2019 Beers Criteria

## › **Tricyclic Antidepressants:**

- Highly anticholinergic, sedating, and cause orthostatic hypotension
- Amitriptyline, Desipramine, Doxepin >6 mg/day, Imipramine, Nortriptyline, etc.

## › **Paroxetine (SSRI):** Highly anticholinergic

## › **Antipsychotics**, first (conventional) and second (atypical) generation

- Increased risk of CVA and greater rate of cognitive decline and mortality in persons with dementia
- Avoid antipsychotics for behavioral problems of dementia or delirium unless nonpharmacological options (eg. behavioral interventions) have failed or are not possible and **the older adult is threatening substantial harm to self or others**

## › **Benzodiazepines:**

- Increase risk of cognitive impairment, delirium, falls, fractures, and motor vehicle crashes in older adults.
- May be appropriate for seizure disorders, rapid eye movement sleep behavior disorder, benzodiazepine withdrawal, ethanol withdrawal, severe generalized anxiety disorder, and procedural anesthesia
- If Benzo needs to be used, **Lorazepam, Oxazepam, Temazepam (LOT)** are preferred due to short half-life → less accumulation of drug in the blood → less side effects.

## › **Nonbenzodiazepine**, benzodiazepine receptor agonist hypnotics (ie, “Z-drugs”)

- Similar side effects as Benzodiazepines
- Eszopiclone (Lunesta), Zaleplon (Sonata), Zolpidem (Ambien)





## AGS 2019 Beers Criteria

- › **Androgens:** Methyltestosterone, Testosterone
  - Potential for cardiac problems; contraindicated in men with prostate cancer
  - Avoid unless indicated for confirmed hypogonadism with clinical symptoms
  
- › **Estrogens with or without progestins:**
  - Evidence of carcinogenic potential (breast and endometrium)
  - VTE risk
  - Lack of cardioprotective effect and cognitive protection in older women.
  - **Avoid systemic estrogen** (eg. oral and topical patch)
  - **Vaginal cream or vaginal tablets (low-dose intravaginal estrogen) are acceptable** for management of dyspareunia, recurrent lower UTI, and other vaginal symptoms



# AGS 2019 Beers Criteria

- › Desiccated thyroid: Concerns about cardiac effects; safer alternatives available

Table 1: Equivalent doses of desiccated thyroid and levothyroxine

Desiccated Thyroid (T3 + T4) (derived from porcine thyroid gland)	T4 (levothyroxine)
30mg	50µg (approximate range 25µg - 88µg)
60mg	100µg (approximate range 88µg - 112µg)
90mg	150µg (approximate range 112µg - 175µg)
125mg	200µg (approximate range 175µg - 300µg)

- › Check TSH 6 weeks later and adjust dose appropriately



# AGS 2019 Beers Criteria

## › Insulin, sliding scale

- Avoid insulin regimens that include only short or rapid-acting insulin dosed according to current blood glucose levels without concurrent use of basal or long-acting insulin.
- This recommendation does not apply to regimens that contain basal insulin or long-acting insulin
- Higher risk of hypoglycemia without improvement in hyperglycemia management regardless of care setting.

## › Megestrol

- Minimal effect on weight
- Increases risk of thrombotic events and possibly death in older adults
- Adrenal suppression: “May suppress hypothalamic-pituitary-adrenal (HPA) axis during chronic administration; consider the possibility of adrenal suppression in any patient receiving or being withdrawn from chronic therapy when signs/symptoms suggestive of hypoadrenalism are noted (during stress or in unstressed state.” **Recommend tapering when discontinuing Megestrol**



## AGS 2019 Beers Criteria

### › **Sulfonylureas, long acting:**

- Chlorpropamide, **Glimepiride, Glyburide**
- Long half-life in older adults; can cause prolonged hypoglycemia
- Glipizide is ok, but hypoglycemia can still occur.

### › **Metoclopramide:**

- Can cause extrapyramidal effects, including tardive dyskinesia; risk may be greater in frail older adults and with prolonged exposure
- Avoid, unless for gastroparesis with duration of use not to exceed 12 weeks except in rare cases

### › **Mineral oil, given orally**

- Potential for aspiration and adverse effects; safer alternatives available



# AGS 2019 Beers Criteria

- › **Proton-pump inhibitors:** Omeprazole, Pantoprazole, Lansoprazole, etc.
  - Risk of Clostridium difficile infection
  - Risk of bone loss and fractures
  - Increased incidence of community-acquired pneumonia (observational studies suggest an association between PPI use and pneumonia)
  - Vitamin B12 deficiency
  - Hypomagnesemia
  - Avoid scheduled use for >8 weeks unless for high-risk patients (eg, oral corticosteroids or chronic NSAID use), erosive esophagitis, Barrett esophagitis, pathological hypersecretory condition, or demonstrated need for maintenance treatment (eg, because of failure of drug discontinuation trial or H2-receptor antagonists)
  - **When discontinuing PPI (after >8 weeks therapy), taper PPI over 2 weeks to avoid acid reflux rebound**
  - **Routine H2 blockers with PPI can cause tachyphylaxis after several weeks of use**
  - Concomitant PPI and clopidogrel does not appear to increase risk for adverse cardiovascular events. (Strong recommendation, high level of evidence).



## AGS 2019 Beers Criteria

- › **NSAIDs (Non-cyclooxygenase-selective NSAIDs) oral & Aspirin >325 mg/day**
  - Increased risk of GI bleeding or peptic ulcer disease
  - Can increase blood pressure
  - Can induce kidney injury
  - Worsen HF
  - Risks are dose related
  - Of all the NSAIDs, **indomethacin has the most adverse effects including adverse CNS effects**
  - **Ketorolac: [US Boxed Warning]: Ketorolac can cause peptic ulcers, GI bleeding, and/or perforation of the stomach or intestines, which can be fatal**
    - › **Maximum combined duration of treatment (for parenteral and oral) is 5 days**



# AGS 2019 Beers Criteria

## › Skeletal muscle relaxants

- Carisoprodol, Chlorzoxazone, Cyclobenzaprine, Metaxalone, Methocarbamol, Orphenadrine
- Anticholinergic adverse effects, sedation, increased risk of fracture
- Effectiveness at dosages tolerated by older adults questionable

## › Desmopressin

- US Box Warning: High risk of hyponatremia. Severe hyponatremia can be life-threatening, leading to seizures, coma, respiratory arrest, or death. Desmopressin is contraindicated in patients at increased risk of severe hyponatremia.
- Avoid for treatment of nocturia or nocturnal polyuria
- Safer alternative treatments



## Drug-Disease Interactions - AGS 2019 Beers Criteria

### › Heart Failure

- Potential to promote fluid retention and/or exacerbate heart failure
- Avoid Cilostazol, Nondihydropyridine CCBs (diltiazem, verapamil), NSAIDs, COX-2 inhibitors (Celebrex), pioglitazone, rosiglitazone), Dronedarone





# Drug-Disease Interactions - AGS 2019 Beers Criteria

## › Delirium

- Avoid in older adults with or at high risk of delirium because of potential of inducing or worsening delirium
  - › Anticholinergics
  - › Antipsychotics (Avoid antipsychotics for behavioral problems of dementia and/or delirium unless nonpharmacological options (eg, behavioral interventions) have failed or are not possible and the older adult is threatening substantial harm to self or others. Antipsychotics are associated with greater risk of CVA and mortality in persons with dementia.)
  - › Benzodiazepines
  - › Corticosteroids (oral and parenteral)c
  - › **H2-receptor antagonists:** Cimetidine, Famotidine, Nizatidine, Ranitidine
  - › Meperidine
  - › Nonbenzodiazepine, benzodiazepine receptor agonist hypnotics: (eszopiclone, zaleplon, zolpidem)



# Drug-Disease Interactions - AGS 2019 Beers Criteria

## › **Syncope**

- Acetylcholinesterase inhibitor (AChEI) cause bradycardia and should be avoided in older adults whose syncope may be due to bradycardia.
- Nonselective peripheral alpha-1 blockers (ie, doxazosin, prazosin, terazosin): risk for orthostatic hypotension
- TCAs - increase the risk of orthostatic hypotension or bradycardia
- Antipsychotics: - increase the risk of orthostatic hypotension or bradycardia
  - › Chlorpromazine
  - › Thioridazine
  - › Olanzapine



# Drug-Disease Interactions - AGS 2019 Beers Criteria

## › **Parkinson disease**

- Dopamine-receptor antagonists have potential to worsen parkinsonian symptoms.
- Avoid antiemetics: Metoclopramide, Prochlorperazine, Promethazine
- Avoid all antipsychotics (except quetiapine, clozapine, pimavanserin)
- Exceptions:
  - › Pimavanserin and clozapine appear to be less likely to precipitate worsening of Parkinson disease.
  - › Quetiapine has only been studied in low-quality clinical trials



# Drug-Disease Interactions - AGS 2019 Beers Criteria

## › **History of falls or fractures**

- Antiepileptics
- Antipsychotics
- Benzodiazepines
- Nonbenzodiazepine, benzodiazepine
  - › Eszopiclone
  - › Zaleplon
  - › Zolpidem
- receptor agonist hypnotics
  - › Eszopiclone
  - › Zaleplon
  - › Zolpidem
- Antidepressants
  - › TCAs
  - › SSRIs
  - › SNRIs
- Opioids



# Drugs To Be Used With Caution in Older Adults

## AGS 2019 Beers Criteria

- › **Aspirin for primary prevention of cardiovascular disease and colorectal cancer**
  - Increase of major bleeding in older age
  - Aspirin is generally indicated for secondary prevention in older adults with established CVD

### Beer's Criteria 2019

- Adults  $\geq 70$  yo: Use aspirin with caution for primary prevention of cardiac events
- Beer's Criteria Rationale:
  - › Risk of major bleeding increases with age
  - › Lack of net benefit in older adults with CV risk factors
  - › Evidence is not conclusive
- No recommendations for adults  $< 70$  yo

### ACC/AHA 2019

- For primary prevention of ASCVD in higher ASCVD adults 40-70 years old who are NOT at increased risk of bleeding, 75-100 mg ASA **might be** considered (Level of Evidence A)
- For primary prevention of ASCVD among adults  $> 70$  years old, **75-100 mg of ASA should not be administered** (Level of Evidence B)
- For primary prevention among adults of any age who have a high risk of bleeding, **75-100 mg of ASA should not be administered** (Level of Evidence C)



# Drugs To Be Used With Caution in Older Adults

## AGS 2019 Beers Criteria

### › **Dabigatran, Rivaroxaban**

- Increased risk of gastrointestinal bleeding compared with warfarin and reported rates with other direct oral anticoagulants when used for long-term treatment of VTE or atrial fibrillation in adults  $\geq 75$  years.


### › **Prasugrel (Effient)**

- Increased risk of bleeding in older adults
- “Benefit in highest-risk older adults (eg, those with prior myocardial infarction or diabetes mellitus) may offset risk when used for its approved indication of acute coronary syndrome to be managed with percutaneous coronary intervention”



# Drugs To Be Used With Caution in Older Adults

## AGS 2019 Beers Criteria

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- › Drugs that may exacerbate or cause SIADH or **hyponatremia**
    - Antipsychotics
    - Carbamazepine
    - Diuretics
    - Mirtazapine
    - Oxcarbazepine
    - SNRIs
    - SSRIs
    - TCAs
    - **Tramadol**
  - › Monitor sodium level closely when starting or changing dosages in older adults

# Drugs To Be Used With Caution in Older Adults

## AGS 2019 Beers Criteria

- › **Dextromethorphan/quinidine (NUEDEXTA)**
  - Limited efficacy in patients with behavioral symptoms of dementia
  - May increase risk of falls and concerns with clinically significant drug interactions
  - Does not apply to treatment of pseudobulbar affect (PBA)
- › **Trimethoprim/sulfamethoxazole (Bactrim, Septra)**
  - Increased risk of hyperkalemia when used concurrently with an ACEI (Lisinopril) or ARB (Losartan) in presence of decreased creatinine clearance (CrCl)
  - Check renal and potassium labs






# Drug-Drug interactions (DDI)

## See Beers Criteria - Table 5

- › Lithium & ACE inhibitor: Increased risk of lithium toxicity
  - › Lithium & Loop diuretics: Increased risk of lithium toxicity
  - › Interactions between CNS active drugs (opioid & benzodiazepine) - Increased risk of falls and of fracture
  - › Warfarin & NSAID - Increased risk of bleeding
  - › Warfarin & Amiodarone - Increased risk of bleeding
- 
- › See more drug interactions on Table 5





Medications That Should Be Avoided or Have Their  
Dosage Reduced With Varying Levels of Kidney Function in Older Adults -  
Table 6

- › Trimethoprim/sulfamethoxazole (Bactrim, Septra)
  - Increased risk of worsening of renal function and hyperkalemia
  - Reduce dose if CrCl 15-29 mL/min
  - Avoid if CrCl <15 mL/min
- › Spironolactone:
  - Increased potassium
  - Avoid if CrCl < 30 mL/min
- › Tramadol:
  - Increased CNS adverse effect
  - If CrCl < 30 mL/min
    - › Immediate release: reduce dose; every 12 hours; maximum: 200 mg/day
    - › Avoid Extended Release
- › DOACs have renal dosing
- › See more renally dosed medications on Table 6

# Goal of AGS 2019 Beers Criteria

## Goals:

- › Improve care by decreasing exposure to POTENTIALLY inappropriate medications (PIMs)
- › Review medications at each visit/encounter
- › Assess benefits vs. risks





## References

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