Medication Appropriateness Index

Patient ID# __________   Evaluator __________________ Date ________________
Drug Code ____________ Drug__________________________________________

To assess the appropriateness of the drug, please answer the following questions and circle the applicable rating:

1. Is there an indication for the drug?       A______  B______  C______  Z
   Comments:
   Indicated
   Not Indicated
   DK

2. Is the medication effective for the condition?
   A______  B______  C______  Z
   Comments:
   Effective
   Ineffective
   DK

3. Is the dosage correct?
   A______  B______  C______  Z
   Comments:
   Correct
   Incorrect
   DK

4. Are the directions correct?
   A______  B______  C______  Z
   Comments:
   Correct
   Incorrect
   DK

5. Are the directions practical?
   A______  B______  C______  Z
   Comments:
   Practical
   Impractical
   DK

6. Are there clinically significant drug-drug interactions?
   A______  B______  C______  Z
   Comments:
   Insignificant
   Significant
   DK

7. Are there clinically significant drug-disease/condition interactions?
   A______  B______  C______  Z
   Comments:
   Insignificant
   Significant
   DK

8. Is there unnecessary duplication with other drug(s)?
   A______  B______  C______  Z
   Comments:
   Necessary
   Unnecessary
   DK

9. Is the duration of therapy acceptable?
   A______  B______  C______  Z
   Comments:
   Acceptable
   Not acceptable
   DK

10. Is this drug the least expensive alternative compared to others of equal utility?
    A______  B______  C______  Z
    Comments:
    Least expensive
    Most expensive
    DK

Comments:
USE OF THE MEDICATION APPROPRIATENESS INDEX (MAI)
For further information/articles using the MAI, address inquiries to Joseph T. Hanlon, PharmD, MS, Department of Medicine (Geriatrics), University of Pittsburgh, Kaufmann Medical Building-Suite 514, 3471 Fifth Ave, Pittsburgh, PA 15213, Email: jth14@pitt.edu

A. General Instructions
This instrument is intended to assess the appropriateness of medications prescribed by a health care provider and to evaluate patients’ self-medication practices. To appropriately apply the MAI, both a list of medical problems and of medications is required. Medication history information obtained from patients may also be helpful. Before evaluating any medications, review the case information and medication profile for each patient. Clinical judgment must always be applied with regard to patient preference and life expectancy. Complete the scale for each regularly scheduled, active medication and any “as needed” medications used frequently. Each question in the scale pertains to the individual patient and drug in question. Read each question carefully and circle the score (A, B, C or Z). If you do not understand the question, consult the specific instructions below for clarification. If you do not know the answer to the question, consult a standard medication text or software such as the AHFS Drug Information, Drug Facts and Comparisons, Micromedex®, Clinical Pharmacology (an electronic drug reference), or UpToDate®, unless the specific instructions for the question indicate an alternative source. At times, you may require additional information from the patient's chart to answer a question. In that case, circle Z and specify the necessary information in the comments section. Some regimens contain combination drugs. If the individual components are available and can be used as single entities, then complete the scale for each individual drug. Finally, please note your reasons for any rating of end of life B or C in the comments section.

B. Scoring
For items coded as inappropriate (C), apply the following weights for individual criterion to calculate a summated MAI score per drug:

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Relative Weight Applied to Inappropriate Ratings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is there an indication for the drug?</td>
<td>3</td>
</tr>
<tr>
<td>Is the medication effective for the condition?</td>
<td>3</td>
</tr>
<tr>
<td>Is the dosage correct?</td>
<td>2</td>
</tr>
<tr>
<td>Are the directions correct?</td>
<td>2</td>
</tr>
<tr>
<td>Are there clinically significant drug-drug interactions?</td>
<td>2</td>
</tr>
<tr>
<td>Are there clinically significant drug-disease interactions?</td>
<td>2</td>
</tr>
<tr>
<td>Are the directions practical?</td>
<td>1</td>
</tr>
<tr>
<td>Is this drug the least expensive alternative compared to others of equal utility?</td>
<td>1</td>
</tr>
<tr>
<td>Is there unnecessary duplication with other drugs?</td>
<td>1</td>
</tr>
<tr>
<td>Is the duration of therapy acceptable?</td>
<td>1</td>
</tr>
</tbody>
</table>

To calculate a weighted MAI score *per patient*, add MAI scores for *each drug* in the patient’s regimen.\(^3\)

**C. Other measures that may be used to assess suboptimal prescribing**

To implicitly assess *unnecessary use* of medications (i.e., polypharmacy), one may combine MAI ratings for questions 1, 2, and 8.\(^4\) To assess the *underuse* of medications, consider using the implicit Assessment of Underutilization (AOU) of Medication tool.\(^5\) For other measures, please refer to the review articles by Dimitrow,\(^6\) Matanovic,\(^7\) O’Mahony,\(^8\) as well as the 2015 American Geriatrics Society (AGS) Beers Criteria.\(^9\)

**D. Specific Instructions For Rating**

**Question 1:** Is there an indication for the drug?

<table>
<thead>
<tr>
<th>A</th>
<th>B</th>
<th>C</th>
<th>Z</th>
</tr>
</thead>
<tbody>
<tr>
<td>indicated</td>
<td>marginally indicated</td>
<td>not indicated</td>
<td>do not know</td>
</tr>
</tbody>
</table>

*Definition:* Indication is defined as the sign, symptom, disease, or condition for which the medication is prescribed. The question assesses whether there is sufficient reason to use the drug. Sufficient reason includes not only curative and palliative therapy, but also preventive therapy for a disease, condition or drug effect.

*Instructions:* A drug is not indicated if no condition exists for its use. Answer the question with the conditions found in the problem list or an alternative standard listing (e.g., health conditions checked as “yes” on the Minimum Data Set). If score = C, then questions 9 and 10 are scored C.

*Examples:* Hydrochlorothiazide (HCTZ) is prescribed and hypertension is recorded on the problem list = A. Olanzapine is prescribed but psychosis, schizophrenia, etc. is not documented = C. Potassium chloride (KCl) for prevention of hypokalemia in the setting of digoxin and diuretic use = A. Isoniazid (INH) and positive PPD plus immunosuppressive condition = A. KCl and diuretics alone without hypokalemia = B.


**Question 2:** Is the medication effective for the condition?

A________________________B________________________C____ Z
effective marginaly effective ineffective do not know

*Definition:* Effective is defined as producing a beneficial result. The question assesses whether the drug prescribed is capable of being effective for the indication in a *population* of patients.

*Instructions:* Indication and effectiveness are tightly but not perfectly linked items. Physicians may prescribe a drug for a given condition because of theoretical and standard practice reasons (indication) but investigators may demonstrate in clinical trials that the drug is ineffective (e.g., ergot mesylate [Hydergine®] and memory enhancement). Conversely, an indication may not be documented for a drug, yet the drug may work well for the intended effect (e.g., KCl to prevent hypokalemia when using diuretics). In those cases, the reviewer must note the assumed indication in the comments. Also, drugs in which the potential risks outweigh the potential benefits, and thus are incapable of being effective in actual practice, should be rated as ineffective (C). For example, those classified by as high risk drugs by AGS 2015 Beers Criteria should be rated as ineffective (C) (Appendix I). The exception would be the use of drugs from this list that are essential medications in palliative care.10

*Examples:* HCTZ for hypertension = A. Histamine type 2 receptor antagonist (H2RA) prophylaxis in a person with a history of nonsteroidal anti-inflammatory drug (NSAID) induced gastric ulcer = C. Meperidine (Demerol®) for pain = C.

**Question 3:** Is the dosage correct?

A________________________B________________________C____ Z
correct marginaly correct incorrect do not know

*Definition:* Dosage is defined as the total amount of medication taken per 24-hour period for regularly scheduled medications.

*Instructions:* Amounts within the dosage range for initial and maintenance therapy noted in the specified texts are correct. Other sources may specify newer, more appropriate therapeutic class specific ranges (e.g., American College of Chest Physicians [ACCP] consensus conference on antithrombotic therapy) or specific geriatric dosage ranges (e.g., American Pharmacists Association [APhA] Geriatric Drug Dosage Handbook). These ranges should supersede the standard texts as long as the reference is given. Hence, one should also take into account known age-related changes in drug pharmacokinetics and pharmacodynamics. Some patients may have drug labs/levels/vital signs to help assess whether the dosage is appropriate. If dosage is too low then circle C-. If the dosage is too high then circle C+. In summary, a dosage is incorrect if it is outside the accepted geriatrics dose range. If there is no accepted geriatrics dose range, then to be incorrect it must be outside the standard adult range. A dosage may also be incorrect if not adjusted for drug levels and laboratory or vital signs outcomes (Appendix II). For dosing of select medications that are primarily renally cleared, see Appendix III. For drugs being tapered to discontinuation (e.g., anticonvulsants), low dosage and/or low levels will be considered correct.

Examples: Glyburide in patient with estimated creatinine clearance of 42ml/min = C (reason: decreased renal clearance of drug in the elderly). Captopril 6.25-37.5 mg bid for heart failure (HF) = A. Furosemide 20-40 mg a day for hypertension (HTN) = B. Ranitidine 150 mg bid for peptic ulcer disease (PUD) > 8 weeks = C+ (reason: maintenance therapy dose is 150 at bedtime). Atorvastatin at highest end of usual dosage range but cholesterol remains elevated = B (reason: drug is necessary but additional therapy is warranted). Patient with chronic cancer pain taking 4 g acetaminophen in divided doses, but who still rates pain as moderate to severe = B (reason: drug is necessary but additional therapy is warranted). Warfarin 1 mg daily for mechanical valve with INR of 1.2= C- (reason: INR not at target goal for this anticoagulation indication). Alternating warfarin 5mg and 7.5 mg every other day for atrial fibrillation with INR of 2.8 = A (reason: although lab value is above standard normal range, it is within the therapeutic range of 2.0-3.0 for this anticoagulation indication; therefore, the dosage is correct).

Question 4: Are the directions correct?

A________________________B________________________C____             Z

correct  marginally correct  incorrect  do not know

Definition: Directions are defined as the instructions in the use of a medication by a patient. The question assesses the route of administration, relationship to food and liquid, the schedule and time of the day.

Instructions: The directions are incorrect when they specify the wrong route of administration, give wrong or no instructions regarding food and liquid (when specific directions regarding relationship to food or liquid exist), or specify the wrong schedule or the wrong time of day (when specific directions regarding relationship to schedule and time of day exist). See Appendix IV for medications with food and fluid requirements, schedule/time of day requirements, and those medications that should not be taken with grapefruit juice.11 For new drugs, consult the latest edition of the Drugs, Supplements, and Herbal Information.12 For information regarding meds that should not be crushed and given via enteral tube, refer to the Institute of Safe Medication Practices.13 When the MAI is used to evaluate patients in institutional care settings, route, food liquid, schedule and time of day requirements do not apply. If the patient transitions from institutional to ambulatory care settings, application may be limited to only medications requiring a specific schedule/time of day for consistency purposes.

Examples: Captopril 25 mg TID = C (reason: should be taken on an empty stomach). Glipizide 10 mg daily = C (reason: should specify “before breakfast”). Ibuprofen 400mg TID with meals and at bedtime with snack = A. Furosemide 20 mg daily = C (reason: should specify “in the morning”). K-Dur® without directions regarding food/liquid = C. Nitropaste® 1” four times daily = C (reason: must specify nitrate-free interval). Nifedipine XL 60 mg daily with 8oz of grapefruit at breakfast = C (reason: should not take with grapefruit juice).

13www.ismp.org/tools/donotcrush.pdf
Question 5: Are the directions practical?

A_______________________B________________________C_____                      Z
practical               marginally practical    impractical    do not know

**Definition:** Practical is defined as capable of being used or put into practice. This question assesses whether the directions for use are practical, so the patient appropriately take or a caregiver may appropriately administer the medication. This reflects the potential for patient adherence without sacrificing efficacy. Additionally, consideration of whether the drug is available on formulary is important when applicable.

**Instructions:** A drug schedule is considered impractical if the drug can be administered less frequently and still maintain efficacy. Irregular day-to-day schedules that have more regular alternatives are also impractical. In addition, medications specified to be given around the clock on a fixed interval when a more flexible schedule is sufficient is impractical.

**Examples:** Warfarin 5 mg daily except Tuesday and Sunday 10 mg daily = C (reason: 6 mg daily is easier). Glipizide 5 mg bid = C (reason: 10 mg every morning is equally effective). Trazodone 75mg at bedtime = A (reason: dosed once daily and can cue into bedtime routine). Nifedipine 10mg TID = C (reason: equally effective alternative, Nifedipine XL 30mg daily, is simpler to administer). Albuterol metered dose inhaler (MDI) 2 puffs q6h = C (reason: four times daily is sufficient).

Question 6: Are there clinically significant drug-drug interactions?

A_______________________B________________________C_____                      Z
insignificant        marginally insignificant    significant    do not know

**Definition:** A drug-drug interaction is defined as the effect the administration of one medication has on another drug. Clinical significance connotes a harmful interaction. This question assesses whether the drug in question interacts with another drug in the patient's regimen by affecting its pharmacokinetics (i.e., absorption, distribution, metabolism and excretion) or pharmacodynamics (i.e., the effect that it has on the body).

**Instructions:** A drug interaction text (e.g., Hansten's Drug Interactions and Updates), software program (e.g. Micromedex®, UpToDate®), review articles like Malone (2004)14 or Hines (2011),15 the 2015 AGS Beers Criteria (Appendix V) may be used as the reference for significant interactions. If no interaction exists, then an insignificant (A) rating is automatic. A marginally significant (B) rating should be given when the reference/program indicates an interaction exists but there is no clinical evidence for toxicity or adverse effects. If the reference/program indicates an interaction exists and sufficient clinical evidence of toxicity or adverse effects (including lack of effect) is available, then the interaction is significant (C). If the reference/program indicates an interaction exists and clinical information is not available, then the interaction may also be considered significant (C). Of note, the drug that causes the

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change in pharmacokinetics or pharmacodynamics is the medication that merits the significant (C) rating.  

Examples: Cimetidine added to warfarin in a patient with a prolonged PT or signs of bleeding = C (reason: significant pharmacokinetic interaction). A tricyclic antidepressant (TCA) or an opioid added to a benzodiazepine = C (reason: two central nervous system (CNS) drugs can result in a patient having increased falls or confusion [significant pharmacodynamics interaction]). In the absence of sufficient clinical information, if a patient taking digoxin and is started on verapamil without a concomitant reduction in digoxin dose = C for verapamil. NSAID (e.g., naproxen) for osteoarthritis started on a patient taking warfarin chronically for atrial fibrillation = C for NSAID (reason: increases bleed risk).

Question 7: Are there clinically significant drug-disease/condition interactions?

A ______________________ B ______________________ C __________ Z __________

insignificant marginally insignificant significant do not know

Definition: Drug-disease interaction is defined as the effect that the drug has on a pre-existing disease or condition. Clinical significance connotes a harmful interaction. This question assesses whether the drug in question may worsen the patient's disease or condition. A previous history of an idiosyncratic allergic reaction to a drug (e.g., penicillin, sulfa drugs, etc.) is considered a pre-existing condition.

Instructions: Information about drug-disease interactions is listed in the precautions or contraindications sections of the above specified texts/software. If no interaction exists according to the references, then an insignificant (A) rating is automatic. If the drug is contraindicated or highly risky (e.g., "extreme caution" is recommended) for a condition, then the drug-disease is significant (C). Appendix VI lists drug-disease interactions to avoid based on a consensus survey of an expert panel of health care professionals. If a drug-disease combination is listed then the drug receives a score of “C;” otherwise, the drug receives an “A.” If the drug requires routine caution ("warning, precaution") in the setting of a particular condition, and the patient shows clinical evidence of the disease worsening following the drug is prescribed, then the drug-disease interaction is also significant (C). If the reference indicates an interaction ("warning, precaution") exists but the patient shows no evidence of worsening disease, then the rating is marginal (B).

Examples: Non-aspirin, non-cyclooxygenase-2 (COX-2) NSAIDs in a patient with recent history of PUD and no proton pump inhibitor (PPI) = C. Highly-anticholinergic TCAs (i.e., doxepin, amitriptyline, imipramine) initiated in a patient with lower urinary tract symptoms = C. Dicloxacillin prescribed in a patient with previous history of penicillin rash = C (reason: clinically significant cross-reaction between dicloxacillin and penicillin). Codeine prescribed in a patient with a history of gastrointestinal distress = B. Lamotrigine prescribed for new-onset epilepsy in a patient with a history of falls/fractures = B (reason: although listed in Appendix VI, treatment is necessary).
**Question 8:** Is there unnecessary duplication with other drug(s)?

A __________________________ B __________________________ C ______ Z
necessary marginally necessary unnecessary do not know

**Definition:** Unnecessary duplication is defined as nonbeneficial or risky overlap of drug(s). Unnecessary duplication exists when two drugs from the same chemical or pharmacological class are prescribed simultaneously.

**Instructions:** The Veterans Affairs (VA) Medication Classification System is available at the VA Pharmacy Benefits Manager website (see Appendix VII for exceptions). The evaluator should look up the generic names of all regularly-scheduled medications in the index to determine the drug class, then refer to Appendix VII to see if modifications must be considered. In general, unnecessary duplication occurs when 2 drugs from the same subclass of the major therapeutic classifications are simultaneously prescribed. In some instances, all subclasses (e.g., sedative/hypnotics) should be considered one class. In other cases, subclasses are broken down into discrete categories (e.g., antihypertensives). If at least 2 drugs from the same class are prescribed simultaneously and the order of prescribing is known, then the last drug added is rated “C” and the other drug is rated “B.” If the order of prescribing is not known, then a “B” and “C” rating should be randomly assigned.

**Examples:** Ranitidine added to a regimen that already includes cimetidine = C for ranitidine (reason: same pharmacologic class). Flurazepam 15 mg at bedtime and diazepam 5 mg TID = C for one drug, B for the other (randomly assigned). Cimetidine and sucralfate prescribed simultaneously for peptic ulcer disease = C for one drug, B for the other (randomly assigned).

**Question 9:** Is the duration of therapy acceptable?

A __________________________ B __________________________ C ______ Z
acceptable marginally acceptable unacceptable do not know

**Definition:** Duration is defined as the length of therapy. This question assesses whether the length of time that the patient has received the drug is acceptable.

**Instructions:** If the duration of therapy is outside the information source specified range, then the length is unacceptable (C). If it is within the range, or no data exists to make a clear decision, then the length is marginally (B) or fully acceptable (A). Other sources, including the medical record, may specify newer, more acceptable durations of therapy, especially in geriatric conditions. Those sources supersede the specified texts if the reference is available. Generally for a chronic condition, a prolonged duration of therapy will be acceptable. A medication prescribed to a patient with life expectancy less than the time to therapeutic benefit for the medication should be rated as unacceptable (C). (See Appendix VIII for Specific Drugs)

**Examples:** Haloperidol in a patient with longstanding dementia but no psychotic features = C. Digoxin in a patient with remote history of HF but in normal sinus rhythm = B. INH prophylaxis

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for 12 months in recent skin test converter = A. Ampicillin for 10 to 14 days for urinary tract infection (UTI) = A. Nitrofurantoin for 12 months in a patient with indwelling urinary catheter = C. Statin newly prescribed for LDL > 130mg/dl in patient with severe dementia who has 12-month life expectancy = C (reason: statin time to thereapeutic benefit is 1.5 to 3 years.).

**Question 10:** Is this drug the least expensive alternative compared to others of equal utility?

A________________________B____________________C_______ Z
less expensive equally expensive more expensive do not know

**Definition:** This question assesses how the cost of the drug compares to other agents of equal efficacy and safety.

**Instructions:** A drug is more expensive if it costs at least 10% more than the average cost/charge of alternatives of equal utility. Alternatives should be considered as medications within the same therapeutic class (see Question 8 for definition). To operationalize, the evaluator can use the local institutional setting prices (e.g., cost per month, per day supply, or per dose) as the standard. If site-specific cost data is not available for assessment, evaluators are encouraged to utilize the Average Wholesale Price (AWP) or the cost index in Drug Facts and Comparisons as their standard. If drug is not indicated (Question 1), then expense is automatically rated “C.”

**Examples:** Ciprofloxacin for an E. coli UTI sensitive to ampicillin = C (reason: ciprofloxacin is more expensive than ampicillin). Lactulose for constipation before trying psyllium = C (reason: lactulose is more expensive than psyllium). Morphine SR in a hospice patient = A (reason: although may be more expensive than IR form, it is more convenient and may be preferred by patient and therefore demonstrates greater utility).

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### Appendix I. 2015 AGS Beers Do Not Use Criteria

<table>
<thead>
<tr>
<th>Organ system &amp; Therapeutic Class</th>
<th>Medication</th>
</tr>
</thead>
</table>
| Central Nervous System & Psychotropic Drugs | Anticholinergics (e.g., 1st generation antihistamines, benztropine, trihexyphenidyl to treat side effects of neuroleptics)  
Antipsychotics (1st or 2nd generation) as first-line therapy for behavior problems associated with dementia  
Benzodiazepine receptor agonists (i.e., benzodiazepines, eszopiclone, zaleplon, zolpidem)  
Barbiturates |
| Cardiovascular | Antithrombotics (i.e., dipyridamole ir only)  
Antiarrhythmics (i.e., digoxin or amiodarone as 1st line therapy for atrial fibrillation, disopyramide, dronaderone)  
Peripheral α₁ blockers for treatment of hypertension  
Digoxin as first-line therapy for heart failure  
Nifedipine immediate release for hypertension |
| Endocrine | Antidiabetic agents (i.e., sliding scale insulin only, long-acting Sulfonylureas [chlorpropamide, glyburide, glimeperide]  
Desiccated thyroid  
Hormones (i.e., androgens, estrogens, growth hormone, megestrol) |
| Musculoskeletal | Meperidine  
Nonsteroidal anti-inflammatory drugs (e.g., noncycloxygenase-selective, indomethacin, ketorolac)  
Skeletal muscle relaxants |
| Gastrointestinal & Genitourinary | Metoclopramide unless for gastroparesis  
Mineral oil (oral)  
Proton pump inhibitors for > 8 weeks unless high-risk  
Desmopressin for nocturia  
Nitrofurantoin in those with creatinine clearance < 30 mL/min or for long-term suppression of bacteriuria |


### Appendix II. Drug Dosage Rules

**Outside of dosage range**

- High dose + high lab³/level⁴/VS = C
- High dose + normal lab/level/VS = B
- High dose + low lab/level/VS = C

- Low dose + high lab³/level⁴/VS = C
- Low dose + normal lab/level/VS = B
- Low dose + low lab/level/VS = C

Within dosage range

Normal dose + high lab\(^a\)/level\(^b\)/VS = C
Normal dose + normal lab/VS = A
Normal dose + low lab/VS = C

\(^a\)Except warfarin or heparin unless PT-INR > 3.5 or 2.5 times control PT, respectively. \(^b\)Unless clinical evidence that patient needs higher levels to control a condition (i.e., digoxin and atrial fibrillation). \(^c\)Unless medication being tapered to be discontinued. VS = vital signs; high VS: systolic blood pressure (BP) > 160 and/or diastolic BP > 90 or pulse > 100. In institutional settings where patients may be clinically unstable, may consider high BP as systolic BP > 180 and/or diastolic BP > 110. Low VS: systolic BP < 90 or pulse < 40.

Appendix III. Recommendations for Renally Cleared Medications in Older Patients with Chronic Kidney Disease\(^1\)-\(^5\)

<table>
<thead>
<tr>
<th>Medication/Class</th>
<th>eCrCl (mL/min)</th>
<th>Maximum Dosing Recommendation (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>using Cockcroft-Gault equation</td>
<td></td>
</tr>
<tr>
<td>Acyclovir (for Zoster)</td>
<td>10-29</td>
<td>800 every 8 hours</td>
</tr>
<tr>
<td></td>
<td>&lt;10</td>
<td>800 every 12 hours</td>
</tr>
<tr>
<td>Amantadine</td>
<td>30-59</td>
<td>100 daily</td>
</tr>
<tr>
<td></td>
<td>15-29</td>
<td>100 every 48 hours</td>
</tr>
<tr>
<td></td>
<td>&lt;15</td>
<td>100 every 7 days</td>
</tr>
<tr>
<td>Amiloride</td>
<td>&lt;30</td>
<td>Avoid use</td>
</tr>
<tr>
<td>Aminoglycosides</td>
<td>&lt;60</td>
<td>Dose based on drug levels</td>
</tr>
<tr>
<td>(amikacin, gentamicin, tobramycin)</td>
<td></td>
<td>unless 1/kg dose for &lt; 5 days</td>
</tr>
<tr>
<td>Apixaban</td>
<td>&lt;25</td>
<td>Avoid use</td>
</tr>
<tr>
<td>Chlorpropamide</td>
<td>&lt;50</td>
<td>Avoid use</td>
</tr>
<tr>
<td>Cimetidine</td>
<td>&lt;50</td>
<td>400 every 12 hours</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>&lt;30</td>
<td>500 every 24 hours</td>
</tr>
<tr>
<td>Colchicine</td>
<td>&lt;30</td>
<td>0.3 daily</td>
</tr>
<tr>
<td>Colchicine</td>
<td>&lt;10</td>
<td>Avoid use</td>
</tr>
<tr>
<td>Cotrimoxazole</td>
<td>15-29</td>
<td>1 DS tablet daily</td>
</tr>
<tr>
<td></td>
<td>&lt;15</td>
<td>Avoid use</td>
</tr>
<tr>
<td>Dabigatran</td>
<td>&lt;30</td>
<td>Avoid use</td>
</tr>
<tr>
<td>Digoxin</td>
<td>&lt;60</td>
<td>Dose based on drug levels or ≤ 0.125 mg daily for heart failure</td>
</tr>
<tr>
<td>Dofetilide</td>
<td>&lt;20</td>
<td>Avoid use</td>
</tr>
<tr>
<td>Duloxetine</td>
<td>&lt;30</td>
<td>Avoid use</td>
</tr>
<tr>
<td>Edoxaban</td>
<td>15-50</td>
<td>30 daily</td>
</tr>
<tr>
<td></td>
<td>&lt;15(^a)</td>
<td>Avoid use</td>
</tr>
<tr>
<td>Enoxaparin (for prophylaxis)</td>
<td>&lt;30</td>
<td>30 daily</td>
</tr>
<tr>
<td>(for other indications)</td>
<td>&lt;30</td>
<td>1/kg daily</td>
</tr>
<tr>
<td>Ethambutol (for treatment)</td>
<td>&lt;10</td>
<td>15-25/kg every 48 hours</td>
</tr>
<tr>
<td>Fampiclovir (for Zoster)</td>
<td>40-59</td>
<td>500 twice daily</td>
</tr>
<tr>
<td></td>
<td>20-39</td>
<td>500 daily</td>
</tr>
<tr>
<td></td>
<td>&lt;20</td>
<td>250 daily</td>
</tr>
<tr>
<td>Medication/Class</td>
<td>eCrCl (mL/min)</td>
<td>Maximum Dosing Recommendation (mg)</td>
</tr>
<tr>
<td>------------------</td>
<td>---------------</td>
<td>----------------------------------</td>
</tr>
<tr>
<td><strong>Famotidine</strong></td>
<td>&lt;50</td>
<td>20 daily</td>
</tr>
<tr>
<td><strong>Fluconazole (for esophageal infection)</strong></td>
<td>&lt;50</td>
<td>200 daily</td>
</tr>
<tr>
<td><strong>Fondaparinux</strong></td>
<td>&lt;30</td>
<td>Avoid use</td>
</tr>
<tr>
<td><strong>Gabapentin (for pain)</strong></td>
<td>30-59</td>
<td>600 twice daily</td>
</tr>
<tr>
<td></td>
<td>15-29</td>
<td>300 twice daily</td>
</tr>
<tr>
<td></td>
<td>&lt;15</td>
<td>300 daily</td>
</tr>
<tr>
<td><strong>Glyburide</strong></td>
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<td>Avoid use</td>
</tr>
<tr>
<td><strong>Lithium</strong></td>
<td>&lt;60</td>
<td>Dose based on drug levels</td>
</tr>
<tr>
<td><strong>Levetiracetam</strong></td>
<td>50-80</td>
<td>500-1000 every 12 hours</td>
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<tr>
<td></td>
<td>30-49</td>
<td>250-750 every 12 hours</td>
</tr>
<tr>
<td></td>
<td>&lt;30</td>
<td>250-500 every 12 hours</td>
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<tr>
<td><strong>Levofloxacin (for UTI)</strong></td>
<td>&lt;20</td>
<td>250 every 48 hours</td>
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<td><strong>Memantine</strong></td>
<td>&lt;30</td>
<td>5 twice daily</td>
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<td><strong>Metformin</strong></td>
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<tr>
<td><strong>Meperidine</strong></td>
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<td>Avoid use</td>
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<tr>
<td><strong>Nizatadine</strong></td>
<td>20-50</td>
<td>150 every other day</td>
</tr>
<tr>
<td></td>
<td>&lt;20</td>
<td>150 every 3 days</td>
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<tr>
<td><strong>NSAIDs</strong></td>
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<tr>
<td><strong>Oseltamivir (for treatment)</strong></td>
<td>10-30</td>
<td>75 daily</td>
</tr>
<tr>
<td><strong>(for prevention)</strong></td>
<td>10-30</td>
<td>75 every other day</td>
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<td><strong>Pregabalin</strong></td>
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<td></td>
<td>15-29</td>
<td>150</td>
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<td></td>
<td>&lt;15</td>
<td>75</td>
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<td><strong>Probenecid</strong></td>
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<td><strong>Procainamide</strong></td>
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<td><strong>Rimantadine</strong></td>
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<td><strong>Rivaroxaban</strong></td>
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<td>&lt;15</td>
<td>Avoid use</td>
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<tr>
<td><strong>Spironolactone</strong></td>
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<tr>
<td><strong>Tramadol immediate release</strong></td>
<td>&lt;30</td>
<td>50-100 every 12 hours</td>
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<td><strong>Tramadol extended release</strong></td>
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<td><strong>Triamterene</strong></td>
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<td>1000 every 12 hours</td>
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<td></td>
<td>&lt;10</td>
<td>500 every 24 hours</td>
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<td><strong>Vancomycin</strong></td>
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<td>Dose based on drug level</td>
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**Abbreviations:** eCrCl = estimated creatinine clearance; UTI = urinary tract infection; NSAID = nonsteroidal anti-inflammatory drug. *Use is not recommended for anticoagulation for non-valvular atrial fibrillation if eCrCl > 95 mL/min.
References:

Appendix IV. Medications with specific food, liquid, schedule, and time of day requirements†

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<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
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<td>Captopril</td>
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<td>Demeclocycline</td>
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<td>Didronel®</td>
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<td>Crixivan®</td>
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<td>Isosorbide dinitrate</td>
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<td>Lapatinib</td>
<td>Tykerb</td>
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<td>Cytomel®</td>
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<td>Quinolones</td>
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<td>Sonata®</td>
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<td>Zolpidem</td>
<td>Ambien®</td>
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**Medications That Should Be Taken With Water/Fluid**

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<tr>
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<td>Chloral Hydrate</td>
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<td>Deferasirox</td>
<td>Exjade®</td>
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<td>Everolimus</td>
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<td>Ibandronate</td>
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<td>Metamucil®</td>
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<td>Actonel®</td>
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<td>Sildosin</td>
<td>Rapaflo®</td>
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<td>Sodium Citrate &amp; Citric Acid</td>
<td>Oracit®, Shohl’s Solution</td>
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<td>Nexavar®</td>
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<td>Tapentadol</td>
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# Medications That Should Be Taken With Food

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<td>Artemether/Lumefantrine</td>
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<td>Reyataz®</td>
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<td>Atovaquone</td>
<td>Mepron®</td>
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<tr>
<td>Bromocriptine</td>
<td>Parlodel®, Cycloset®</td>
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<tr>
<td>Butalbital/codeine</td>
<td>Fiorinal® with codeine</td>
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<td>Calcium Acetate</td>
<td>PhosLo®</td>
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<td>Calcium Supplements</td>
<td>Os-Cal®</td>
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<td>Carbamazepine</td>
<td>Tegretol®</td>
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<td>Cefditoren</td>
<td>Spectracef®</td>
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<td>Cefpodoxime (suspension)</td>
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<td>Cefuroxime (doses &gt; 400 mg/day)</td>
<td>Celebrex®</td>
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<td>Clarithromycin XL</td>
<td>Biaxin® XL</td>
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<td>Fenofibrate</td>
<td>TriCor®</td>
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<td>Fluvastatin</td>
<td>Lescol®</td>
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<td>Galantamine ER</td>
<td>Razadyne® ER</td>
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<td>Griseofulvin</td>
<td>Grifulvin V®, Gris-PEG®</td>
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<td>Itraconazole</td>
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<td>Lanthanum carbonate</td>
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<td>Levodopa/Carbidopa</td>
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<td>Lithium CR</td>
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<td>Nitrofurantoin</td>
<td>Macrobid®, Macroductin®</td>
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<td>Nonsteroidal Anti-Inflammatory Drugs</td>
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<td>Olsalazine</td>
<td>Dipentum®</td>
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<td>Oxaprozin</td>
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<td>Sapropterin</td>
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**Medications That Should Not Be Taken With Grapefruit Juice**

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<td>*Apixaban</td>
<td>Eliquis®</td>
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<td>*Atorvastatin</td>
<td>Lipitor®</td>
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<td>*Buspirone</td>
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<td>Carbamazepine</td>
<td>Carbatrol®, Tegretol®</td>
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<td>*Cilostazol</td>
<td>Pletal®</td>
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<td>*Clopidogrel</td>
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<td>*Cyclosporine</td>
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<td>*Dextromethorphan</td>
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<td>*Pazopanib</td>
<td>Votrient®</td>
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<td>*Primaquine</td>
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Medications That Should Be Taken On A Specific Schedule

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<tr>
<td>Alfuzosin (Uroxatral®)</td>
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</tr>
<tr>
<td>Artemether/Lumefantrine (Coartem®)</td>
<td>4 tablets at hr 0 and hr 8 on day 1, then 4 tablets twice daily on day 2 and day 3</td>
</tr>
<tr>
<td>Atazanavir (Reyataz®)</td>
<td>2 hr before or 1 hr after Videx chewable tablets</td>
</tr>
<tr>
<td>Acarbose (Precose®)</td>
<td>With the first bite of food at each main meal</td>
</tr>
<tr>
<td>Capecitabine (Xeloda®)</td>
<td>Within 30 minutes after a meal</td>
</tr>
<tr>
<td>Cefpodoxime (Vantin®)</td>
<td>Every 12 hrs</td>
</tr>
<tr>
<td>Cilostazol</td>
<td>½ hr before or 2 hr after breakfast and dinner</td>
</tr>
<tr>
<td>Disopyramide</td>
<td>Every 6 hrs</td>
</tr>
<tr>
<td>Disopyramide SR</td>
<td>Every 8-12 hrs</td>
</tr>
<tr>
<td>Entecavir (Baraclude®)</td>
<td>At least 2 hrs before or 2 hrs after a meal</td>
</tr>
<tr>
<td>Esomeprazole (Nexium®)</td>
<td>At least 1 hr before meals</td>
</tr>
<tr>
<td>Etravirine (Intelence®)</td>
<td>After meals</td>
</tr>
<tr>
<td>Exenatide (Byetta®)</td>
<td>Within 60 min of morning and evening meals</td>
</tr>
<tr>
<td>Famiclovir (Famvir®)</td>
<td>Every 8 hrs</td>
</tr>
<tr>
<td>Gabapentin (Neurontin®)</td>
<td>Three times daily (doses should not be &gt; 12 hrs apart)</td>
</tr>
<tr>
<td>Gemfibrozil (Lopid®)</td>
<td>½ hr before meals</td>
</tr>
<tr>
<td>Heparin (subcutaneous)</td>
<td>Every 8-12 hrs</td>
</tr>
<tr>
<td>Indecainide</td>
<td>Every 12 hrs</td>
</tr>
</tbody>
</table>

17
<table>
<thead>
<tr>
<th>Medication Name</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin</td>
<td>½ hr before meals and at bedtime</td>
</tr>
<tr>
<td>Isosorbide mononitrate</td>
<td>Twice daily (7 hrs apart)</td>
</tr>
<tr>
<td>Lansoprazole (Prevacid®)</td>
<td>Before meals</td>
</tr>
<tr>
<td>Levofoxacin (Levaquin®)</td>
<td>1 hr before or 2 hrs after eating</td>
</tr>
<tr>
<td>Methscopolamine (Pamine®)</td>
<td>½ hr before meals and at bedtime</td>
</tr>
<tr>
<td>Methylphenidate (Ritalin®)</td>
<td>30-45 min before meals</td>
</tr>
<tr>
<td>Metoclopramide (Reglan®)</td>
<td>30 minutes after meals and at bedtime</td>
</tr>
<tr>
<td>Metronidazole ER (Flagyl®)</td>
<td>1 hr before or 2 hrs after meals</td>
</tr>
<tr>
<td>Migliol (Glyset®)</td>
<td>With the first bite of food at each main meal</td>
</tr>
<tr>
<td>Moricizine</td>
<td>Every 8 hrs (occasionally every 12 hrs)</td>
</tr>
<tr>
<td>Nateglinide (Starlix®)</td>
<td>1-30 min before meals</td>
</tr>
<tr>
<td>Nitrates (Isordil®, NTP)</td>
<td>Specify nitrate free-interval</td>
</tr>
<tr>
<td>Nitroglycerin Patch</td>
<td>Specify nitrate free-interval</td>
</tr>
<tr>
<td>Norfloxacin (Noroxin®)</td>
<td>1 hr before or ≥ 2 hrs after a meal and dairy products</td>
</tr>
<tr>
<td>Omeprazole (Prilosec®)</td>
<td>½ hr before meals</td>
</tr>
<tr>
<td>Pramlintide (Symlin®)</td>
<td>Immediately prior to major meals (&gt;250 kcal or &gt; 30g carbs)</td>
</tr>
<tr>
<td>Procainamide</td>
<td>Every 4-6 hrs</td>
</tr>
<tr>
<td>Procainamide SR</td>
<td>Every 6-8 hrs</td>
</tr>
<tr>
<td>Promethazine</td>
<td>Before meals and/or prior to bedtime</td>
</tr>
<tr>
<td>Propafenone</td>
<td>Every 8 hrs</td>
</tr>
<tr>
<td>Propranolol (Inderal®)</td>
<td>Before meals and at bedtime</td>
</tr>
<tr>
<td>Quinidine gluconate</td>
<td>Every 8-12 hrs</td>
</tr>
<tr>
<td>Quinidine sulfate</td>
<td>Every 6 hrs</td>
</tr>
<tr>
<td>Quinidine sulfate SR</td>
<td>Every 8-12 hrs</td>
</tr>
<tr>
<td>Ramelteon (Rozerem®)</td>
<td>Within 30 min of bedtime (avoid taking with high-fat meals)</td>
</tr>
<tr>
<td>Repaglinide (Prandin®)</td>
<td>15-30 min before the start of a meal</td>
</tr>
<tr>
<td>Salmeterol (Serevent®)</td>
<td>Every 12 hrs</td>
</tr>
<tr>
<td>Saquinavir (Invirase®)</td>
<td>Three times daily within 2 hrs of full meals</td>
</tr>
<tr>
<td>Selegiline</td>
<td>With breakfast and lunch</td>
</tr>
<tr>
<td>Stavudine (Zerit®)</td>
<td>Every 12 hrs</td>
</tr>
<tr>
<td>Sucralfate</td>
<td>After meals and at bedtime</td>
</tr>
<tr>
<td>Tamsulosin (Flomax®)</td>
<td>½ hour before meal</td>
</tr>
<tr>
<td>Tacrolimus (Prograf®)</td>
<td>Every 12 hrs</td>
</tr>
<tr>
<td>Theophylline</td>
<td>Every 6 hrs</td>
</tr>
<tr>
<td>Theophylline SR</td>
<td>Every 8-12 hrs</td>
</tr>
<tr>
<td>Tildudronate (Skelid®)</td>
<td>2 hrs before or 2 hrs after meals</td>
</tr>
<tr>
<td>Voriconazole (Vfen®)</td>
<td>Every 12 hrs and 1 hr before or after meal</td>
</tr>
<tr>
<td>Zilueton CR (Zyflo CR®)</td>
<td>Within 1 hr after morning or evening meals</td>
</tr>
</tbody>
</table>
### Medications That Should Be Taken At A Specific Time Of Day

<table>
<thead>
<tr>
<th>Medication Name/Class</th>
<th>Time of day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antidepressants (except SSRIs, bupropion)</td>
<td>Bedtime</td>
</tr>
<tr>
<td>Chloral Hydrate</td>
<td>Bedtime</td>
</tr>
<tr>
<td>Cimetidine</td>
<td>Bedtime (if twice daily, give 2nd dose in the morning)</td>
</tr>
<tr>
<td>Clomipramine</td>
<td>Bedtime</td>
</tr>
<tr>
<td>Corticosteroids (oral)</td>
<td>Morning (between 6-10 AM)</td>
</tr>
<tr>
<td>Diuretics</td>
<td>Morning (if twice daily, give 2nd dose before 4 pm)</td>
</tr>
<tr>
<td>Donepezil (Aricept®)</td>
<td>Bedtime</td>
</tr>
<tr>
<td>Doxazosin XL (Cardura XL®)</td>
<td>Morning</td>
</tr>
<tr>
<td>Flurazepam</td>
<td>Bedtime</td>
</tr>
<tr>
<td>Fluvastatin IR, lovastatin IR, simvastatin</td>
<td>Evening</td>
</tr>
<tr>
<td>Lisdexamfetamine (Vyvanse®)</td>
<td>Morning</td>
</tr>
<tr>
<td>Mirtazapine (Remeron®)</td>
<td>Bedtime</td>
</tr>
<tr>
<td>Niacin/Lovastatin, ER (Advicor®)</td>
<td>Bedtime</td>
</tr>
<tr>
<td>Oral Hypoglycemics bid</td>
<td>Before breakfast (if twice daily, give 2nd dose before evening meal)</td>
</tr>
<tr>
<td>Paliperidone (Invega®)</td>
<td>Morning</td>
</tr>
<tr>
<td>Phenobarbital (Luminal®)</td>
<td>Bedtime</td>
</tr>
<tr>
<td>Phenytoin (Dilantin®)</td>
<td>Bedtime</td>
</tr>
<tr>
<td>Proton Pump Inhibitors</td>
<td>After meals in the morning</td>
</tr>
<tr>
<td>Quinine</td>
<td>Bedtime</td>
</tr>
<tr>
<td>Ranitidine</td>
<td>Bedtime (if twice daily, give 2nd dose in the morning)</td>
</tr>
<tr>
<td>Ramelteon (Rozerem®)</td>
<td>Within 30 minutes of bedtime</td>
</tr>
<tr>
<td>Rasagiline (Azilect®)</td>
<td>Early in the day</td>
</tr>
<tr>
<td>Simvastatin (Zocor®)</td>
<td>Bedtime</td>
</tr>
<tr>
<td>Terazosin</td>
<td>Bedtime</td>
</tr>
<tr>
<td>Triazolam</td>
<td>Bedtime (on an empty stomach)</td>
</tr>
<tr>
<td>Zaleplon (Sonata®)</td>
<td>Bedtime</td>
</tr>
<tr>
<td>Zolpidem, CR (Ambien®, Ambien CR®)</td>
<td>Bedtime (should not be taken with or immediately after a meal)</td>
</tr>
</tbody>
</table>

*High risk medication. †For drugs marketed in the United States after 2010 or for drugs not available in United States but available in other countries, consult current pharmacotherapy reference.
### Appendix V. Clinically Important Drug-Drug Interactions\(^1-3\)

<table>
<thead>
<tr>
<th>Drug Affected</th>
<th>Precipitant Drug (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACEI/ARB</td>
<td>K supplements, K sparing diuretics (amiloride, triamterene), aliskiren</td>
</tr>
<tr>
<td>α blockers, peripheral</td>
<td>Loop diuretics</td>
</tr>
<tr>
<td>Anticholinergic</td>
<td>Anticholinergic</td>
</tr>
<tr>
<td>Antiplatelet(^a)</td>
<td>NSAIDs (unless patient also prescribed PPI)</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>Erythromycin, clarithromycin, fluoxetine, diltiazem, verapamil, rifampin</td>
</tr>
<tr>
<td>CNS med(^b)</td>
<td>≥2 other CNS meds</td>
</tr>
<tr>
<td>Corticosteroid</td>
<td>NSAIDs</td>
</tr>
<tr>
<td>Cyclosporine</td>
<td>Rifampin</td>
</tr>
<tr>
<td>Dextromethorphan</td>
<td>MAOI</td>
</tr>
<tr>
<td>Disopyramide</td>
<td>Cimetidine</td>
</tr>
<tr>
<td>Digoxin</td>
<td>Amiodarone, clarithromycin, propafenone, quinidine, verapamil</td>
</tr>
<tr>
<td>Ergots for migraine</td>
<td>Macrolide antibiotics (clarithromycin, erythromycin)</td>
</tr>
<tr>
<td>Estrogen/progestin OC</td>
<td>Rifampin</td>
</tr>
<tr>
<td>Ganciclovir</td>
<td>Zidovudine</td>
</tr>
<tr>
<td>Lithium</td>
<td>ACEI, loop diuretics</td>
</tr>
<tr>
<td>MAOI</td>
<td>Buspirone, Opioids (fentanyl, meperidine, tramadol, tapentadol), SSRIs, SNRIs, sympathomimetics</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>Trimethoprim</td>
</tr>
<tr>
<td>Opioid</td>
<td>BZD RA, Gabapentinoid</td>
</tr>
<tr>
<td>Pimozide</td>
<td>Macrolides (clarithromycin, erythromycin), azoles (fluconazole, itraconazole, ketoconazole)</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>Amiodarone, imidazoles, TMP/SMX</td>
</tr>
<tr>
<td>Procainamide</td>
<td>Amiodarone, cimetidine, ranitidine, TMP/SMX</td>
</tr>
<tr>
<td>Quinidine</td>
<td>Cimetidine</td>
</tr>
<tr>
<td>SSRI</td>
<td>St John’s wort, tramadol</td>
</tr>
<tr>
<td>Statins</td>
<td>Cyclosporine, gemfibrozil</td>
</tr>
<tr>
<td>Statins (CYP3A4-, Ator-, lo-, sim-, vastatin)</td>
<td>Diltiazem. imidazoles, macrolides, nefazadone, verapamil(^c), imidazoles, macrolides, nefazadone</td>
</tr>
<tr>
<td>Sulfonylureas</td>
<td>Imidazoles</td>
</tr>
<tr>
<td>Theophylline</td>
<td>Barbiturates, cimetidine, fluvoxamine, imidazoles, Mexilitene, quinolones (ciprofloxacin), ciprofloxacin</td>
</tr>
<tr>
<td>Tizanidine</td>
<td>Ciprofloxacin</td>
</tr>
<tr>
<td>Triazolam</td>
<td>imidazoles, macrolides, nefazadone</td>
</tr>
<tr>
<td>Thiopurines</td>
<td>Allopurinol, febuxostat</td>
</tr>
<tr>
<td>Warfarin</td>
<td>Amiodarone, barbiturates, imidazoles, macrolides, NSAIDs, quinolones (ciprofloxacin), TMP/SMX</td>
</tr>
</tbody>
</table>

**Abbreviations:** ACEI = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; K = potassium; NSAIDs = nonsteroidal anti-inflammatory drugs; PPI = proton pump inhibitor; CNS = central nervous system medications; MAOI = monoamine oxidase inhibitors; OC = oral contraceptive; SSRI = selective serotonin reuptake inhibitor; \(^a\)Includes aspirin. \(^c\)CNS medications include: opioid, anticonvulsants, antipsychotics, benzodiazepine receptor agonists (i.e., benzodiazepines, zolpidem, zaleplon, eszopiclone), tricyclic antidepressants, selective serotonin reuptake inhibitors. \(^c\)Only atorvastatin, lovastatin, and simvastatin
**References:**

**Appendix VI. Clinically significant drug-disease interactions**

<table>
<thead>
<tr>
<th>Disease Domain</th>
<th>Drug Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CKD (stages III-IV)</strong></td>
<td>NSAID, all</td>
</tr>
<tr>
<td><strong>Chronic constipation</strong></td>
<td>Anticholinergics</td>
</tr>
<tr>
<td></td>
<td>Diltiazem</td>
</tr>
<tr>
<td></td>
<td>Opioid receptor agonists (without concomitant stimulant laxative)</td>
</tr>
<tr>
<td></td>
<td>Verapamil</td>
</tr>
<tr>
<td><strong>Delirium</strong></td>
<td>Anticholinergics</td>
</tr>
<tr>
<td></td>
<td>Benzodiazepine receptor agonists&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Chlorpromazine</td>
</tr>
<tr>
<td></td>
<td>Corticosteroids</td>
</tr>
<tr>
<td></td>
<td>Histamine type 2 receptor antagonists</td>
</tr>
<tr>
<td></td>
<td>Meperidine</td>
</tr>
<tr>
<td></td>
<td>Thioridazine</td>
</tr>
<tr>
<td></td>
<td>Tricyclic antidepressants</td>
</tr>
<tr>
<td><strong>Dementia and Cognitive Impairment</strong></td>
<td>Antihistamines, 1&lt;sup&gt;st&lt;/sup&gt; generation</td>
</tr>
<tr>
<td></td>
<td>Antipsychotics (chronic and as-needed use)</td>
</tr>
<tr>
<td></td>
<td>Benzodiazepine receptor agonists&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Bladder antimuscarinic drugs</td>
</tr>
<tr>
<td></td>
<td>Gastrointestinal antispasmodics (e.g., dicyclomine, hyoscyamine)</td>
</tr>
<tr>
<td></td>
<td>Histamine type 2 receptor antagonists</td>
</tr>
<tr>
<td></td>
<td>Skeletal muscle relaxants (orphenadrine, cyclobenzaprine)</td>
</tr>
<tr>
<td></td>
<td>Tricyclic antidepressants</td>
</tr>
<tr>
<td><strong>Heart Failure</strong></td>
<td>Nondihydropyridine calcium channel blockers (diltiazem, verapamil) &lt;i&gt;in systolic HF only&lt;/i&gt;</td>
</tr>
<tr>
<td></td>
<td>Cilostazol</td>
</tr>
<tr>
<td></td>
<td>Dronaderone</td>
</tr>
<tr>
<td></td>
<td>NSAID</td>
</tr>
<tr>
<td></td>
<td>Thiazolidinediones (pioglitazone, rosiglitazone)</td>
</tr>
<tr>
<td><strong>History of Falls/Fractures</strong></td>
<td>Anticonvulsants</td>
</tr>
<tr>
<td></td>
<td>Antipsychotics</td>
</tr>
<tr>
<td></td>
<td>Benzodiazepines receptor agonists</td>
</tr>
<tr>
<td></td>
<td>Opioid receptor agonists</td>
</tr>
<tr>
<td></td>
<td>Selective serotonin reuptake inhibitors</td>
</tr>
<tr>
<td>Selective norepinephrine reuptake inhibitors</td>
<td></td>
</tr>
<tr>
<td>--------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>Tricyclic antidepressants</td>
<td></td>
</tr>
</tbody>
</table>

### History of Peptic Ulcer Disease
- Aspirin > 325mg/day without gastroprotection
- NSAID, non-COX-2-selective, without gastroprotection

### Insomnia
- Decongestants, oral (i.e., pseudoephedrine, phenylephrine)
- Stimulants (e.g., amphetamine, methylphenidate, pemoline)
- Theobromines (i.e., theophylline, caffeine)

### Lower Urinary Tract Symptoms
- Anticholinergics

### Parkinson’s Disease
- Antipsychotics, all (except for clozapine or pimavanserin)
  - Metoclopramide
  - Prochlorperazine
  - Promethazine

### Seizures
- Antipsychotics, atypical (i.e., clozapine, olanzapine)
- Antipsychotics, conventional (e.g., chlorpromazine, thioridazine, thiothixene)
  - Bupropion
  - Maprotiline
  - Tramadol

### Syncope
- Acetylcholinesterase inhibitors
  - α blockers, peripheral (i.e., doxazosin, prazosin, terazosin)
- Antipsychotics (i.e., chlorpromazine, olanzapine thioridazine)
- Tricyclic antidepressants, all

### Urinary Incontinence
- α blockers (avoid in women)
  - Estrogen oral and transdermal dosage forms only (applies to women)

*Refers to benzodiazepines, eszopiclone, zaleplon, and zolpidem.*
Appendix VII. Modifications of Veterans Affairs Medication Classification System

<table>
<thead>
<tr>
<th>Code</th>
<th>Class</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>AH100</td>
<td>Antihistamines</td>
<td>Consider all subclasses as one</td>
</tr>
<tr>
<td>CN300</td>
<td>Sedative/Hypnotics</td>
<td>Consider all subclasses as one</td>
</tr>
<tr>
<td>CN400</td>
<td>Anticonvulsants</td>
<td>Exclude - therapeutic category</td>
</tr>
<tr>
<td>CN500</td>
<td>Antiparkinson</td>
<td>Exclude - therapeutic category</td>
</tr>
<tr>
<td>CN600</td>
<td>Antidepressants</td>
<td>Combine CN601, CN603, CN609 into one</td>
</tr>
<tr>
<td>CN700</td>
<td>Antipsychotics</td>
<td>Combine CN701, CN709 into one</td>
</tr>
<tr>
<td>CV250</td>
<td>Antianginals</td>
<td>Consider as nitrates (only ones starred)</td>
</tr>
<tr>
<td>CV300</td>
<td>Antiarrhythmics</td>
<td>Exclude consideration as therapeutic category as combination therapy can be appropriate</td>
</tr>
<tr>
<td>CV359</td>
<td>Antilipemics Agents, Other</td>
<td>Split into discrete categories as indicated (Bile Acid Sequestrants, Others)</td>
</tr>
<tr>
<td></td>
<td>Bile Acid Sequestrants</td>
<td>Colestipol, cholestyramine</td>
</tr>
<tr>
<td></td>
<td>Others</td>
<td>Examples: niacin, gemfibrozil, probucol</td>
</tr>
<tr>
<td>CV409</td>
<td>Antihypertensives</td>
<td>Split into discrete categories as indicated (Central/peripheral (\alpha) blockers, Vasodilators)</td>
</tr>
<tr>
<td></td>
<td>Central/Peripheral (\alpha) Blockers</td>
<td>Examples: clonidine, methyldopa, reserpine</td>
</tr>
<tr>
<td></td>
<td>Vasodilators</td>
<td>Minoxidil (count as CV402)</td>
</tr>
<tr>
<td>GA300</td>
<td>Antiulcer agents</td>
<td>Combine GA301, GA302 &amp; GA304, into one</td>
</tr>
<tr>
<td>MS400</td>
<td>Antigout agents</td>
<td>Exclude - therapeutic category</td>
</tr>
<tr>
<td>RE000</td>
<td>Respiratory</td>
<td>Combine RE120 and RE125 into one</td>
</tr>
<tr>
<td>RE120</td>
<td>Respiratory</td>
<td>No therapeutic duplication between long- and short-acting (\beta_2) agonists</td>
</tr>
<tr>
<td>BL117</td>
<td>Platelet Aggregation Inhibitors</td>
<td>Aspirin indicated for antiplatelet effects</td>
</tr>
<tr>
<td>CN103</td>
<td>Non-opioid Analgesics</td>
<td>Aspirin indicated for minor pain</td>
</tr>
<tr>
<td>CN104</td>
<td>Non-steroidal Anti-inflammatoryities</td>
<td>Aspirin indicated for anti-inflammatory</td>
</tr>
</tbody>
</table>

Appendix VIII  Drugs to Consider Duration of Use “Unacceptable” For Those At EOL

- Anti-dementia agents
- Anti-platelet agents (not asa)
- Cytotoxic chemotherapy
- Hormone antagonists
- Immunomodulators (e.g., etanercept)
- Leukotriene receptor antagonists
- Lipid-lowering agents (e.g., statins)
- Others- ACEI/ARB, Allopurinol, Alpha blockers (for BpH), Anticoagulants, Antidepressants, antiinfectives, antipsychotics, antivertigo, ARB, ASA, Bisphosphonates, BP meds, BZDRA, CCB, Calcium/Vit. D, CNS stimulants, DM drugs, Estrogen, , expectorants, GU antispasmodics, H2 RA, Iron, MVIs, Minerals, NSAIDs, PPIs, Rubefacients, SERMs, Theophylline, Vitamins?
References
2. van Nordennen RT. Drugs Aging 2014; 31:501–12.