POTENTIALLY SAFER ALTERNATIVES TO HIGH-RISK MEDICATIONS

The use of ***potentially inappropriate high-risk medications*** **(HRM)** in adults aged 65 and older can lead to poor health outcomes, including adverse drug events which may lead to confusion, falls, hospitalizations, and death. Certain medications are associated with increased risk of harm from drug side-effects and pose a concern for patient safety. The risk of harm arises not just from drugs used as monotherapy but also multiple drugs when given in combination.

The American Geriatrics Society (AGS) Beers Criteria identified several categories of medications that have an increased risk of adverse effects to elderly patients. When prescribing, please consider the **potentially safer treatment alternatives** below. Providers should evaluate the use of high-risk medications and prescribe safer treatment alternatives when medically appropriate. Due to the altered physiology of elderly patients these high-risk medications can be potentially dangerous if not adjusted. It is recommended for the provider to consult a geriatrician on the safest alternative agent to use if possible.

Additionally, prescribing practitioner and/or clinical pharmacist should regularly review and document a comprehensive medication list of ***all*** the member's medication(s) *(including prescription medications, OTC medications, herbal or supplemental therapies, and medication samples*).

Evaluation of medication appropriateness should be made based on the totality of elderly patients' medication regimen.

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Coding Guidelines

Using the assessment codes below, prescribers should review, sign, and date the member's complete medication list in the medical record (or indicate if the member is not taking any medication).

Medication Review	Medication List
90863, 99483, 99605, 99606, 1160F	**1159F, G8427**

Most Used High-Risk Medications	Potential Risks	Potentially Safer Alternatives†
Anticholinergics *Anti-Parkinson's Agent:* ■ *BENZTROPINE* *First Generation Antihistamine:* ■ *HYDROXYZINE* ■ *CHLORPHENIRAMINE* ■ *DIPHENHYDRAMINE*	Higher anticholinergic side effects (confusion, dry mouth, constipation, urinary retention). Medication clearance reduced with advanced age and tolerance develops when used as a hypnotic. Cumulative exposure to anticholinergic drugs is associated with risk of falls, delirium, and dementia.	■ *BENZTROPINE* **>** amantadine **>** carbidopa/levodopa **>** entacapone **>** pramipexole **>** rasagiline **>** ropinirole **>** selegiline **>** *Kynmobi** *(Available in brand name drug only)* **>** *Neupro** *(Available in brand name drug only)* ■ *HYDROXYZINE, CHLORPHENIRAMINE, DIPHENHYDRAMINE* **>** loratadine **>** levocetrizine **>** cetirizine
Benzodiazepines ■ *ALL BENZODIAZEPINES* *(e.g., ALPRAZOLAM, CHLORAZEPATE, CHLORDIAZEPOXIDE, CLONAZEPAM, DIAZEPAM, ESTAZOLAM, FLURAZEPAM, LORAZEPAM, OXAZEPAM, QUAZEPAM, TEMAZEPAM, TRIAZAOLAM)*	Risks of abuse, misuse, and addiction. Concomitant use with opioids may result in increased risk of sedation, respiratory depression, coma, and death. Older adults have increased sensitivity to benzodiazepines and decreased metabolism of long-acting agents. In general, all benzodiazepines increase risk of cognitive impairment, delirium, falls, fractures, and motor vehicle crashes ****May be appropriate for seizure disorders, rapid eye movement sleep behavior disorder, benzodiazepine withdrawal, ethanol withdrawal, severe generalized anxiety disorder.***	**For panic disorder or antidepressant:** **>** fluoxetine **>** sertraline **>** venlafaxine **For absence seizures:** **>** ethosuxamide **For seizures:** **>** divalproex sodium **>** lacosamide **>** lamotrigine **>** levetiracetam **>** primidone **>** topiramate **>** valproic acid
Endocrine System, Desiccated Thyroid Medications ■ *THYROID (USP)*	May increase the risk of cardiovascular events, especially those with coronary artery disease.	**>** levothyroxine **>** liothyronine

†Please note: The listing of safer treatment alternatives represents potential options; this table is not all inclusive.
†If the prescriber deems a high-risk medication necessary for a patient, prior authorization can be requested through the Pharmacy Utilization Management at: 1 (800) 303-9626.
†Prior authorization form can also be found in: **metroplus.org/providers/provider-forms**
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Most Used High-Risk Medications (Continued)	Potential Risks	Potentially Safer Alternatives†
Endocrine System, Sulfonylureas ■ *GLYBURIDE* ■ *GLIPIZIDE* ■ *GLIMEPIRIDE* ■ *CHLORPROPAMIDE*	Sulfonylureas have a higher risk of cardiovascular events including ischemic stroke and cardiovascular related death, all-cause mortality, and hypoglycemia than alternative agents.	**>** metformin **>** nateglinide **>** pioglitazone **>** repaglinide
Nonbenzodiazepine Hypnotics ■ *ESZOPICLONE* ■ *ZALEPLON* ■ *ZOLPIDEM*	Adverse events similar to benzodiazepines in elderly (delirium, falls, fractures, etc.) Increase in ER visits, motor vehicle crashes, and hospitalizations. ***Exclusions: Psychosis, Schizophrenia, Schizoaffective Disorder, Bipolar Disorder, Major Depressive Disorder, Seizure Disorder***	**For insomnia with or without narcolepsy who have a history of falls and dementia**: **>** mirtazapine **>** trazodone **For insomnia without narcolepsy:** **>** *Belsomra** *(Available in brand name drug only)*
Pain medications, Skeletal Muscle Relaxants ■ *CARISOPRODOL* ■ *METAXALONE* ■ *CHLORZOXAZONE* ■ *METHOCARBAMOL* ■ *CYCLOBENZAPRINE* ■ *ORPHENADRINE*	Most muscle relaxants are poorly tolerated in older adults due to anticholinergic effects, risk of sedation and fractures	**>** duloxetine **>** pregabalin
Pain Medications, Opioids (Narcotics) ■ *MEPERIDINE (DEMEROL)* ■ *PENTAZOCINE (TALWIN or TALACEN)*	Meperidine can increase the risk of seizures and can cause confusion Elderly patients may be more sensitive to the effects of pentazocine injection than younger adults, and are more likely to have age-related kidney problems	**For acute mild pain:** **>** acetaminophen **>** NSAIDs (e.g., ibuprofen) **For acute moderate to severe pain:** **>** Tramadol (Ultram) **>** Morphine **>** Oxycodone immediate release with acetaminophen
Antiarrhythmics ■ *DISOPYRAMIDE* ■ *AMIODARONE*	Disopyramide may increase the risk of heart failure due to potent negative inotropic action. Disopyramide can also cause anticholinergic side effects (xerostomia, abdominal discomfort, nausea, constipation, urinary hesitancy, and retention) Amiodarone may induce QT prolongation and torsades de pointes. The risk of organic specific toxicity is greater in elderly patients due to physiological deterioration in renal and hepatic function.	**For rate control of atrial fibrillation:** **>** Nondihydropyridine Calcium Channel Blockers (e.g., diltiazem) **>** Beta-Blockers **For rhythm control of atrial fibrillation:** **>** Dofetilide **>** Flecainide **>** Propafenone **>** Long acting Dihydropyridine Calcium Channel Blockers (e.g., amlodipine)

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Antihypertensives ■ *Peripheral Alpha-1 Blockers (e.g., DOXAZOSIN, PRAZOSIN, TERAZOSIN)* ■ *Centrally Acting Agents (e.g., CLONIDINE, GUANABENZ, GUANFACINE, METHYLDOPA, RESPERINE)* ■ *IMMEDIATE RELEASE NIFEDIPINE*	Peripheral Alpha-1 blockers have a high risk of orthostatic hypotension Centrally Acting agents have a high risk of adverse CNS effects, bradycardia, and orthostatic hypotension Immediate release formulation of nifedipine is associated with potential for hypotension, myocardial infarction, stroke, and arrhythmias	**For hypertension (first line):** **>** ACE-inhibitors (e.g., lisinopril, benazepril) **>** ARBs (e.g., Losartan, valsartan) **>** Calcium Channel Blockers (e.g., amlodipine, diltiazem) **>** Thiazide Diuretics (e.g., chlorthalidone, hydrochlorothiazide) **For hypertension with another indication or resistant hypertension to first line agent:** **>** May consider beta-blocker (e.g., metoprolol, atenolol) **>** Selective beta-blockers (e.g., acebutolol, atenolol, betaxolol, bisoprolol, metoprolol, nebivolol) can be considered for those with fall risk **For immediate release nifedipine consider:** **>** Amlodipine **>** Felodipine ER **>** Nifedipine ER
Cardiac Glycosides ■ *DIGOXIN (> 0.125mg/day)*	For atrial fibrillation there are safer and more effective agents when rate control is needed For heart failure there are better alternatives to digoxin that reduce mortality and hospitalization Elderly patients with renal insufficiency have a greater risk of digoxin related toxicity when used at higher doses	**For atrial fibrillation:** **>** Refer to antiarrhythmic section for rate and rhythm control alternatives **>** Re-evaluate digoxin dosage and avoid doses > 0.125mg/day **For heart failure:** **>** Avoid digoxin as first line therapy for heart failure **>** Re-evaluate appropriateness and avoid doses > 0.125mg/day
Potentially Harmful Drug-Disease Interactions	**Potential Risks**	**Potentially Safer Alternatives†**
History of Falls and a prescription for Antiepileptics ■ *GABAPENTIN*	May cause ataxia, impaired psychomotor function, syncope. Increased risk of falls and fractures, severe sedation-related adverse events, including respiratory depression and death. ***Exclusions: Psychosis, Schizophrenia, Schizoaffective Disorder, Bipolar Disorder, Major Depressive Disorder, Seizure Disorder***	**For neuralgia:** **>** lidocaine patches
Dementia and a prescription of Anticholinergic agents, antimuscarinics (oral) ■ *OXYBUTYNIN*	Strong anticholinergic side effects (confusion, dry mouth, constipation, urinary retention). Cumulative exposure to anticholinergic drugs is associated with increased risk of falls, delirium, and dementia. ***Exclusions: Psychosis, Schizophrenia, Schizoaffective Disorder, Bipolar Disorder***	**>** *Mybetriq* (Available in brand name drug only)*

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Chronic Kidney Disease and a prescription for NSAIDs ■ *ASPIRIN (>325 mg/day), DICLOFENAC, DIFLUNISAL, ETODOLAC< IBUPROFEN, KETOPROFEN, MELOXICAM, NABUMETONE, NAPROXEN, OXAPROZIN, PIROXICAM, SULINDAC, INDOMETHACIN, KETOROLAC*	Increased risk of GI bleeding or peptic ulcer disease in high-risk groups. Increased risk of blood pressure which may induce kidney injury (except aspirin). ***No Exclusions**	**>** acetaminophen
Potentially Harmful Drug-Drug Interactions	**Potential Risks**	**Recommendation**
■ *RAS INHIBITORS (ACEIs, ARBs, ALISKIREN) or POTASSIUM SPARING DIURETICS (AMILORIDE, TRIAMTERENE) – ANOTHER RAS INHIBITOR (ACEIs, ARBs, ALISKIREN)*	Combination of these agents can increase the risk of hyperkalemia	**>** Avoid use in those with chronic kidney disease Stage 3a or higher
■ *OPIOIDS – BENZODIAZEPINES* ■ *OPIOIDS – GABAPENTIN or PREGABALIN*	Increased risk of overdose and severe sedation-related adverse events, including respiratory depression and death when combining an opioid with either a benzodiazepine or gabapentinoid	For Opioids – Benzodiazepines: **>** Avoid combination For Opioids – Gabapentin or Pregabalin: **>** Avoid combination ***Exclusions: When transitioning from opioid therapy to gabapentin or pregabalin, or when using gabapentinoids to reduce opioid dose, although caution should be used in all circumstances**
■ *ANTICHOLINERGIC – ANTICHOLINERGIC*	Using more than one anticholinergic drug can increase the risk of cognitive decline, delirium, and falls or fractures	**>** Avoid or minimize the number of anticholinergic drugs
Potentially Harmful Drug-Drug Interactions	**Potential Risks**	**Recommendation**
■ *LITHIUM -- ACEIs or ARBs* ■ *LITHIUM – LOOP DIURETICS*	Combination of lithium with either an ACEI/ARB or loop diuretic can increase the risk of lithium toxicity	**>** Avoid or monitor lithium concentrations
■ *PERIPHERAL ALPHA-1 BLOCKERS – LOOP DIURETICS*	Older women are at increased risk of urinary incontinence when these two drug classes are used concurrently.	**>** Avoid concurrent use in older women, unless clinical scenario warrants use of both drugs
■ *WARFARIN – AMIODARONE, or CIPROFLOXACIN, or MACROLIDES (EXCLUDING AZITHROMYCIN), or SULFAMETHOXAZOLE TRIMETHOPRIM, or SSRIs*	Combination of warfarin with these agents can result in increased risk of bleeding	**>** Avoid if possible or if used together INR should be closely monitored

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