



## PATIENT SAFETY:

### At the core of evidence-based guidelines for older adults

#### Evidence suggests polypharmacy can create measurable health challenges, including an 88% increased risk of experiencing an adverse drug event<sup>1</sup>

The American Geriatrics Society (AGS) recommends avoiding the concurrent use of the following in older adults:<sup>2,3</sup>

- Three or more central nervous system (CNS) medications. Multiple studies have reported an increased risk of falls and possible fractures.<sup>4,5,6,7</sup>
  - In older adults taking **two or more** CNS-active medications, there is approximately a **200% increased risk of recurrent falls vs control**.<sup>6</sup>
  - In older adults taking **higher doses** of CNS-active medications, there is a **300% increased risk of recurrent falls vs control**.<sup>6</sup>
- Two or more anticholinergic (ACH) medications. Multiple studies have reported an **increased risk** of cognitive decline with concurrent use.<sup>8,9,10</sup>



Based on this evidence, the Pharmacy Quality Alliance™ (PQA) developed and endorsed two polypharmacy measures in older adults.<sup>11</sup>

#### Polypharmacy measures in older adults<sup>11</sup>

	<b>Polypharmacy</b> Use of Multiple CNS-active Medications in Older Adults	<b>Polypharmacy</b> Use of Multiple ACH Medications in Older Adults
<b>Risks of polypharmacy use</b>	CNS medications increase the risk of falls	ACH medications are associated with an increased risk of cognitive decline
<b>Description</b>	Percentage of older adults with concurrent use of 3 or more unique CNS-active medications	Percentage of older adults with concurrent use of 2 or more unique ACH medications
<b>Calculation (numerator/denominator) x 100%; lower rate is better</b>	Concurrent use of 3 or more unique* CNS-active medications, each with 2 or more fills All patients ≥ 65 years old with 2 or more fills for the same CNS-active medication	Concurrent use of 2 or more unique* anticholinergic medications, each with 2 or more fills All patients ≥ 65 years old with 2 or more fills for the same ACH medication
<b>Exclusion</b>	Seizure disorder and hospice	Hospice
<b>Measurement period</b>	Calendar year	Calendar year
<b>General trend</b>	Lower is better	Lower is better

**Note:** Concurrent use = overlapping days' supply for 30 or more days in measurement year.

\*Unique = different active ingredients

## ACH Medications

### Possible alternatives<sup>^</sup> (if clinically appropriate)

<b>Antihistamines</b>	<ul style="list-style-type: none"> <li>• brompheniramine</li> <li>• carbinoxamine</li> <li>• chlorpheniramine</li> <li>• clemastine</li> <li>• cyproheptadine</li> <li>• dexbrompheniramine</li> <li>• dexchlorpheniramine</li> </ul>	<ul style="list-style-type: none"> <li>• dimenhydrinate</li> <li>• diphenhydramine (oral)</li> <li>• doxylamine</li> <li>• hydroxyzine</li> <li>• meclizine</li> <li>• pyrilamine</li> <li>• triprolidine</li> </ul>	<ul style="list-style-type: none"> <li>• intranasal normal saline</li> <li>• second-generation antihistamine (e.g., levocetirizine, cetirizine, desloratadine)</li> <li>• steroid nasal spray (e.g., fluticasone, flunisolide, mometasone)</li> </ul>
<b>Antiparkinsonian agents</b>	<ul style="list-style-type: none"> <li>• benztropine</li> </ul>	<ul style="list-style-type: none"> <li>• trihexyphenidyl</li> </ul>	<ul style="list-style-type: none"> <li>• pramipexole immediate-release, ropinirole immediate-release</li> </ul>
<b>Skeletal muscle relaxants</b>	<ul style="list-style-type: none"> <li>• cyclobenzaprine</li> </ul>	<ul style="list-style-type: none"> <li>• orphenadrine</li> </ul>	<ul style="list-style-type: none"> <li>• acetaminophen, celecoxib, ibuprofen, naproxen</li> </ul>
<b>Antidepressants</b>	<ul style="list-style-type: none"> <li>• amitriptyline</li> <li>• amoxapine</li> <li>• clomipramine</li> <li>• desipramine</li> <li>• doxepin (&gt; 6 mg/day)</li> </ul>	<ul style="list-style-type: none"> <li>• imipramine</li> <li>• nortriptyline</li> <li>• paroxetine</li> <li>• protriptyline</li> <li>• trimipramine</li> </ul>	<ul style="list-style-type: none"> <li>• selective serotonin reuptake inhibitors (SSRIs)* e.g., sertraline, except paroxetine</li> <li>• serotonin and norepinephrine reuptake inhibitors (SNRIs) (e.g., duloxetine)</li> </ul>
<b>Antipsychotics</b>	<ul style="list-style-type: none"> <li>• chlorpromazine</li> <li>• clozapine</li> <li>• loxapine</li> <li>• olanzapine</li> </ul>	<ul style="list-style-type: none"> <li>• perphenazine</li> <li>• thioridazine</li> <li>• trifluoperazine</li> </ul>	<ul style="list-style-type: none"> <li>• low-dose non-anticholinergic antipsychotics (e.g., aripiprazole, risperidone, ziprasidone)</li> </ul>
<b>Antiarrhythmic</b>	<ul style="list-style-type: none"> <li>• disopyramide</li> </ul>		<ul style="list-style-type: none"> <li>• diltiazem, verapamil</li> </ul>
<b>Antimuscarinics</b>	<ul style="list-style-type: none"> <li>• darifenacin</li> <li>• fesoterodine</li> <li>• flavoxate</li> <li>• oxybutynin</li> </ul>	<ul style="list-style-type: none"> <li>• solifenacin</li> <li>• tolterodine</li> <li>• trospium</li> </ul>	<ul style="list-style-type: none"> <li>• Myrbetriq<sup>®</sup> (mirabegron), Gemtesa<sup>®</sup> (vibegron)</li> </ul>
<b>Antispasmodics</b>	<ul style="list-style-type: none"> <li>• atropine (excludes ophthalmic)</li> <li>• belladonna alkaloids</li> <li>• clidinium-chlordiazepoxide</li> <li>• dicyclomine</li> <li>• homatropine (excludes ophthalmic)</li> </ul>	<ul style="list-style-type: none"> <li>• hyoscyamine</li> <li>• methscopolamine</li> <li>• propantheline</li> <li>• scopolamine (excludes ophthalmic)</li> </ul>	<ul style="list-style-type: none"> <li>• For constipation: lactulose oral solution. For diarrhea: loperamide</li> </ul>
<b>Antiemetics</b>	<ul style="list-style-type: none"> <li>• prochlorperazine</li> </ul>	<ul style="list-style-type: none"> <li>• promethazine</li> </ul>	<ul style="list-style-type: none"> <li>• ondansetron</li> </ul>

<sup>^</sup>This list may not represent medications covered on your patient's plan. Please check to ensure alternatives are available for your patient.

\*SSRIs, SNRIs, and TCAs are not recommended in patients with a history of falls or fractures.<sup>3</sup>

## CNS-Active Medications

## Recommendation

<p><b>Antiepileptics</b></p>	<ul style="list-style-type: none"> <li>• brivaracetam</li> <li>• cannabidiol</li> <li>• carbamazepine</li> <li>• divalproex sodium</li> <li>• eslicarbazepine</li> <li>• ethosuximide</li> <li>• ethotoin</li> <li>• felbamate</li> <li>• gabapentin</li> <li>• lacosamide</li> <li>• lamotrigine</li> <li>• levetiracetam</li> <li>• methsuximide</li> <li>• oxcarbazepine</li> <li>• perampanel</li> <li>• phenobarbital</li> <li>• phenytoin</li> <li>• pregabalin</li> <li>• primidone</li> <li>• rufinamide</li> <li>• stiripentol</li> <li>• tiagabine</li> <li>• topiramate</li> <li>• valproic acid</li> <li>• vigabatrin</li> <li>• zonisamide</li> </ul>	<ul style="list-style-type: none"> <li>• Avoid unless safer alternatives are not available</li> <li>• Consider reducing use of other CNS-active medications</li> <li>• Consider tapering to avoid symptom recurrence and discontinuation syndromes</li> <li>• Implement strategies to reduce falls risk (e.g., assistive devices, home safety evaluation, balance, and strength training)</li> </ul>
<p><b>Antipsychotics</b></p>	<ul style="list-style-type: none"> <li>• aripiprazole</li> <li>• asenapine</li> <li>• brexpiprazole</li> <li>• cariprazine</li> <li>• chlorpromazine</li> <li>• clozapine</li> <li>• fluphenazine</li> <li>• haloperidol</li> <li>• iloperidone</li> <li>• loxapine</li> <li>• lumateperone</li> <li>• lurasidone</li> <li>• molindone</li> <li>• olanzapine</li> <li>• paliperidone</li> <li>• perphenazine</li> <li>• pimavanserin</li> <li>• pimozone</li> <li>• quetiapine</li> <li>• risperidone</li> <li>• thioridazine</li> <li>• thiothixene</li> <li>• trifluoperazine</li> <li>• ziprasidone</li> </ul>	
<p><b>Benzodiazepines and nonbenzodiazepine sedative/hypnotics</b></p>	<ul style="list-style-type: none"> <li>• alprazolam</li> <li>• chlordiazepoxide</li> <li>• clobazam</li> <li>• clonazepam</li> <li>• clorazepate</li> <li>• diazepam</li> <li>• estazolam</li> <li>• eszopiclone</li> <li>• flurazepam</li> <li>• lorazepam</li> <li>• midazolam</li> <li>• oxazepam</li> <li>• quazepam</li> <li>• temazepam</li> <li>• triazolam</li> <li>• zaleplon</li> <li>• zolpidem</li> </ul>	

## CNS-Active Medications

## Recommendation

<b>Opioids</b>	<ul style="list-style-type: none"><li>• benzhydrocodone</li><li>• buprenorphine</li><li>• butorphanol</li><li>• codeine</li><li>• dihydrocodeine</li><li>• fentanyl</li><li>• hydrocodone</li><li>• hydromorphone</li><li>• levorphanol</li><li>• meperidine</li><li>• methadone</li><li>• morphine</li><li>• opium</li><li>• oxycodone</li><li>• oxymorphone</li><li>• tapentadol</li><li>• tramadol</li></ul>	<ul style="list-style-type: none"><li>• Avoid unless safer alternatives are not available</li><li>• Consider reducing use of other CNS-active medications</li><li>• Consider tapering to avoid symptom recurrence and discontinuation syndromes</li><li>• Implement strategies to reduce falls risk (e.g., assistive devices, home safety evaluation, balance, and strength training)</li></ul>
<b>Selective serotonin and norepinephrine reuptake inhibitors and tricyclic antidepressants</b>	<ul style="list-style-type: none"><li>• amitriptyline</li><li>• amoxapine</li><li>• citalopram</li><li>• clomipramine</li><li>• desipramine</li><li>• desvenlafaxine</li><li>• doxepin</li><li>• duloxetine</li><li>• escitalopram</li><li>• fluoxetine</li><li>• fluvoxamine</li><li>• imipramine</li><li>• levomilnacipran</li><li>• milnacipran</li><li>• nortriptyline</li><li>• paroxetine</li><li>• protriptyline</li><li>• sertraline</li><li>• trimipramine</li><li>• venlafaxine</li></ul>	

## Tapering regimens for CNS-active medications

Drug class	Example of tapering regimen
Antidepressants	Taper 25% every 4–6 weeks <sup>12</sup>
Benzodiazepines/ sedative-hypnotics	Taper 25% every week. Reduce to 10–25% every 2–4 weeks if withdrawal symptoms occur <sup>13</sup>
Antipsychotics	Taper 25–50% every 1–2 weeks. If withdrawal symptoms occur, options are to slow taper further, restart at lowest dose or consider non-medication behavioral support <sup>14</sup>
Opioids	Taper 10% per week (or 10% per month if taking > 1 year) <sup>15</sup>

**Note:** These tapering regimens are only provided as examples. Tapering may vary based on patient factors (e.g., duration of therapy, symptom recurrence) and the regimen should be adjusted based on patient monitoring.

## Clinical best practices to reduce polypharmacy and adverse events

- Before prescribing a new medication, always remember to check if it falls on the POLY-ACH and POLY-CNS measure drug list.
  - If on the drug list, consider nonpharmacological interventions or other medication alternatives.
  - If POLY-ACH and POLY-CNS medications cannot be avoided:
    - Use the lowest dose, frequency, and duration necessary.
    - Minimize overlap with other polypharmacy drugs (e.g., limit supply duration).
    - Document acknowledgement of risk in patient's medical chart.
- Educate patients about the risk of falls, drug interactions, and adverse drug events when taking multiple medications.
- Review medications each visit for polypharmacy and consider removal or replacement with a clinical alternative.
  - Consider starting with medications that have the highest risk but lowest benefits.
  - Consider stopping medications with the lowest likelihood of withdraw reactions or disease rebound.
- If deprescribing is an option, implement a plan and monitor progress.
  - Consider the need to taper medications if taken for long term or at a high dose. This may take several weeks or months.
  - Educate patient/caregiver with clear instructions.
  - Stop one medication at a time so that harms and benefits can be properly documented and addressed, as needed.
  - Follow up on plan after implementation (consider a shorter interval for visits and/or telephone support).

## References

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