Focus on Seizure Disorder in Older Adults: Part 2
- by Carrie Allen

This focus article is part 2 of 2 articles dedicated to seizure disorder/epilepsy (SDE) in older adults. Part 1 focused on background information/general concepts related to SDE, while part 2 focuses on selected medications used to treat SDE, including side effects and monitoring.

Medication Therapy for SDE

The treatment of acute seizures, such as status epilepticus, is beyond the scope of this article; however, long-term care (LTC) facilities should have education and protocols to handle such situations. Mortality rates increase with age, anoxia, duration of status epilepticus, and are greater than 50% in people over 80 years old. Managing non-acute seizures with antiepileptic drugs (AED) in older adults should be approached with the following goals in mind:

- Freedom from seizures
- Minimization of AED side effects (including drug-drug/drug-disease interactions)
- Maintenance of a normal lifestyle
- Sustained quality of life (QOL)

Older adults have a higher risk of therapeutic failure and adverse drug reactions (ADR) with AED. In fact, AED are the fourth leading cause of ADR among nursing home residents (NHR). Despite the fact that newer AED with better side effect profiles are available in generic forms, phenytoin remains the most prescribed AED in the nursing home setting, followed by carbamazepine and valproic acid. The Centers for Medicare and Medicaid Services (CMS) has included phenytoin and valproic acid as high-risk medications in their Adverse Event Trigger tool, with information on how to monitor for ADR. Additionally, age-related decline in renal and hepatic function may precipitate ADR, and require lower doses of some AED. Virtually all AED can cause sedation, ataxia, and lethargy upon initiation, but some tolerance typically develops in 7 – 10 days. Therefore, in non-emergency situations, AED should be started at low doses and gradually increased until seizure control is achieved (unless intolerable side effects occur).

Effectiveness should be monitored primarily by seizure control, rather than the achievement of therapeutic serum drug concentrations. However, there are many reasons why therapeutic drug monitoring of AED is performed in older adults such as toxicity associated with older AED, drug-drug interactions that impact AED concentrations, unstable medical conditions, fluctuating renal/hepatic status, malnutrition, and recent changes to the drug regimen. AED are implicated in numerous drug-drug and drug-disease interactions; therefore, ongoing evaluation is warranted when medication changes or changes in condition occur. The Table on pages 2-3 lists selected AED and their side effects/ADR, as well as if dose adjustment for renal impairment is required. Monitoring for side effects and ADR should be ongoing during therapy with AED.
Establishing the optimal AED regimen requires time and effort to determine the best choice of AED, dose, and administration times. Many individuals require more than one AED to control their seizures; recommended strategies for when first-line monotherapy fails in patients with SDE include the following.

- increasing the dose of the first-line drug if there is a lack of seizure control but no toxicity
- lowering the dose of the first-line drug and adding another drug if there is poor seizure control at the maximal dose tolerated
- performing a rapid substitution if there are unacceptable dose-related ADR at the lowest possible maintenance dose
- prescribing an immediate substitution if the patient is experiencing unacceptable idiosyncratic reactions

<table>
<thead>
<tr>
<th>Selected AED Used in the LTC Setting*</th>
<th>Notable Side Effects/ADRa</th>
<th>Suggested Monitoring and Other Considerations*</th>
</tr>
</thead>
</table>
| Carbamazepine (Tegretol)             | - Dose related: diplopia, drowsiness, nausea, sedation  
- Other: rash, SJS, DRESS, blood dyscrasias, SIADH, ↑ risk of OP with long-term use | - Monitor CMP, CBC + differential, at baseline and at least annually  
- Discontinue if WBC < 3000/mm³ or ANC <1500/mm³  
- Serum carbamazepine concentration within 1 week after initiation/dosing changes, then every 6 months |
| Eslicarbazepine (Aptiom)             | - Dose related: hyponatremia, cognitive dysfunction somnolence, fatigue, dizziness, gait disturbance, incoordination, vision changes  
- Other: N/V, headache, tremor | - Monitor LFT, BMP, CrCl at baseline and at regular intervals; monitor for S/S of hyponatremia (especially during the first 8 weeks of therapy)  
- Do not use with oxcarbazepine or in patients allergic to oxcarbazepine or carbamazepine  
- Dose modifications of Aptiom or other AED may be needed when taken as combination therapy (e.g., carbamazepine, phenobarbital, phenytoin)  
- Renal dosing considerations  
- Discontinue if significant liver injury occurs |
| Ezogabine (Potiga)                   | - Dose related: dizziness, somnolence  
- Other: vision abnormalities/loss, vertigo, hallucinations, confusion, psychosis, tremor, abnormal coordination, memory impairment, aphasia, gait and balance disturbances, dysartrhia, urinary retention | - Monitor LFT, BMP, CrCl at baseline and annually  
- Monitor vision at baseline and every 6 months, continue treatment if retinal pigmentary abnormalities or vision changes are detected, unless benefits outweigh the risk of vision loss  
- Monitor for grey-blue or brown discoloration in the skin, mucus membranes or nailbeds; changing to another AED should be seriously considered if detected  
- Renal and hepatic dosing considerations in patients ≥ 65 years old |
| Gabapentin (Neurontin)               | - Dose related: diplopia, slurred speech, drowsiness, lethargy, and diarrhea  
- Other: somnolence, dizziness, ataxia, tremor, peripheral edema, nystagmus, DRESS | - Monitor CrCl at baseline and every 6 months  
- Renal dosing considerations  
- Commonly used for treatment of neuropathic pain |
| Lacosamide (Vimpat)                  | - Dose related: prolongations in PR interval  
- Other: CNS depression, diplopia, headache, dizziness, ataxia, nausea, DRESS | - Renal and hepatic dosing considerations |
| Lamotrigine (Lamictal)               | - Dose related: rash, N/V, life-threatening rashes/ SJS; risk factors include:  
- coadministration with valproate  
- exceeding recommended initial dose  
- exceeding rate of recommended dose escalation  
- Other: headache, dizziness, ataxia, somnolence, incoordination, insomnia | - Monitor LFT, CBC, CrCl at baseline and annually  
- Monitor for S/S of rash and discontinue at the first sign of rash, unless the rash is clearly not drug related  
- Caution if a history of rash exists with other AED, especially carbamazepine, ethosuximide, phenobarbital, and phenytoin  
- Renal and hepatic dosing considerations |
| Levitiracetam (Keppra)               | - Dose related: nausea, headache  
- Other: somnolence, dizziness, depression, nervousness, ataxia, vertigo, amnesia, psychiatric symptoms (e.g., psychosis, emotional lability, agitation, aggression), blood dyscrasias | - Monitor CrCl at baseline and annually  
- Use cautiously in patients with psychosis, consider discontinuation if psychotic symptoms emerge |
<table>
<thead>
<tr>
<th>Selected AED Used in the LTC Setting*</th>
<th>Notable Side Effects/ADR†</th>
<th>Suggested Monitoring and Other Considerations‡</th>
</tr>
</thead>
</table>
| Oxcarbazepine (Trileptal, Oxtellar XR) | • **Dose related:** nausea, headache  
• **Other:** dizziness, somnolence, abnormal vision, ataxia, abdominal pain, tremor, rash, hyponatremia | • Monitor BMP and CrCl at baseline, serum electrolytes monthly for 3 months, every 3 months for 1 year, then annually (risk of hyponatremia)  
• Renal dosing considerations |
| Perampanel® (Fycompa) | • **Dose related:** serious and/or life threatening neuropsychiatric events  
• **Other:** dizziness, somnolence, irritability, falls, N/V, weight gain, vertigo, ataxia, confusion, abdominal pain, anxiety | • Monitor LFT, CBC, CrCl, at baseline and annually  
• Ongoing monitoring for psychiatric and behavioral adverse reactions  
• Renal and hepatic dosing considerations |
| Phenobarbital® | • **Dose/concentration related:** respiratory depression, hypotension, coma  
• **Other:** somnolence, confusion, cognitive impairment | • Monitor LFT, CBC + differential, BMP at baseline and at regular intervals  
• Monitor serum phenobarbital concentrations every 6 months  
• Use cautiously in renal or hepatic impairment |
| Phenytoin (Dilantin) | • **Dose/concentration related:** nystagmus, N/V, vision problems, ataxia, slurred speech, dizziness, drowsiness, lethargy, coma, rash, fever, confusion, mood changes  
• **Other:** SJS, blood dyscrasias, gingival hyperplasia, cardiac arrhythmias, folic acid deficiency, peripheral neuropathy, † risk of OP with long-term use | • Monitor LFT, CBC, CrCl at baseline and every 6 months  
• Monitor serum phenytoin concentrations at regular intervals, 7 days after dose changes, and observe for S/S of toxicity on an ongoing basis  
• Some patients may require monitoring serum albumin every 6 months  
• Dosing considerations if CrCl <25 mL/min |
| Pregabalin (Lyrica®) | • **Dose related:** weight gain, blurred vision  
• **Other:** dizziness, somnolence, ataxia, impaired concentration, peripheral edema | • Renal dosing considerations, monitor CrCl every 6 months  
• Commonly used for treatment of neuropathic pain |
| Topiramate (Topamax, Trokendi XR, Quedexy XR) | • **Dose related:** nausea, weight-loss, metabolic acidosis, nephrolithiasis  
• **Other:** anemia, cognitive impairment (e.g., problems with memory, concentration, and language), somnolence, dizziness, ataxia, paresthesia, psychomotor slowing, depression, edema | • Monitor CBC, BMP, CrCl at baseline and every 6 months  
• Consider another AED if metabolic acidosis occurs  
• Concomitant use with valproic acid may cause hyperthermia ± hyperammonemia ± encephalopathy  
• Renal dosing considerations |
| Valproic Acid/ Divalproex Sodium (Depakene/Depakote) | • **Dose related:** N/V, weight gain, alopecia, thrombocytopenia  
• **Other:** somnolence, dizziness, insomnia, nervousness, tremor, vision problems, amnesia, ataxia, depression, peripheral edema, hyperammonemia/encephalopathy, dyspnea, rash, SJS, DRESS  
• **Risk for toxicity is increased with:**  
  − hepatic and/or renal impairment  
  − concurrent use of: antidepressants, benzodiazepines, or antibiotics | • Monitor LFT, CBC, CrCl, valproic acid concentration at baseline and every 6 months  
• Risk for toxicity is increased with:  
  − hepatic and/or renal impairment  
  − concurrent use of: antidepressants, benzodiazepines, or antibiotics |
| Vigabatrin (Sabril) | • **Dose related:** weight gain, insomnia  
• **Other:** permanent vision loss (risk increases with dose, but is present at any dose), somnolence, headache, fatigue, depression | • Restricted access due to risk of vision loss  
• Monitor vision at baseline, every 3 months, and repeat 3 to 6 months after discontinuation  
• Monitor CrCl at baseline and every 6 months  
• Renal dosing considerations |
| Zonisamide (Zonegran) | • **Dose related:** N/V, weight loss, paresthesias  
• **Other:** somnolence, dizziness, confusion, mental slowing, tremor, agitation/irritability, ataxia, nephrolithiasis, metabolic acidosis | • Monitor LFT, BMP CrCl, at baseline and every 6 months  
• Discontinue in acute renal failure and when estimated GFR < 50 mL/min |

*This table is not all inclusive; refer to facility prescribing patterns, prescribing information, and clinical guidelines for more information.  
† Renamed as “Focal Seizure” or “Focal Onset” by the International League Against Epilepsy (ILAE) in 2017.  
‡Controlled substance  
§Renamed as “Focal Seizure” or “Focal Onset” by the International League Against Epilepsy (ILAE) in 2017.  
¶All AED have a class warning for an increased risk of suicidality.  
¶More common in Asian populations and/or those who are positive for the HLA-B*1502 allele.  
ANC = absolute neutrophil count, BMP = basic metabolic panel, CBC = complete blood count, CMP = comprehensive metabolic panel, CMS = Centers for Medicare and Medicaid Services, CrCl = creatinine clearance, DRESS = drug reaction with eosinophilia and systemic symptoms, GFR = glomerular filtration rate, LFT = liver function tests, N/V = nausea/vomiting, OP = osteoporosis, SIADH = syndrome of inappropriate antidiuretic hormone secretion, SJS = Stevens-Johnson Syndrome, S/S = signs and symptoms, WBC = white blood cell count.
Strategies to Reduce Vaccine Administration Errors

Vaccine administration errors can result in a resident receiving an ineffective immunization and, therefore, leaving them vulnerable to infection. Vaccine errors may also lead to adverse events, increased costs (due to revaccination and staff time), and diminished patient confidence in vaccines and healthcare providers. Common vaccine administration errors include:

- Wrong vaccine, dosage, patient age for vaccine, route of administration, or vaccine interval
- Wrong diluent used to reconstitute the vaccine or only administering the diluent
- Administering expired vaccine
- Administering a vaccine which was not stored properly
- Administering a vaccine to a patient with a contraindication

Examples of vaccine errors include: administering the high-dose trivalent influenza vaccine in adults less than 65 years of age, administering zoster [shingles] live vaccine in residents who are immunosuppressed due to certain medical conditions or treatment, administering the wrong type of pneumococcal vaccine (e.g., due to PCV13 and PPSV23 confusion), and inappropriate time interval between pneumococcal vaccine doses. Among the most frequently confused vaccine abbreviations or acronyms are those for tetanus, diphtheria, with or without pertussis (i.e., DT, DTaP, Tdap, and Td). Ongoing training and education of staff is key in preventing and reducing vaccine administration errors. Additional strategies include:

- Ask the following prior to vaccine administration: Is this the right patient, vaccine, diluent (when applicable), timing interval between vaccines, dosage, route of administration (e.g., intramuscular, subcutaneous), needle gauge and length, and technique?
- Check that the vaccine is appropriate for the patient's age and medical history (e.g., no contraindications).
- Do not store sound-alike and look-alike vaccines next to each other.
- Use standardized vaccine abbreviations, if abbreviations are permitted (e.g., from the CDC)
- Do not combine vaccines into a single syringe unless specifically FDA approved for that purpose.
- Do not transfer vaccines from one syringe to another or draw partial doses from separate vials to obtain a full dose.
- Check expiration dates frequently. Rotate vaccines so those with shortest expiration dates are used first.
- Display current reference sheets for timing and spacing, recommended sites, routes, and needle lengths.
- Avoid interruptions when selecting and preparing vaccines.
- Never administer vaccines you have not personally prepared.
- Check your work (e.g., vial label) three times before administering a vaccine.

Risk of Serious Allergic Reaction with Topical Chlorhexidine Gluconate by Allen Lefkovitz

Following a significant increase in reports of serious allergic reactions and two associated deaths, the U.S. Food and Drug Administration (FDA) has requested manufacturers of over-the-counter (OTC) topical chlorhexidine gluconate (CHG) products to add a warning about this risk to the product labeling. Topical products include both generic and brand products (e.g., Bioscrub, Chloraprep, Hibicleans, Hibistat) and are used to clean and prepare the skin before surgery in order to reduce bacteria that cause infection. In addition to topical formulations, CHG is also available in medical devices (e.g., dressings, intravenous lines) and as prescription products to treat gum disease (e.g., Peridex rinse); however, other forms of CHG have carried warnings about serious allergic reactions for several years.

Healthcare professionals are advised to:

- Closely monitor patients for signs of wheezing, difficulty breathing, swelling of the face, hives, a severe rash, and/or severe hypotension. If an allergic reaction is suspected, use should be discontinued immediately and respiratory and cardiovascular support should be provided as needed.
- Always ask if a patient has ever had a reaction to CHG or any antiseptic product prior to using CHG.

Additional information about the FDA's warning are available at: www.fda.gov/Drugs/DrugSafety/ucm530975.htm.
Using Morphine Milligram Equivalents (MME) to Evaluate Opioid Adverse Event Risk

Opioids can improve function and quality of life in residents with pain, but their use is not without risk. The Centers for Disease Control and Prevention (CDC) uses MME* to identify the risk of overdose in non-cancer patients receiving opioid therapy, with a higher MME conferring a greater risk of overdose (see Table below). In addition to MME, risk is increased in those with sleep apnea, renal or hepatic insufficiency, age ≥ 65 years, and those with psychiatric diagnoses (e.g., depression, anxiety). Concurrent benzodiazepine use [e.g., lorazepam (Ativan)] increases the risk of opioid adverse effects at every MME, as reflected in the FDA boxed warning to limit their use. MME calculation is now available on Omniview and through your Consultant Pharmacist.

<table>
<thead>
<tr>
<th>MME</th>
<th>CDC Monitoring and Management Recommendations</th>
<th>Overdose risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-19</td>
<td>Evaluate benefits and harms within 1-4 weeks of starting opioid therapy and at least every 3 months. Monitor for nausea, sedation, confusion, falls, constipation and physical dependence. This MME has a relatively low risk for overdose events and death, but risk is not eliminated. This MME provides a baseline for risk evaluation.</td>
<td>Baseline risk</td>
</tr>
<tr>
<td>20-49</td>
<td>• Evaluate benefits and harms within 1-4 weeks of increasing dose and at least every 3 months; monitor as above • Ensure naloxone access (e.g., EDK) for those at increased risk (benzodiazepine use, age ≥ 65 years, etc.) • Examples: hydrocodone/acetaminophen (Norco) 5/325 mg four times a day = 20 MME daily; oxycodone ER (Oxycontin) 10 mg twice daily = 30 MME</td>
<td>1.4 times baseline</td>
</tr>
<tr>
<td>50-99</td>
<td>• Assess benefits and harms before increasing opioid dose beyond 50 MME; evaluate at least every 3 months • Ensure naloxone access (e.g., via EDK) for all residents at this MME • Example: fentanyl patch 25 mcg/hr = 60 MME</td>
<td>3.7 times baseline</td>
</tr>
<tr>
<td>≥100</td>
<td>Avoid ≥ 90 MME or carefully document risk-benefit evaluation. If pain and function do not improve at this MME, prescribers are encouraged to optimize other pain management strategies, consider opioid tapering and/or consult a specialist. Ensure naloxone access for this very high risk use,</td>
<td>8.9 times baseline</td>
</tr>
</tbody>
</table>

* MME is not a tool for conversion between opioid medications, and is not intended for use in those with active cancer or under palliative and/or end-of-life care. CDC Guidelines for Prescribing Opioids for Chronic Pain are available at: www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm.
EDK - Emergency Drug Kit

Regulatory Recap: State Operations Manual Appendix PP: Guidance to Surveyors for Long Term Care Facilities

Example of a Severity Level 3 (Actual Harm) Event – Seizure Activity by Carrie Allen

The State Operations Manual (SOM) Appendix PP provides examples of events that result in harm to residents. One such example is related to the facility assessment of recent seizure activity.

It is recognized by the SOM that seizures can be caused by a precipitating event, such as ingestion of a toxin or a medication. The example below is excerpted from the SOM, to illustrate that facilities should have a process in place to rule out adverse drug events as a cause of seizure activity, before prescribing ongoing medications to treat a seizure disorder, where one may not actually exist.

**Excerpt from SOM Appendix PP:** Level 3 indicates noncompliance that resulted in actual harm, and may include, but is not limited to, clinical compromise, decline, or the resident’s inability to maintain and/or reach his/her highest practicable well-being.

**Example:** Facility failure to evaluate the medication regimen as a potential cause of seizure activity resulting in the addition of anticonvulsants to treat recent-onset seizures that can be adverse consequences of medications.
Qtern® Tablet

<table>
<thead>
<tr>
<th>Brand Name (Generic Name)</th>
<th>Qtern [CUE-turn] (dapagliflozin and saxagliptin) [dap-ag-li-FLOE-zin &amp; sax-a-GLIP-tin]</th>
</tr>
</thead>
<tbody>
<tr>
<td>How Supplied</td>
<td>Dapagliflozin 10 mg/Saxagliptin 5 mg tablet</td>
</tr>
<tr>
<td>Therapeutic Class</td>
<td>Combination sodium-glucose cotransporter 2 (SGLT-2) inhibitor and a dipeptidyl peptidase-4 (DPP-4) inhibitor.</td>
</tr>
<tr>
<td>Approved Indication</td>
<td>Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (T2DM) who have inadequate control with dapagliflozin or already treated with dapagliflozin and saxagliptin.</td>
</tr>
<tr>
<td>Usual Dosing</td>
<td>One tablet orally once daily in the morning with or without food. Swallow whole and do not split or cut. Use only in patients who tolerate 10 mg dapagliflozin.</td>
</tr>
<tr>
<td>Select Drug Interactions</td>
<td>Do not coadminister strong cytochrome P450 3A4/5 inhibitors (e.g., clarithromycin)</td>
</tr>
<tr>
<td>Most Common Side Effects</td>
<td>Upper respiratory tract infection, urinary tract infection, and dyslipidemia</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>Contraindicated with moderate to severe renal impairment (eGFR &lt; 45 mL/min/1.73 m²), end-stage renal disease, or on dialysis. Assess renal function before initiation of therapy then periodically. Prior to starting Qtern assess volume status and correct hypovolemia.</td>
</tr>
<tr>
<td>Website</td>
<td><a href="http://qtern-hcp.com">http://qtern-hcp.com</a></td>
</tr>
</tbody>
</table>

NEW Generic Medications

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
<th>Date Generic Available</th>
</tr>
</thead>
<tbody>
<tr>
<td>Desvenlafaxine 25 mg, 50 mg, and 100 mg Extended-Release Tablet</td>
<td>Pristiq® Tablet ER</td>
<td>3/1/17</td>
</tr>
<tr>
<td>Methylphenidate 60 mg Extended-Release Capsule</td>
<td>Ritalin LA® Capsule ER</td>
<td>2/17/17</td>
</tr>
</tbody>
</table>
HealthLine Quiz - by Steve Law

1. Which statement about antiepileptic drugs (AED) is FALSE?
   a. Valproic Acid is the most prescribed AED in the nursing home setting
   b. AED are the fourth leading cause of adverse drug reactions among nursing home residents
   c. AED should be started at low doses and gradually increased until seizure control is achieved
   d. Age-related decline in renal and hepatic function may precipitate an adverse drug reaction

2. Which is NOT a notable AED adverse drug reaction?
   a. Carbamazepine – SIADH
   b. Phenytoin – Gingival hyperplasia
   c. Valproic Acid – Thrombocytopenia
   d. Topiramate – Weight gain

3. Which suggested monitoring parameters of AED is most appropriate?
   a. Monitor an LFT yearly while on gabapentin
   b. Monitor a CBC with differential every 6 months while on levetiracetam
   c. Monitor a serum phenobarbital level every 6 months while on phenobarbital
   d. Monitor a BMP every quarter while on phenytoin

4. Which is a common vaccine administration error?
   a. Administering an expired vaccine
   b. Administering a vaccine to the wrongly approved age group
   c. Administering a vaccine that was not stored properly
   d. Administering a vaccine to a patient with a contraindication for that vaccine
   e. All of the above

5. An MME is used to compare the risk of overdose between doses of the same opioid and different opioid medications?
   a. True  b. False

6. Which is FALSE about the new medication Qtern®?
   a. A common side effect is dyslipidemia
   b. It is a combination of a GLP-1 agonist and a DPP-4 inhibitor
   c. It is contraindicated in patients with moderate to severe renal impairment
   d. It should be given once a day in the morning

*Please note, the HealthLine Quiz is designed to help readers retain information that is relevant to their care setting. It is not an approved source of continuing education credits for healthcare professionals.

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Contributing Authors for This Issue
Carrie Allen, PharmD, BCGP, BCPS, BCPP, CCHP
Clinical Advisor, CVS Health
Yamini Shah, PharmD
Clinical Pharmacist, Clinical Development, CVS/caremark
Allen L. Lefkovitz, PharmD, BCGP, FASCP
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