Louisiana Medicaid

Provider Update

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Louisiana Medicaid Electronic Health Records Incentive Program Launched

Louisiana is among the first states to offer incentive payments to Medicaid providers for adopting, implementing or upgrading electronic health record (EHR) technology to treat patients more efficiently, to reduce their administrative work and to share health information securely among medical facilities. The Department of Health and Hospitals launched the Louisiana Medicaid EHR Incentive Program on January 3, 2011 through funding from the Health Information Technology for Economic and Clinical Health (HITECH) Act, which established programs under Medicare and Medicaid encouraging health care providers to adopt and effectively use EHR and health information technology.

Eligible Medicaid physicians and other healthcare providers could receive up to $63,750 in incentive payments over a six-year period. Eligible providers include physicians (primarily doctors of medicine or osteopathy), nurse practitioners, certified nurse-midwives, dentists and physician assistants (either practicing in federally qualified health centers or leading in rural health clinics). Providers can receive incentive payments in the first year for adopting EHR in their practices, and then are eligible for an additional five years of incentive payments if they demonstrate meaningful use of EHR. Acute care hospitals (including critical access and cancer hospitals) and Children's hospitals that treat Medicaid patients may also be eligible for incentive payments. Hospital incentive payments are based on many factors, but begin with a $2 million base payment.

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Like physicians and other healthcare providers, hospitals can receive incentive payments in the first year for adopting EHR and they are eligible for an additional three years of incentive payments if they demonstrate meaningful use to EHR.

Providers interested in the program can visit the Centers for Medicare and Medicaid Services (CMS) at http://www.cms.gov/EHRIncentivePrograms/15_Eligibility.asp#TopOfPage to determine if they meet the requirements for participation. Eligible providers must meet Medicaid patient encounter volume criteria and must also adopt, implement, or update certified EHR technology to qualify. A product list of certified EHR technology can be found at http://onc-chpl.force.com/ehrcert.

Eligible providers should begin by registering with the National Level Repository through the CMS site at https://ehrincentives.cms.gov/hitech/login.action. After completing the CMS registration, eligible participants will be directed to the Louisiana Medicaid Web site via e-mail to complete the application process. Medicaid program staff will contact eligible providers and hospitals to complete their enrollment.

For more information about how to participate in this program and receive payments, contact Louisiana Medicaid EHR Incentive Payment Program at ehrincentives@la.gov or 225-342-4810, or visit the Louisiana Medicaid EHR Incentive Payment Program online at http://www.lamedicaid.com/provweb1/EHR/EHRIndex.htm.

The Louisiana Health Care Quality Forum is offering assistance through its Louisiana Health Information Technology Center. Providers should contact the center at rec@lhcqf.org to inquire about training and certification.

'ClaimCheck' News and Editing Updates

Part of the on-going DHH process related to the implementation of the 'ClaimCheck' claims editing capabilities is to assess and compare Louisiana Medicaid policies and processes alongside national standards. This is especially important as we prepare for the incorporation of the CMS mandated National Correct Coding Initiative (NCCI) editing for Medicaid services. As a result of continued evaluation and in an effort to improve processing accuracy, providers may note updates in the following areas effective with processing reflected on the Remittance Advice (RA) of December 21, 2010:

- Units of service updated related to select allergy immunotherapy procedure codes to reflect the CPT definition.
- Age restrictions updated (where applicable) on procedure codes to match the CPT definition.
- Procedure codes included in the 'new visit' frequency editing updated to reflect the appropriate evaluation and management codes.

- Adopting the recognized national standard for pre/post operative editing of evaluation and management codes related to obstetrical delivery services. For those services that include postpartum care, the post operative period is 45 days from the date of delivery.
- Inclusion of pertinent procedure codes from the "Medicine" section of CPT in multiple surgery reduction processing (application of modifier -51 when appropriate). Those medicine codes that have the Medicare Multiple Surgery Indicator for the physician service and/or professional component of the procedure are included. This involves mainly cardiovascular diagnostic and intervention procedures.

Providers are reminded that 'ClaimCheck' editing is based on the date of processing, regardless of the service date. Changes made as a result of this process supersede previously published policy where different. For the latest information related to 'ClaimCheck', please continue to monitor the Louisiana Medicaid website home-page at www.lamedicaid.com under the 'ClaimCheck' icon on the same website as well as RA messages. For any further questions, please contact Molina Provider Relations at (800) 473-2783 or (225) 924-5040.

Primary Care Case Management Program Enriched

CommunityCARE, Medicaid's primary care case-management program that links Medicaid recipients to a primary care provider, transitioned January 1, 2011 to an enhanced version that incorporates pay-for-performance (P4P) measures. The new program, known as CommunityCARE 2.0 (CC 2.0), provides greater coordination of care for Louisiana's Medicaid populations and creates a bridge toward the implementation of Coordinated Care Networks. Primary care providers must meet basic participation requirements to be part of the CC 2.0 Program and may earn enhanced rates by meeting P4P measurements. Additional information about this change can be found at www.la-communitycare.com.

Office of Inspector General to Hold Free Compliance Training

The Department of Health and Human Services (HHS), Office of Inspector General (OIG) is offering free, half-day compliance training sessions in Houston, Tampa, Kansas City, Baton Rouge, Denver and Washington, DC for local health care providers, compliance professionals and their legal counsel. The training sessions are a key component of the commitment by the Health Care Fraud Prevention and Enforcement Action Team (HEAT), a joint initiative of HHS and the U.S. Department of Justice to prevent fraud, waste, and abuse in the Medicare and Medicaid programs.

The sessions, which will feature government experts from the OIG, Centers for Medicare and Medicaid Services, United States Attorneys' Offices and State Medicaid Fraud Control Units, will focus on a three-pronged message about provider compliance:

- Understanding the fraud and abuse laws and the consequences of violating them,
- Making a plan to cultivate a culture of compliance within your organization, and
- Knowing what to do when noncompliance is discovered.

Training will be held in Baton Rouge, Louisiana on Tuesday, April 12, 2011 at the Hilton Baton Rouge Capitol Center. Space is limited so the OIG encourages providers, compliance professionals and their legal counsel to visit their website, http://compliance.oig.hhs.gov, for more information and to request enrollment now.

Avoid Hiring or Employing Excluded Individuals

As a condition of participation in the Louisiana Medicaid Program, providers are responsible for ensuring that current as well as potential employees and/or contractors have not been excluded from participation in the Medicaid or Medicare Program by Louisiana Medicaid and/or the Office of Inspector General (OIG). Providers who employ or contract with excluded individuals or entities may be subject to penalties of $10,000 for each item or service the excluded individual or entity furnished.

Providers should check the following two websites prior to hiring or contracting with an individual or entity and should routinely check the websites for determining the exclusion status of current employees and contractors. All current and previous names used such as first, middle, maiden, married or hyphenated names and aliases for **all owners, employees and contractors** should be checked.

- http://exclusions.oig.hhs.gov/search.aspx
- http://www.epls.gov/epls/search.do

If an individual's or entity's name appears on either website, this person or entity is considered excluded and is barred from working with Medicare and/or the Louisiana Medicaid Program in any capacity. The provider must notify the Department of Health and Hospitals with the following information:

- Name of the excluded individual or entity, and
- Status of the individual or entity (applicant or employee/contractor).

If the individual or entity is an employee or contractor, the provider should also include the following information:

- Beginning and ending dates of the individual's or entity's employment or contract with the agency,
- Documentation of termination of employment or contract, and
- Type of service(s) provided by the excluded individual or entity.

These findings should be reported to:

Department of Health and Hospitals
Program Integrity - Special Investigations Unit
P. O. Box 91030
Baton Rouge, LA 70821-9030
Fax: (225) 219-4155

Medicaid providers should review the information provided in the SPECIAL ADVISORY BULLETIN titled "The Effect of Exclusion from Participation in Federal Healthcare Programs" at http://www.oig.hhs.gov/fraud/docs/alertsandbulletins/effected.htm.

Sections E, F, and G of the bulletin explain the prohibition against hiring excluded individuals or entities and the fines and penalties involved when an excluded individual or entity is hired or contracted.

Office of Aging and Adult Services Seeking Providers for New Community Choices Waiver

The Office of Aging and Adult Services (OAAS) received approval from the Centers for Medicare and Medicaid Services to implement a new home and community based services waiver called the Community Choices Waiver. Implementation is expected by the summer of 2011. Once implemented, the Community Choices Waiver will replace the current Elderly and Disabled Adult (EDA) Waiver.

The Community Choices Waiver will include all of the services currently provided in the EDA Waiver plus several new services. Services that will be offered include:

- Support Coordination
- Transition Intensive Support Coordination
- Transition Service (provided to individuals leaving a nursing facility)
- Personal Assistance Service

- Adult Day Health Care
- Environmental Accessibility Adaptations
- Assistive Devices and Medical Supplies (includes Personal Emergency Response Systems)
- Skilled Maintenance Therapy Services (Physical, Occupational, Speech and Respiratory Therapies)
- Nursing Services
- Home Delivered Meal Services
- Caregiver Temporary Support Services (Respite)
- Non-Medical Transportation

OAAS will begin outreach to provider groups offering more information about the Community Choices Waiver and how to become a provider for these services. Providers of Adult Day Health Care, Nursing Facility, Adult Residential Care and Respite services are encouraged to enroll as providers of Caregiver Temporary Support Services. OAAS asks that providers of the following types of services also consider enrolling in the waiver:

- Occupational, Physical, Speech/Language and Respiratory Therapy,
- Home Health,
- Nurse Practitioner,
- Home Delivered Meals, and
- Non-Medical Transportation.

Additional information about provider enrollment will be forthcoming in future editions of the *Provider Update* and on the OAAS website at http://www.dhh.louisiana.gov/offices/?ID=105.

Remittance Advice Corner

The following is a compilation of messages that were recently transmitted to providers through Remittance Advices (RA):

Attention Providers of Immunizations

Effective with dates of service January 1, 2011 and forward, providers should no longer use procedure codes 90465, 90466, 90467 and 90468 to report immunization administration services as they have been deleted from the 2011 Current Procedural Terminology (CPT) manual and therefore these codes will be in non-payable status. Providers should continue to use procedure codes 90471, 90472, 90473 and 90474 per current Louisiana Medicaid policy to report all immunization administration services. At this time Louisiana Medicaid will not be using new immunization administration CPT codes 90460 and 90461, and these two new procedure codes will be in non-payable status. Contact Molina Provider Relations at (800) 473-2783 or (225) 924-5040 with any questions.

Attention Dental Providers

Effective for dates of service on or after January 1, 2011, the dental procedure code D0272 will be reim bursable by Medicaid in the Early and Periodic Screening, Diagnosis and Treatment (EPSDT) Dental Program only once a year. Complete details can be located on the www.lamedicaid.com website under the "Dental Providers" link. Contact the LSU Dental Medicaid Unit at (504) 941-8206 or 1-866-263-6534 (toll-free) with any questions.

Attention Professional Service Providers
Pediatric Critical Care Codes Omitted from 9/22 and 10/6 Claim Adjustments

It has come to our attention that some claims for pediatric critical care codes were omitted from the systematic budget adjustments that occurred on the 9/22/10 and 10/6/10 RAs. Please note that the fees for these codes were implemented correctly and have been reimbursing appropriately since that time. Claims that required adjustment due to delayed implementation of the fee changes were not performed systematically. Providers wishing to adjust their claims can do so on an individual basis. Please contact the Provider Relations unit at (800) 473-2783 or (225) 924-5040 with questions concerning this issue and for assistance with adjustment of claims if needed.

Attention Professional Services Providers
Procedure Codes Payable to Optometrists (Updated 12/30/10)

The Department recently updated programming logic for procedure codes payable to optometrists effective for dates of service Jan 1, 2007 forward. Claims that previously denied with errors 210 "PROVIDER NOT CER-TIFIED FOR THIS PROCEDURE", 298 "INVALID PROCEDURE CODES FOR DATE OF SERVICE," and 299 "PROC/DRUG NOT COVERED BY MEDICAID" were systematically adjusted on the RA of December 21, 2010. As a result of this update, claims for eyeglasses (V codes) inadvertently denied on the RAs of 12/14/10, 12/21/10, 12/28/10 and 1/4/11. We are working to repair this issue so that claims should process correctly on the RA of 1/11/11. Claims that previously denied due to this issue will be systematically adjusted on the RA of 1/11/11. Continue to monitor www.lamedicaid.com and weekly RAs for further updates. Please contact the Provider Relations unit at (800) 473-2783 or (225) 924-5040 with questions concerning this issue.

Attention Immunization Pay-for-Performance Providers

Effective immediately, CommunityCARE PCPs participating in the Immunization Pay-for-Performance (P4P) initiative are encouraged to enter the Medicaid ID numbers of children linked to their practice into the 'Demographics' page of the LINKS Immunization Registry. The Medicaid ID number along with the currently used Social Security Number (if present), name and date of birth will assist Medicaid in ensuring Medicaid eligible children are matched with their corresponding LINKS immunization record (if present) for use in the P4P incentive payment calculation. For assistance with questions related to the LINKS registry, contact the OPH Immunization Consultant for your region (see https://linksweb.oph.dhh.louisiana.gov/linksweb/main.jsp) or call the OPH Immunization Office at (504) 838-5300. For assistance with questions not related to LINKS, contact Molina Provider Relations at (800) 473- 2783 or (225) 924-5040.

Attention Hospital Providers
Reimbursement of Vagus Nerve Stimulators (VNS)

Effective June 14, 2010, a PA-01 Form is no longer required for hospital providers for the VNS device. However, reimbursement of the device continues to be dependent upon approval of the surgeon to perform the procedure. Hospitals should confirm that the surgeon has received an authorization for the procedure prior to submitting their claim in order to prevent denials.

The hospital will bill their VNS claim using HCPCS procedure code C1767 (VNS generator) and/or C1778 (VNS leads) to Molina on a CMS 1500 claim form with the words DME written in red on the top of the form. The claim will pend to the Molina Medical Review Department for review of the surgeon's approved PA request. If approved, the hospital claim will be allowed to process for payment; if there is no valid authorization, the hospital claim will deny with edit 191 (PA required).

If the recipient is a Chisholm class member, the authorization for the device will be referred to PAL to assist the recipient in obtaining the necessary documentation to process the request. This may include identifying the surgeon to contact in order to assist with the submission of his/her prior authorization request.

All Providers

Online Medicaid Provider Manual Chapters

The following Medicaid Provider Manual Chapters are available on the Louisiana Medicaid website at www.lamedicaid.com under the "Provider Manual" link.

- Administrative Claiming
- Adult Day Health Care Waiver
- Ambulatory Surgical Centers
- American Indian 638 Clinics
- Dental
- Durable Medical Equipment
- Elderly and Disabled Adult Waiver
- Family Planning Waiver (Take Charge)
- Federally Qualified Health Centers
- Home Health
- ICF/DD
- Medical Transportation
- Mental Health Clinics
- Mental Health Rehabilitation
- Multi-Systemic Therapy
- Personal Care Services
- Pharmacy
- Psychological Behavioral Services
- Rural Health Clinics

This list will be updated periodically as other Medicaid program chapters become available online.

Durable Medical Equipment Providers

Standardized Seating Evaluation Form Issued

The Medicaid Durable Medical Equipment Program has issued a standardized wheelchair evaluation form to be used with all power or motorized wheelchair requests. A completed Medicaid Power Wheelchair Evaluation Form (PWC-Form-1) is now required for the seating evaluation requirement on all prior authorization requests for power or motorized wheelchairs.

Beginning March 1, 2011, Molina's Prior Authorization Unit will deny all prior authorization requests for power or motorized wheelchairs that do not include the PWC-Form-1. Therefore, providers should begin using the new form immediately when developing their requests.

A copy of the PWC-Form-1 is available at www.lamedicaid.com following the Forms/Files/User Guides link. Questions regarding the use of this new form should be directed to Rene Huff at (225) 342-3935.

Pharmacologic Management of Epilepsy

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Introduction

Epilepsy is a chronic neurological disorder resulting in recurrent, unprovoked seizures, with or without convulsions.[1, 2] Almost 3 million people in the United States suffer from epilepsy, inclusive of more than 300,000 school children through age 15 and more than 300,000 persons over the age of 65.[3] The exact cause of epilepsy in nearly 80% of patients is unknown (idiopathic or cryptogenic etiology), but some identifiable causes include stroke, trauma, brain tumors, infections, and degenerative disorders.[4] Epilepsy is readily treatable; however to date, it remains a challenge. Patients are often unaware of their seizures and may significantly underestimate the number of seizures that occur, especially those that occur during sleep or that disrupt consciousness.[5]

Pathophysiology

A seizure results when there is an abnormal firing of a group of neurons in the cerebral cortex or from a sudden imbalance between the excitatory and inhibitory forces within the network of cortical neurons in favor of a sudden-onset net excitation.

Classification of Seizures

The International League Against Epilepsy (ILAE) developed an international classification system to identify epileptic seizures according to site of origin within the brain (see Table 1).[1,7] Seizures are initially divided into two major classes, partial seizures and generalized seizures, based on their clinical and electroencephalogram (EEG) presentations. Partial seizures begin in a focal or localized area of the cerebral cortex (one hemisphere), whereas generalized seizures involve both cerebral hemispheres. Not all seizure types can be classified as partial or generalized. The subtypes of partial seizures were revised in 2010 and because of the difficulty in scientifically defining these subtypes, the authors of the classification system recommend only using these as descriptive terms if needed for treatment or research purposes and emphasize that the subtypes are not natural classes of seizures.[6]

Table 1: ILAE International Classification of Epileptic Seizures with General Descriptions of Seizures [1, 7]

Seizure Type	General Description
Partial seizures	Involve one hemisphere of the brain at onset, focal
Simple	Consciousness not impaired, clinical manifestation related to area involved
Complex	Consciousness impaired
Secondarily generalized	Simple or complex partial seizures evolving into generalized tonic-clonic seizures or simple seizures evolving into complex partial seizures, then to generalized tonic-clonic seizures
Generalized seizures	Involve both hemispheres of the brain at onset
Absence	Brief loss of consciousness; consist of staring spells, unresponsiveness, eyelid fluttering, lip smacking, twitching of hands, or mouth
Myoclonic	Brief shock-like muscular contractions of the face, trunk
Tonic	Results in mainly muscle stiffness and rigidity
Clonic	Rhythmic jerking movements of the arms and legs
Tonic-clonic	Sudden loss of consciousness; violent muscle contractions, post-ictal exhaustion, sleep disorientation, incontinence
Atonic	Sudden loss of postural muscle tone
Unclassified seizures	Cannot be classified as partial or generalized

Pharmacotherapy

Management of patients with epilepsy focuses on three main goals: controlling seizures, avoiding treatment side effects, and maintaining or restoring quality of life. In selecting an antiepileptic drug (AED) that is most appropriate for the individual patient, it is important to consider: seizure type, side effects, patient profile (e.g., sex, age, and childbearing potential), ease of medication use, and cost.[8] A balance between efficacy, tolerability, and safety must be obtained. Overall, up to 80 percent of patients can become seizure free on AED treatment.[9, 10] Epilepsy may be a lifetime diagnosis for some patients (e.g., mentally challenged, inoperable brain tumors, etc), but antiepileptic therapy is not necessarily lifelong.

AED therapy is as likely to fail from adverse effects of medication as from lack of efficacy.[11] To effectively evaluate therapeutic outcomes, patients should be monitored for seizure control, side effects, social adjustment, drug interactions, adherence, quality of life, and toxicity. Monotherapy with AEDs is preferred and combination AED therapy should be considered only after a patient has failed at least 2 AEDs in monotherapy. A 2005 survey by experts in the field of epilepsy attempted to determine which treatment options might be best in a number of clinical situations (idiopathic generalized epilepsy and symptomatic localization- related epilepsy). Figure 1a demonstrates findings related to an overall treatment strategy for idiopathic generalized epilepsy and Figure 1b demonstrates findings related to an overall treatment strategy for symptomatic localization-related epilepsy.[12]

Figure 1a: Overall Strategy for Idiopathic Generalized Epilepsy[12]

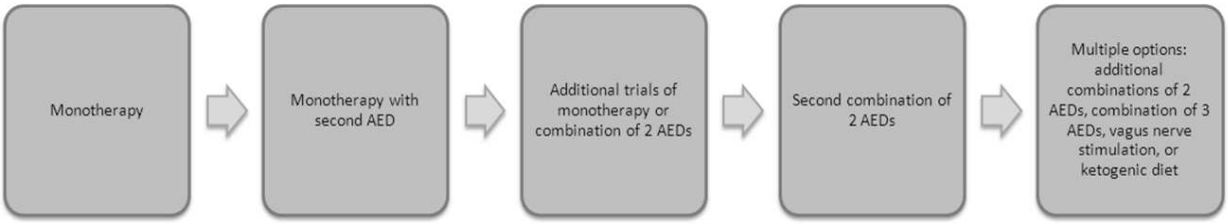
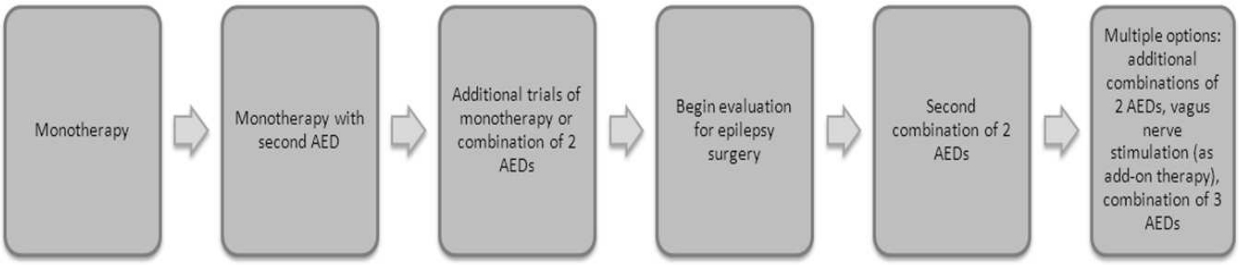


Figure 1b: Overall Strategy for Symptomatic Localization-Related Epilepsy[12]



The mechanism of action of many AEDs is not well understood and several AEDs act via multiple mechanisms. However, antiepileptic drugs can be divided into 9 groups based upon their proposed mechanisms of action: [7,13]

1. Blockers of repetitive activation of sodium channel - phenytoin, carbamazepine, oxcarbazepine, lamotrigine, topiramate
2. Enhancer of slow inactivation of sodium channel - lacosamide
3. GABA-A receptor enhancers - phenobarbital, benzodiazepines
4. Glutamate modulators - topiramate, lamotrigine, felbamate
5. Calcium channel blockers:
   T-calcium channel blockers - ethosuximide, valproate
   N- and L-calcium channel blockers - lamotrigine, topiramate, zonisamide, valproate
6. H-current modulators - gabapentin, lamotrigine
7. Blockers of unique binding sites - gabapentin, levetiracetam
8. Inhibition of GABA-T - vigabatrin
9. Carbonic anhydrase inhibitors - topiramate, zonisamide

Detailed information on labeled indications, dosing, and selected adverse effects for each AED is provided in Tables 2a and 2b. Table 3 summarizes selected pharmacokinetic parameters (half-life and target serum concentration) for individual AEDs.

Table 2a: Antiepileptic Drugs with Generics Available[13]

Medication	Labeled Indication (seizure type)	Adult Dosage Range: Usual Initial mg/d (Max mg/d)	Selected Adverse Effects & Boxed Warnings
Carbamazepine (CBZ) (Carbatrol®, Tegretol®)	Tonic-clonic, complex partial, mixed	400 (1600 divided BID-QID)	Diplopia, drowsiness, nausea, sedation, hyponatremia (**Boxed Warnings**: blood dyscrasias, dermatologic reactions)
Ethosuximide (Zarontin®)	Absence	500 (1500 in divided doses)	Ataxia, aggressiveness, sedation, rash, headache, abdominal pain
Gabapentin (Neurontin®)	Adjunctive therapy partial with and without secondary generalization	900 (2400 divided TID)[a]	Drowsiness, sedation, dizziness , ataxia, fatigue
Lamotrigine (Lamictal®)	Partial, tonic-clonic, adjunctive	25 (225-375 divided BID)[a,b,c]	Ataxia, dizziness, diplopia, headache, nausea, vomiting (**Boxed Warnings**: Life-threatening skin rash)
Levetiracetam (Keppra®)	Adjunctive therapy with tonic-clonic, myclonic, partial	1000 (3000 divided BID)[a]	Somnolence, dizziness, headache, behavior symptoms
Oxcarbazepine (Trileptal®)	Partial	600 (1200 divided BID)	Diplopia, somnolence, dizziness, headache, tremor, nausea, vomiting
Phenobarbital (C-IV)	Tonic-clonic, partial	1-3 mg/kg/d (50-100 mg BID-TID)	Sedation, cognitive impairment, ataxia, headache, hyperactivity, attention deficit behavior, mood changes, sleep problems, rash
Phenytoin (Dilantin®, Phenytex®)	Complex partial, generalized tonic-clonic , prevention of seizures following head trauma/neurosurgery	5-6 mg/kg/d (divided TID)	Nystagmus, ataxia, cognitive impairment, lethargy, sedation, fatigue, headache, dizziness, behavior changes, visual blurring, gingival hyperplasia, hirsutism, coarsening of facial features, acne, folate deficiency, rash (**Boxed Warnings IV**: hypotension)
Primidone (Mysoline®)	Generalized tonic-clonic, partial	100-125 (2000 divided TID or QID)	Anemia, granulocytopenia, agranulocytosis
Topiramate (Topamax®)	Monotherapy or adjunctive therapy partial, or generalized tonic-clonic	25-50 (200 BID)[a]	Sedation, confusion, mental slowing, word-finding difficulty, anorexia, serum bicarbonate decreased
Valproic Acid (Depakene®, Stavzor®-delayed capsules) Divalproex sodium (Depakote®)	Complex partial, absence	10-15 mg/kg/d (60 mg/kg/d)	GI upset, headache, lethargy, tremor, thrombocytopenia, sedation, alopecia (**Boxed Warnings**: hepatic failure, pancreatitis, pregnancy)
Zonisamide (Zonegran®)	Adjunctive therapy partial	100-200 (400 QD)	Somnolence, ataxia, fatigue, anorexia, dizziness, headache

Abbreviations: BID-twice daily; QD-once daily; QID-four times daily; TID-three times daily; VPA-valproic acid; C-IV-Schedule IV controlled substance

[a]Dosage adjustment needed in renal impairment

[b]Dosage adjustment needed in hepatic impairment

[C]Dosage adjustment needed if taken in conjunction with other AEDs.

Table 2b: Antiepileptic Drugs-Generics Not Available[13]

Medication	Labeled Indication (seizure type)	Adult Dosage Range: Usual Initial mg/d (Max mg/d)	Selected Adverse Effects & Boxed Warnings
Felbamate (Felbatol®)	Partial, with or without generalization	1200 (3600 divided TID or QID)	Anxiety, insomnia, nausea, anorexia, headache, dizziness, somnolence (**Boxed Warnings**: aplastic anemia, hepatotoxicity)
Lacosamide(Vimpat®) (C-V)	Partial (adjunct)	100 (400 divided BID)[a,b]	Ataxia, dizziness, diplopia, headache, nausea, PR interval prolongation
Pregabalin (Lyrica®) (C-V)	Partial (adjunct)	150 (600 divided BID or TID)[a]	Ataxia, blurred vision, dizziness, nausea, headache, somnolence, peripheral edema, weight gain
Tiagabine (Gabitril®)	Partial (adjunct)	4 (56 divided BID to QID)	Dizziness, somnolence, irritability, slowed thinking, exacerbation of generalized seizures
Vigabatrin (Sabril®)[c]	Refractory complex partial	1000 (3000 divided BID)[a]	Seizure, dizziness, headache, insomnia, tremor, pharyngitis, somnolence, weight gain (**Boxed Warning**: permanent vision loss)

Abbreviations: BID-twice daily; QID-four times daily; TID-three times daily; C-V-Schedule V controlled substance
[a]Dosage adjustment needed in renal impairment
[b]Dosage adjustment needed in hepatic impairment
[c]Must be obtained via SHARE program - a special restricted distribution program. More information available at www.lundbeckshare.com.

Table 3: Pharmacokinetics of AEDs in Adults[13]

Medication	Half-life (hrs)	Target Serum Concentration (mg/L)
Carbamazepine	25-65 initially then 12-17 after repeated doses [a]	4-12
Ethosuximide	50-60	40-100
Felbamate	20-23	Not established
Gabapentin	5-7	Not established
Lacosamide	13	Not established
Lamotrigine	25-33	Not established
Levetiracetam	6-8	Not established
Oxcarbazepine	~2 (parent drug) 9 (metabolite)	Not established
Phenobarbital	53-140	20-40
Phenytoin	~22 (7-42)	10-20 (total) 1-2.5 (free)
Pregabalin	6.3	Not established
Primidone	5-15	5-12 (must monitor phenobarbital if on both)
Tiagabine	2-5 (with enzyme inducers) 7-9 (without enzyme inducers)	Not established
Topiramate	21	Not established
Valproic acid	9-16	50-100
Vigabatrin	7.5 12-13 (elderly)	Not established
Zonisamide	~63	Not established

[a] Half-life is variable because of autoinduction which is usually complete 3-5 weeks after initiation of a fixed carbamazepine regimen

Special Topics

Generic Substitution of AEDs

Generic substitution is allowed if medications are bioequivalent (A-rated) as determined by the FDA. This determination always involves comparing the generic to the reference listed drug (RLD), which is usually the brand-name drug. To be considered A-rated, the 90% confidence interval for maximum concentration (Cmax) and area under the curve (AUC) must be within 80 to 125% of the values listed for the RLD. Therefore, two generic versions of the same drug could have as much as a 45% difference in AUC and Cmax and still be considered bioequivalent.[14]

A small number of case reports and national surveys of patients with epilepsy and physicians treating epilepsy, like those reported by Berg, et al. in 2008, suggest that generic substitution of antiepileptic drugs is a potential problem.[15, 16] As reported by Berg et al., results of a survey of physicians who treat patients with epilepsy (n=606) and adult patients with self-reported epilepsy (n=550) indicated that 75% of physicians and 65% of patients reported concern over the efficacy of generic medications, 88% of physicians reported a specific concern that generic interchange in controlled patients could result in a breakthrough seizure, and 65% of physicians reported they had cared for a patient who had experienced a breakthrough seizure that could be associated with a switch from a branded to a generic agent.[16] In a second study, Berg et al. reported results of a chart audit survey completed by neurologists of 50 cases where loss of seizure control was attributed to generic AED interchange. In 21 or 26 cases where data were available for comparison, AED levels were on average 33% lower at the time of the seizure (on generic AED) as compared to the AED level at baseline (on brand AED). [15]

Further evidence that generic interchange is a potential problem is seen in three large case-control studies that found A-rated antiepileptic drug substitution was a risk factor for emergency or hospital-level treatment of epilepsy (OR: 1.78 to 1.81).[17-19] Studies using medical and pharmacy claims databases have found that generic interchange of AEDs is associated with higher epilepsy-related medical utilization rates, such as hospitalizations.[20-22]

In contrast, a meta-analysis of 7 randomized controlled trials (n=204) found no difference in the chance of a patient on generic AEDs experiencing loss of seizure control compared to patients taking brand-name medications (aggregate odds ratio: 1.1, 95% CI 0.9, 1.2). The drugs in these trials included brand-name and generic versions of carbamazepine (5 studies), phenytoin (3 studies) and valproic acid (1 study). Although these studies were primarily short in duration and in small patient populations, they suggest that for most patients, generic substitution is not associated with increased risk of seizures.[23]

Generic substitution is often not avoidable, since generic medications are usually less expensive and sometimes required by insurance providers. For many patients, use of generic medications presents no problems. However, variations in pharmacokinetics between brand-name drugs and their generic equivalents, and within generics, as allowed by the FDA can result in breakthrough seizures or toxicity for a subset of patients.[24-27] Patients at higher risk include elderly patients, patients with liver or kidney disease, comorbid conditions, and patients taking medications that may interact with AEDs, leading to altered AED pharmacokinetics.[26] The Epilepsy Foundation issued a position statement in 2009 recommending that both the physician and patient be informed if interchange occurs.[28]

Pharmacists can be a key resource for patients and physicians by providing information on generic availability of AEDs and by recognizing changes in generic manufacturers. Providing this information allows patients and physicians to monitor for possible changes in efficacy or side effects which may be attributable to AED substitution.

Suicidality and AEDs

An increased risk of suicidal behavior and ideation has been linked to several AEDs in randomized placebo-controlled studies of patients with epilepsy according to a January 2008 FDA report.[29] The FDA's actions are based on the agency's review of 199 clinical trials of 11 AEDs.[30] The elevated risk (0.43 versus 0.24 %) was observed as early as one week after starting medication and continued though the 24 weeks of study observation.[31] The effect was consistent in the 11 AEDs studied (carbamazepine, felbamate, gabapentin, lamotrigine, levetiracetam, oxcarbazepine, pregabalin, tiagabine, topiramate, valproate, and zonisamide), and the FDA considers this risk likely to be shared by all AEDs. A literature review that was not affiliated with the FDA estimated that the overall standardized mortality ratio for suicide was 3.3. This increased risk appeared to be present among most subgroups of individuals with epilepsy.[32] The FDA has required updated labeling for these AEDs and medication guides describing the increased risk are required to be provided to patients at the time of dispensing. Updated medication guides are currently available for AEDs through the FDA website.[33]

Conclusion

- Individual patient characteristics (eg, age, sex, type of seizures, health insurance coverage, etc) must be considered when choosing an AED.
- Potential side effects and drug interactions should also be carefully considered.
- Monotherapy with an appropriate AED is the preferred treatment when possible.
- Pharmacists can play an important role by providing physicians, patients, and other healthcare professionals with information about potential side effects and available AEDs, especially as new agents and new generics become available.

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