### Anticonvulsant Step Therapy Criteria with Medical Diagnoses Option

**FDA APPROVED INDICATIONS AND DOSAGE**

<table>
<thead>
<tr>
<th>Drug</th>
<th>PO Seizures</th>
<th>GTC Seizures</th>
<th>Other Seizures</th>
<th>Non-Seizure</th>
<th>Dosing</th>
</tr>
</thead>
</table>
| Keppra** (levetiracetam) tablets, solution, injection | ✓ | ✓ | ✓ | MC | Doses/Day – 2 divided doses  
  Adult: Start 1000 mg/day; maximum of 3000 mg/day.  
  PO (Ages 4-15), GTC seizures (Ages 6-15): Start 20 mg/kg/day; maximum dose 60 mg/kg/day  
  Injectable: Start 500 mg twice daily; maximum recommended daily dose of 3000 mg. |
| Keppra XR (levetiracetam) tablets | ✓ | | | | Doses/Day – 1 daily dose  
  PO seizures - Age ≥16: Start 1000 mg/day; maximum -3000 mg/day |
| Lamictal** (lamotrigine) tablets, chewable tabs, ODT (oral disintegrating) tablets | ✓ c,d | ✓ c | ✓ c | LG | Doses/Day – 1-2 divided doses for initial and lower doses; 2 doses/day for higher doses  
  Seizures:  
  Adult - Start 25 - 50 mg every or every other day; maximum dose range 100 – 500 mg daily  
  Age 2-12 - Start 0.15 – 0.6 mg/kg/day; maximum dose range 1 – 15 mg/kg/day  
  BPD: Start 25 - 50 mg every or every other day; maximum dose range 100 – 400 mg daily  
  Dosing depends on concomitant use of other medications, including valproic acid and enzyme-inducing drugs. ab |
| Lamictal XR (lamotrigine) tablets | ✓ f | ✓ f | | | Doses/Day – 1 daily dose  
  Seizures:  
  Start 25 - 50 mg every or every other day; maximum dose range 200 – 600 mg daily  
  Dosing depends on concomitant use of other medications, including valproic acid and enzyme-inducing drugs. ab |
| Lyrica (pregabalin) capsules, solution | ✓ | | | | Doses/Day – 2-3 divided doses  
  Seizures: (Adults) Start at 150 mg/day; titrate up to maximum of 600 mg/day.  
  DPN: Start 150 mg/day; maximum - 300 mg/day  
  PHN: Start 150 mg/day; maximum - 600 mg/day  
  FM: Start 150 mg/day; maximum - 450 mg/day |
| Topamax** (topiramate) tablets, capsules | ✓ g | ✓ g | ✓ g | LGS | Doses/Day – 2 divided doses  
  Seizures:  
  Monotherapy – Adults: Start 50 mg/day; target dose 400 mg/day.  
  Adjuunctive therapy - Adults: Start 25-50 mg/day; target of 200-400 mg/day  
  Adjuunctive therapy - Pediatrics: Start ≤25 mg nightly (1-3 mg/kg/day) for first week; titrate to target of 5-9 mg/kg/day.  
  MP: Start 25 mg nightly for first week; titrate to target of 100 mg/day. |
<table>
<thead>
<tr>
<th>Drug</th>
<th>PO Seizures</th>
<th>GTC Seizures</th>
<th>Other Seizures</th>
<th>Non-Seizure</th>
<th>Dosing</th>
</tr>
</thead>
</table>
| **Trileptal** (oxcarbazepine) tablets, suspension | ✓ | h | | | Doses/Day – 2 divided doses.  
**Adults:** Start 600 mg/day; titrate to 1200 mg – 2400 mg/day.  
*Dosing depends on adjunctive or monotherapy use and previous use of other anticonvulsants.*  
**Pediatrics:** Start 8-16 mg/kg/day, not exceed 600 mg/day for adjunctive therapy; target dose range of 600 mg/day to 2100 mg/day, not to exceed 60 mg/kg/day for age 2-3  
*Pediatric dosing is age and weight based.* |
| **Vimpat** (lacosamide) tablets, injection | ✓ | i | | | Doses/Day – 2 divided doses.  
**PO seizures:** Start 100 mg/day; titrate to 200-400 mg/day. |

GTC=generalized tonic-clonic, PO=partial onset, LGS=Lennox-Gastaut syndrome, BPD=bipolar disorder, DPN=diabetic peripheral neuropathy, PHN=post-herpetic neuralgia, FM=fibromyalgia, MP=migraine prevention, MC=myoclonic, AEDs=antiepileptic drugs  
*adjunctive treatment**  
**generics available**

**a= Valproate has been shown to inhibit glucuronidation, decreasing apparent clearance of lamotrigine.**  
**b= Carbamazepine, phenytoin, phenobarbital, primidone, or primidone induce glucuronidation and increase clearance. Other drugs with similar effects include estrogen containing oral contraceptives. Patients on rifampin or other drugs that induce glucuronidation should follow the same dosing format.**  
**c=Lamictal is indicated for adjunctive therapy in patients age ≥2 for partial seizures, primary generalized tonic clonic seizures, and Lennox-Gastaut seizures.**  
**d=Lamictal is indicated for conversion to monotherapy in patients with partial seizures age ≥16 who are receiving treatment with carbamazepine, phenobarbital, phenytoin, primidone, or valproate as the single antiepileptic drug.**  
**e=Lamictal is indicated for bipolar disorder maintenance treatment in patients age ≥18 to delay time to occurrence of mood episodes in patients treated for acute mood episodes with standard therapy.**  
**f=Lamictal XR is indicated as adjunctive therapy for primary generalized tonic clonic seizures and partial onset seizures with or without secondary generalization in patients ≥13 years of age.**  
**g=Topamax is indicated as monotherapy in patients age ≥10 with partial onset or primary generalized tonic clonic seizures. Topamax is also indicated as adjunctive therapy for adults and pediatric patients (age 2-16) with partial onset seizures or primary generalized tonic-clonic seizures; and in patients age ≥2 with seizures associated with Lennox-Gastaut syndrome.**  
**h=Trileptal is indicated for use as monotherapy or adjunctive therapy in treatment of partial seizures in adults; and as monotherapy in treatment of partial seizures in children age ≥4, and as adjunctive therapy in children age ≥2.**  
**i=Vimpat is indicated for adjunctive therapy of partial onset seizures in patients age ≥17.**
Epilepsy

Epilepsy is a varied disorder with many causes ranging from genetic causes through to acquired brain damage and insults. Disease outcomes are also heterogeneous. Most people have a relatively short-lasting susceptibility to seizures and enter remission shortly after starting treatment on small doses of anticonvulsants. However, 20-30% of people who develop epilepsy will have chronic epilepsy that responds incompletely to one anticonvulsant, and will require treatment with one or more drugs through their life.14

Based on guidelines from the American Academy of Neurology (AAN) and the American Epilepsy Society, and the International League Against Epilepsy (ILAE), as well as current product labeling, the chart below was developed.11-13

<table>
<thead>
<tr>
<th>Antiepileptic Drug Selection by Seizure Type</th>
<th>First or Alternative Monotherapy (Alphabetical Order)</th>
<th>Useful Combinations (Any A + Any B)</th>
<th>Other Useful Alternatives (Monotherapy or Polytherapy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Partial seizures (complex or simple) with or without secondarily generalized seizures</td>
<td>Carbamazepine (CBZ) Lamotrigine (LTG) Levetiracetam (LEV) Oxcarbazepine (OXC) Phenytoin (PHT) Topiramate (TPM) Valproate (VPA) Zonisamide (ZNS)</td>
<td>CBZ LTG OXC PHT GBP LEV TPM VPA ZNS</td>
<td>Acetazolamide (ACZ) Clorazepate (CLZ) Clonazepam (CLN) Phenobarbital (PB) Primidone (PRM) Felbamate (FBM) Vigabatrin (VIG)</td>
</tr>
<tr>
<td>Tonic clonic seizures, tonic seizures, atonic seizures</td>
<td>Carbamazepine Lamotrigine Levetiracetam Oxcarbazepine Phenytoin Topiramate Valproate Zonisamide</td>
<td>CBZ LTG OXC PHT LEV TPM VPA ZNS</td>
<td>Acetazolamide Clorazepate Clonazepam Felbamate (FBM) Phenobarbital Primidone</td>
</tr>
<tr>
<td>Absence seizures</td>
<td>Ethosuximide (ETH) Lamotrigine Valproate Topiramate</td>
<td>LTG VPA ACZ CLN ETH TPM</td>
<td>Acetazolamide Clonazepam Phenobarbital Primidone</td>
</tr>
<tr>
<td>Myoclonic seizures</td>
<td>Clonazepam Valproate Zonisamide Levetiracetam</td>
<td>VPA CLZ ZNS LEV</td>
<td>Phenobarbital Lacosamide (LCO)</td>
</tr>
</tbody>
</table>

Neuropathic Pain

Pregabalin is also FDA approved for treatment of pain associated with diabetic peripheral neuropathy (DPN) and post-herpetic neuralgia (PHN). In clinical studies treatment with pregabalin was associated with >50% reductions in patient reported pain scores compared with placebo in DPN and PHN. There are no trials comparing pregabalin with other agents used to treat diabetic DPN or PHN.15,16

Dworkin et al.26 states that most randomized controlled trials of chronic neuropathic pain have examined only two pain syndromes, DPN and PHN. These authors suggest that while the applicability of the results of clinical trials for one chronic neuropathic pain syndrome to others
cannot be determined, most of the first-line therapies have been tested with multiple types of neuropathic pain and have shown similar results.26

Generally, guidelines and reviews on treatment of neuropathic pain have not been consistent regarding their placement of anticonvulsants as first-, second-, or third-line treatment. Some guidelines and reviews recommend pregabalin and gabapentin [off-label] as first- or second-line treatment. Carbamazepine and lamotrigine [both off-label] have been considered second- or third-line treatments for neuropathic pain. Tricyclic antidepressants (e.g. amitriptyline) are often recommended as a first-line treatment for neuropathic pain.17-33

**Fibromyalgia**
A variety of pharmacologic and nonpharmacologic treatments are offered to patients diagnosed with fibromyalgia syndrome. To date no therapy has proven effective for the entire scope of symptoms and disabilities associated with fibromyalgia.49

A difficulty of assessing therapeutic options for individual fibromyalgia patients is that many of the clinical trials have not accounted for the heterogeneity of fibromyalgia. The presence of comorbidities (e.g. depression) may predict a poor response to treatment. A number of treatments have shown clinical benefit versus placebo, although frequently not in the majority of patients studied. Non-drug approaches (e.g. pool based exercise, aerobics, strength training, physiotherapy, etc) are considered by many physicians to be among the most useful fibromyalgia treatments. Data suggest that when it comes to fibromyalgia therapy there has been a lack of standardization in approach to trials and outcome measures used.50

The heterogeneity of fibromyalgia makes a “one size fits all” approach unlikely to be broadly efficacious. Most fibromyalgia patients exhibit multiple symptoms in addition to pain and tenderness, and therefore require simultaneous treatment for multiple aspects of their illness. While use of combination therapy may offer the best hope in treatment of fibromyalgia, almost all clinical trials for fibromyalgia have tested only single therapies. Fibromyalgia treatment choices are made empirically, informed whenever possible by evidence.50

A meta-analysis (2009) on treatment of fibromyalgia with antidepressants found strong overall evidence for an association of antidepressants with reduction in pain, fatigue, and sleep disturbances, and improvements in health-related quality of life. Effect sizes for pain reduction were large for tricyclic antidepressants (e.g. amitriptyline), medium for monoamine oxidase inhibitors, and small for selective serotonin reuptake inhibitors [SSRIs] (e.g. fluoxetine) and serotonin-norepinephrine reuptake inhibitors [SNRIs] (e.g. duloxetine, milnacipran).52

Systematic reviews and guidelines on treatment of fibromyalgia suggest there are several pharmacologic agents available generically for treatment of this condition. A systematic review (2009) compared recommendations from three evidence based guidelines published by professional organizations on the management of fibromyalgia. See chart below.51
Because evidence for the long-term effects of drugs in treatment of fibromyalgia are lacking, patients should be reevaluated at regular intervals considering the benefits versus side effects of the drug, and if benefits no longer exist, the drug should be discontinued.49

Three agents are FDA approved for treatment of fibromyalgia in the United States: milnacipran (Savella, an SNRI), duloxetine (Cymbalta, an SNRI), pregabalin (Lyrica, an anticonvulsant). Separate clinical trials have shown benefits of these drugs versus placebo through use of varied primary endpoints. The lack of data comparing safety and efficacy of these drugs with each other and with other treatments for fibromyalgia makes it difficult to determine their role in therapy.

The efficacy of pregabalin for management of fibromyalgia was shown in several clinical trials.34-36 The information available shows that pregabalin doses of 300 mg, 450 mg, and 600 mg daily provide a significant improvement in pain score, with evidence of improvement in as early as one week.34-36 The reported response rate varied from about 30% to 60%; the placebo response in studies was also very high. There was no evidence of a greater effect on pain scores for the 600 mg daily dose versus the 450 mg daily dose, but there was evidence of dose-dependent adverse reactions;5,36 in view of these dose-dependent adverse effects, treatment with doses above 450 mg per day are not recommended.5 Gabapentin is structurally similar to pregabalin and has been used off-label for fibromyalgia.53 Comparative safety and efficacy of pregabalin and gabapentin in treatment of fibromyalgia is unclear.

**Migraine Prophylaxis**

Topiramate is indicated for the prophylactic treatment of migraine headache.6 The European Federation of Neurological Societies (EFNS) guidelines from 2009 support the use of β-blockers (propranolol and metoprolol), calcium channel blockers, and valproate as first-line prophylactic agents, as well as topiramate. Amitriptyline, naproxen, and bisoprolol are listed as second choices.39 One review (Silverstein, 2009) lists the following as agents with high efficacy: propranolol, timolol, amitriptyline, valproate, topiramate, flunarizine. This review considers the following to have some efficacy: NSAIDs, atenolol, metoprolol, nadolol, verapamil, gabapentin.37 Medical Letter treatment guidelines (2008) suggest menstrual or other predictable migraine attacks may be prevented by a brief course of NSAID, ergot alkaloid or triptan. For continuous prophylaxis, beta-blockers are commonly used; propranolol and timolol are FDA approved, but metoprolol, nadolol, and atenolol also have been effective. Antiepileptic drugs such as valproate and topiramate have been effective in decreasing migraine frequency in 50% of patients; gabapentin has been used with varying degrees of
A Cochrane review (2004) of anticonvulsant agents for migraine prophylaxis states that valproic acid/sodium valproate has proven efficacy for this use. This review suggested that gabapentin needed further evaluation and that topiramate had reasonable evidence to support its use.

Bipolar Disorder
Lamotrigine is indicated for the maintenance treatment of bipolar I disorder to delay the time to occurrence of mood episodes (depression, mania, hypomania, mixed episodes) in patients treated for acute mood episodes with standard therapy. Although prescribing information states effectiveness of lamotrigine for acute treatment of mood episodes has not been established, several guidelines list lamotrigine as part of first line treatment for acute depressive episodes of bipolar disorder, as well as maintenance treatment. Texas Medication Algorithm Project (TMAP, 2007) guidelines on treatment of bipolar patients with a depressive episode suggest that if depressive symptoms persist after mood stabilizer treatment is optimized, lamotrigine is recommended as a first line medication for depression. Lamotrigine monotherapy is recommended as a first line option only for those patients without a recent and/or severe history of manic symptoms. Other patients should receive lamotrigine plus a mood stabilizer.

For patients presenting with euphoric mania/hypomania or psychotic mania, TMAP (2007) guidelines suggest first-line medication choices are lithium, valproate, aripiprazole, quetiapine, risperidone, and ziprasidone. Lithium is also recommended as first line adjunctive treatment of bipolar depression in patients with history of mania, and is recommended among the first line agents for maintenance treatment of bipolar disorder.

Guidelines include carbamazepine and/or oxcarbazepine mostly as alternative first line, and second or third line treatment choices for acute manic/mixed episodes of bipolar disorder, third line for acute bipolar depression, and second or third line for maintenance treatment. The TMAP consensus panel placed carbamazepine as a potential monotherapy option within a first line sub-category in treatment of acute manic/hypompanic episodes. These sub-category medications have equivalent efficacy as other first line medications, but there are concerns about greater potential adverse events or complexity associated with treatment that makes them not a first choice. Carbamazepine stimulates its own metabolism as well as that of numerous other psychotropic medications. This creates complexity with its own dosing as well as concomitant medications. Use of oxcarbazepine as a mood stabilizing agent for bipolar disorder is supported as an accepted unlabeled use by the pharmaceutical compendia (American Hospital Formulary Service [AHFS], Clinical Pharmacology, Micromedex).

For additional clinical information see Prime Therapeutics Formulary Chapter 11.1: Anticonvulsants.

REFERENCES


53. Medical Letter. Pregabalin (Lyrica) for fibromyalgia. 2007;49(1270):77-78.

Document History
Original Prime Standard (Topamax and Zonegran) approved by UM Committee 02/2005
Prime Standard 06/05 (Gabitril, Topamax, Zonegran)
Prime Standard criteria approved by External UM Committee 08/2005
Initial Client Review Client Specific Criteria (automatic approval if previous history of selected agents) approved by client 11/2005
Annual Review Prime Standard criteria with changes approved by External UM Committee 08/2006
Client Specific Annual Review Client Specific Criteria approved by HCSC Corporate Clinical Committee 11/2006
Annual Review Prime Standard criteria with changes approved by External UM Committee 05/2007
Mid-year Review Prime Standard criteria with changes, addition of Lyrica fibromyalgia indication, approved by External UM Committee 08/2007
Client Specific Annual Review Client Specific Criteria approved by HCSC Corporate Clinical Committee 09/2007
Annual Review Prime Standard criteria with changes approved by P&T UM Committee 08/2008
Mid-year Review Prime Standard criteria with addition of Keppra XR and generic levetiracetam approved by P&T UM Committee 11/2008
Mid-year Review Prime Standard criteria with addition of Vimpat approved by P&T UM Committee 05/2009
Annual Review Prime Standard criteria with changes approved by P&T UM Committee 11/2009
Client Specific Annual Review Client Specific Criteria with changes approved by HCSC Corporate Clinical Committee 12/2009
Administrative Addition (oxcarbazepine suspension generic as prerequisite) 01/2010
Annual Review Prime Standard criteria with changes approved by P&T UM Committee 05/2010
Client Specific Annual Review Client Specific Criteria with changes approved by HCSC Corporate Clinical Committee 09/2010
Anticonvulsant Step Therapy

OBJECTIVE
The intent of the Anticonvulsant Step Therapy (ST) criteria for the brand products Keppra (levetiracetam), Keppra XR (levetiracetam ER), Lamictal (lamotrigine), Lamictal ODT (lamotrigine orally disintegrating), Lamictal XR (lamotrigine ER), Lyrica (pregabalin), Topamax (topiramate), Trileptal (oxcarbazepine), and Vimpat (lacosamide) is to accommodate their use for the treatment of seizure disorders while encouraging use of other generic medications first for their other labeled and accepted unlabeled indications. The criteria for Lyrica encourage its use for neuropathic pain after trial and failure of generic amitriptyline, nortriptyline, imipramine, desipramine, or gabapentin, and for fibromyalgia after a failure of generic amitriptyline, nortriptyline, imipramine, desipramine, cyclobenzaprine, tramadol, or gabapentin. The criteria for Topamax for migraine prevention encourage prior use of two other less-costly preventative medications, such as a beta-blocker, calcium channel blocker, tricyclic antidepressant, divalproex or valproic acid, or gabapentin. Criteria for Lamictal, Lamictal ODT, Lamictal XR, and Trileptal for bipolar disorder encourage use of generic anticonvulsants indicated for bipolar disorder or lithium as first-line agents. Patients who have received and responded to or are currently receiving and responding to one of these brand anticonvulsants and switching could potentially cause harm or a health risk will be approved for continuation of that agent. These brand anticonvulsants may be considered for other indications if the prescriber submits documentation supporting the intended therapeutic use for the patient.

TARGET DRUGS
Keppra® (levetiracetam)a
Keppra XR® (levetiracetam ER)
Lamictal® (lamotrigine)a
Lamictal ODT® (lamotrigine)
Lamictal XR® (lamotrigine ER)
Lyrica® (pregabalin)
Topamax® (topiramate)a
Trileptal® (oxcarbazepine)a
Vimpat® (lacosamide)
a – generic available; generics are not targeted in this step therapy program

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL
Keppra, Keppra XR, or Vimpat will be approved when ANY ONE of the following is met:
1. The patient has received in the past and responded to or is currently receiving and responding to the requested agent and switching could potentially cause harm or a health risk
   OR
2. The patient has a diagnosis of a seizure disorder or history or current use of another anticonvulsant medication
   OR
3. The patient has a diagnosis other than seizure disorder AND the prescriber has submitted documentation in support of therapy with the requested agent for the intended diagnosis which has been reviewed and approved by the Clinical Review pharmacist
Lamictal, Lamictal ODT, Lamictal XR or Trileptal will be approved when ANY ONE of the following is met:

1. The patient has received in the past and responded to or is currently receiving and responding to the requested agent and switching could potentially cause harm or a health risk
   **OR**
2. The patient has a diagnosis of a seizure disorder or history or current use of another anticonvulsant medication
   **OR**
3. The patient has a diagnosis of bipolar disorder AND ONE of the following:
   a. Trial and failure of at least one of the following: generic anticonvulsant indicated for bipolar disorder or lithium **OR**
   b. History of contraindication, allergy, or intolerance to a generic anticonvulsant indicated for bipolar disorder or lithium **OR**
   c. Prescriber has submitted documentation in support of therapy with the requested agent for the intended diagnosis which has been reviewed and approved by the Clinical Review pharmacist
   **OR**
4. The patient has a diagnosis other than seizure disorder or bipolar disorder AND the prescriber has submitted documentation in support of therapy with the requested agent for the intended diagnosis which has been reviewed and approved by the Clinical Review pharmacist

Lyrica will be approved when ANY ONE of the following is met:

1. The patient has received in the past and responded to or is currently receiving and responding to Lyrica and switching could potentially cause harm or a health risk
   **OR**
2. The patient has a diagnosis of a seizure disorder or history or current use of another anticonvulsant medication
   **OR**
3. The patient has a diagnosis of neuropathic pain AND ONE of the following:
   a. Trial and failure of at least one of the following: amitriptyline, nortriptyline, desipramine, imipramine or gabapentin **OR**
   b. History of contraindication, allergy, or intolerance to one of the above agents **OR**
   c. Prescriber has submitted documentation in support of therapy with Lyrica for the intended use which has been reviewed and approved by the Clinical Review pharmacist
   **OR**
4. The patient has a diagnosis of fibromyalgia AND ONE of the following:
   a. Trial and failure of amitriptyline, nortriptyline, imipramine, desipramine, cyclobenzaprine, gabapentin, or tramadol **OR**
   b. History of contraindication, allergy, or intolerance to one of the above agents **OR**
   c. Prescriber has submitted documentation in support of therapy with Lyrica for the intended use which has been reviewed and approved by the Clinical Review pharmacist
   **OR**
5. The patient has a diagnosis other than seizure disorder or neuropathic pain or fibromyalgia AND the prescriber has submitted documentation in support of therapy with Lyrica for the intended diagnosis which has been reviewed and approved by the Clinical Review pharmacist
Topamax will be approved when ANY ONE of the following is met:

1. The patient has received in the past and responded to or is currently receiving and responding to Topamax and switching could potentially cause harm or a health risk OR
2. The patient has a diagnosis of a seizure disorder or history or current use of another anticonvulsant medication OR
3. The patient has a diagnosis of migraine headache AND ONE of the following:
   a. Trial and failure of a minimum of two of the following prophylactic agents: \(\beta\)-blocker, tricyclic antidepressant, divalproex or valproic acid, gabapentin, or calcium channel blocker OR
   b. History of contraindication, allergy, or intolerance to two or more of the above agents OR
   c. Prescriber has submitted documentation in support of therapy with Topamax for the intended use which has been reviewed and approved by the Clinical Review pharmacist OR
4. The patient has a diagnosis other than seizure disorder or migraine headache AND the prescriber has submitted documentation in support of therapy with Topamax for the intended diagnosis which has been reviewed and approved by the Clinical Review pharmacist

Length of approval: 12 months (indefinite for seizure disorder)
Anticonvulsant Step Therapy

ELECTRONIC EDIT
For the anticonvulsant step therapy edit, the 90-day search period was chosen to capture the most recent or current therapy for one preferred agent.

SUMMARY OF ANTICONVULSANT STEP THERAPY

<table>
<thead>
<tr>
<th>Targeted Agent(s)</th>
<th>Keppra, Keppra XR, Lamictal, Lamictal ODT, Lamictal XR, Lyrica, Topamax, Trileptal, Vimpat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is auto-grandfathering implemented?</td>
<td>Y (with look-back time frame)</td>
</tr>
<tr>
<td>Prerequisite Agent(s) – Epilepsy</td>
<td>Any anticonvulsant</td>
</tr>
<tr>
<td>Prerequisite Agent(s) – Neuropathic Pain</td>
<td>amitriptyline, nortriptyline, desipramine, imipramine, gabapentin</td>
</tr>
<tr>
<td>Prerequisite Agent(s) – Fibromyalgia</td>
<td>amitriptyline, nortriptyline, desipramine, imipramine, gabapentin, tramadol, cyclobenzapine</td>
</tr>
<tr>
<td>Prerequisite Agent(s) – Bipolar Disorder</td>
<td>lithium</td>
</tr>
<tr>
<td>Number of prerequisites required</td>
<td>1</td>
</tr>
<tr>
<td>Prerequisite look-back time frame</td>
<td>90 days&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Age-related edit?</td>
<td>NA</td>
</tr>
<tr>
<td>Additional comments</td>
<td>Anticonvulsant prerequisites include all anticonvulsants brand and generic</td>
</tr>
</tbody>
</table>

<sup>a</sup> - The system searches for a claim with a days supply that begins or ends in the past 90 days. For claims with a 30-day supply the system would be able to identify a claim processed for payment between 1 and 120 days prior to the new claim. For claims that are dispensed as an extended days supply (90 days), the system would identify a claim processed between 1 and 180 days.

DETAILS OF ANTICONVULSANT STEP THERAPY

<table>
<thead>
<tr>
<th>Targeted Agents</th>
<th>GPIs (multisource code)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANY ONE of: Keppra, Keppra XR,</td>
<td>72600043******,&lt;br&gt;72600075******,&lt;br&gt;72600036******&lt;br&gt;(M, N, or O)</td>
</tr>
<tr>
<td>Topamax, Vimpat</td>
<td>For Prerequisites, ANY ONE of: any generic or brand anticonvulsant</td>
</tr>
<tr>
<td></td>
<td>72**************,&lt;br&gt;60100060******&lt;br&gt;(M, N, O, or Y)</td>
</tr>
<tr>
<td></td>
<td>Auto-grandfathering, ANY ONE of: Keppra, Keppra XR, Topamax, Vimpat</td>
</tr>
<tr>
<td></td>
<td>72600043******,&lt;br&gt;72600075******,&lt;br&gt;72600036******&lt;br&gt;(M, N, or O)</td>
</tr>
<tr>
<td></td>
<td>Auto-grandfathering look-back time frame:</td>
</tr>
<tr>
<td></td>
<td>90 days&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> - The system searches for a claim with a days supply that begins or ends in the past 90 days. For claims with a 30-day supply the system would be able to identify a claim processed for payment between 1 and 120 days prior to the new claim. For claims that are dispensed as an extended days supply (90 days), the system would identify a claim processed between 1 and 180 days.
## DETAILS OF ANTICONVULSANT STEP THERAPY (cont.)

<table>
<thead>
<tr>
<th>Targeted Agents</th>
<th>GPIs (multisource code)</th>
<th>Prior Agents</th>
<th>GPIs (multisource code)</th>
<th>Look-back Time frames</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ANY ONE of:</strong> Lamictal, Lamictal ODT, Lamictal XR, Trileptal</td>
<td>72600040******, 72600046******, (M, N, or O)</td>
<td><strong>For Prerequisites,</strong> ANY ONE of: any generic or brand anticonvulsant OR lithium</td>
<td>72************, 60100060******, (M, N, O, or Y) OR 5950********** (M, N, O, or Y)</td>
<td><strong>Prerequisite look-back time frame:</strong> 90 days&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>For auto-grandfathering,</strong> ANY ONE of: Lamictal, Lamictal ODT, Lamictal XR, Trileptal</td>
<td>72600040******, 72600046******, (M, N, or O)</td>
<td></td>
<td></td>
<td><strong>Auto-grandfathering look-back time frame:</strong> 90 days&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>ANY ONE of:</strong> Lyrica</td>
<td>72600057****** (M, N, or O)</td>
<td><strong>For Prerequisites,</strong> ANY ONE of: any generic or brand anticonvulsant OR generic gabapentin, amitriptyline, nortriptyline, desipramine, imipramine; tramadol, or cyclobenzaprine</td>
<td>72************, 60100060******, (M, N, O, or Y) OR 7260003000****; 58200010******; 58200060******; 58200050******; 58200030******; 6510009510****, 7510005010****, (Y)</td>
<td><strong>Prerequisite look-back time frame:</strong> 90 days&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>For auto-grandfathering,</strong> ANY ONE of: Lyrica</td>
<td></td>
<td></td>
<td>72600057****** (M, N, or O)</td>
<td><strong>Auto-grandfathering look-back time frame:</strong> 90 days&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

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<sup>a</sup> - The system searches for a claim with a days supply that begins or ends in the past 90 days. For claims with a 30-day supply the system would be able to identify a claim processed for payment between 1 and 120 days prior to the new claim. For claims that are dispensed as an extended days supply (90 days), the system would identify a claim processed between 1 and 180 days.
PRIOR AUTHORIZATION CRITERIA QUESTION SETS

Lyrica (pregabalin)
Initial and Renewal Evaluation

1. Has the patient received and responded to Lyrica (pregabalin) in the past or is the patient currently receiving and responding to Lyrica (pregabalin) and switching could potentially cause harm or a health risk? If yes, approve for 12 months. If no, continue to 2.

2. What is the patient’s diagnosis?
   a. Seizure disorder
   b. Neuropathic pain
   c. Fibromyalgia
   d. Other
   If a, approve indefinitely. If b, continue to 3. If c, continue to 5. If d, continue to 7.

3. Has the patient tried and failed one of the following agents: amitriptyline, nortriptyline, desipramine, imipramine, or gabapentin
   If yes, approve for 12 months. If no, continue to 4.

4. Does the patient have an allergy, intolerance, or contraindication to one of the agents listed in question 3? If yes, approve for 12 months. If no, continue to 7.

5. Has the patient tried and failed one of the following agents: amitriptyline, nortriptyline, desipramine, imipramine, cyclobenzaprine, gabapentin, or tramadol? If yes, approve for 12 months. If no, continue to 6.

6. Does the patient have an allergy, intolerance, or contraindication to one of the agents listed in question 5? If yes, approve for 12 months. If no, continue to 7.

7. Has the prescriber submitted and the pharmacist reviewed documentation in support of the requested therapeutic use for Lyrica (pregabalin) in this patient? If yes, pharmacist must review and may approve for 12 months based on review of information provided. If no, deny.

Topamax (topiramate)
Initial and Renewal Evaluation

1. Has the patient received and responded to Topamax (topiramate) in the past or is the patient currently receiving and responding to Topamax (topiramate) and switching could potentially cause harm or a health risk? If yes, approve for 12 months. If no, continue to 2.

2. What is the patient’s diagnosis:
   a. Seizure disorder
   b. Migraine headache
   c. Other
   If a, approve indefinitely. If b, continue to 3. If c, continue to 5.

3. Has the patient tried and failed a minimum of two of the following agents for prophylaxis of migraine headache; 1) β-blockers, 2) tricyclic antidepressants, 3) divalproex or valproic acid 4) calcium channel blockers, or 5) gabapentin. If yes, approve for 12 months. If no, continue to 4.
4. Does the patient have an allergy, intolerance, or contraindication to two or more of
the above agents?
   If yes, approve for 12 months. If no, continue to 5.

5. Has the prescriber submitted and the pharmacist reviewed documentation in support
of the requested therapeutic use for Topamax (topiramate) in this patient?
   If yes, pharmacist must review and may approve for 12 months based on review of
   information provided.
   If no, deny.

**Lamictal (lamotrigine), Lamictal ODT (lamotrigine orally disintegrating), Lamictal
XR (lamotrigine extended-release), Trileptal (oxcarbazepine)**

**Initial and Renewal Evaluation**

1. Has the patient received and responded to the requested agent in the past or is the
   patient currently receiving and responding to the requested agent and switching
   could potentially cause harm or a health risk?
   If yes, approve for 12 months. If no, continue to 2.

2. What is the patient's diagnosis:
   a. Seizure disorder
   b. Bipolar disorder
   c. Other
   If a, approve indefinitely. If b, continue to 3. If c, continue to 5.

3. Has the patient tried and failed a generic anticonvulsant indicated for bipolar disorder
   or lithium?
   If yes, approve for 12 months. If no, continue to 4.

4. Does the patient have an allergy, intolerance, or contraindication to a generic
   anticonvulsant indicated for bipolar disorder or lithium?
   If yes, approve for 12 months. If no, continue to 5.

5. Has the prescriber submitted and the pharmacist reviewed documentation in support
   of the requested therapeutic use for the requested agent in this patient?
   If yes, pharmacist must review and may approve for 12 months based on review of
   information provided.
   If no, deny.

**Keppra (levetiracetam), Keppra XR (levetiracetam extended-release), Vimpal
(lacosamide)**

**Initial and Renewal Evaluation**

1. Has the patient received and responded to the requested agent in the past or is the
   patient currently receiving and responding to the requested agent and switching
   could potentially cause harm or a health risk?
   If yes, approve for 12 months. If no, continue to 2.

2. What is the patient's diagnosis:
   a. Seizure disorder
   b. Other
   If a, approve indefinitely. If b, continue to 3.

3. Has the prescriber submitted and the pharmacist reviewed documentation in support
   of the requested therapeutic use for the requested agent in this patient?
   If yes, pharmacist must review and may approve for 12 months based on review of
   information provided. If no, deny.
Anticonvulsant Step Therapy – Medical Diagnoses Option

**OBJECTIVE**
The intent of the identification of patients with certain medical diagnoses is to allow coverage of target brand anticonvulsants (Keppra, Keppra XR, Lamictal, Lamictal ODT, Lamictal XR, Lyrica, Topamax, Trileptal, and Vimpat) in patients with a seizure disorder. Medical claims data will be used to identify plan members with the ICD-9 codes listed below:

<table>
<thead>
<tr>
<th>EVENT</th>
<th>ICD-9CM Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epilepsy</td>
<td>345, 345.X, 345.XX</td>
</tr>
</tbody>
</table>

*The Medical Diagnoses Criteria will approve ICD-9 codes of three or more digits as applicable to ensure that patients who have been assigned incomplete codes will be included.

These patients would be exempt from the step therapy process for Keppra, Keppra XR, Lamictal, Lyrica, Topamax, Trileptal, and Vimpat. Medical claims data must be supplied to Prime in order to implement this option.