DRUG DETERMINATION POLICY

Title: DDP-36 Third Generation Anticonvulsants

Effective Date: 6/28/23

Physicians Health Plan
PHP Insurance Company
PHP Service Company

Important Information - Please Read Before Using This Policy

The following policy applies to health benefit plans administered by PHP and may not be covered by all PHP plans. Please refer to the member's benefit document for specific coverage information. If there is a difference between this general information and the member's benefit document, the member's benefit document will be used to determine coverage. For example, a member's benefit document may contain a specific exclusion related to a topic addressed in a coverage policy.

Benefit determinations for individual requests require consideration of:

1. The terms of the applicable benefit document in effect on the date of service.
2. Any applicable laws and regulations.
3. Any relevant collateral source materials, including coverage policies.
4. The specific facts of the particular situation.

Contact PHP Customer Service to discuss plan benefits more specifically.

1.0 Policy:

This policy describes the determination process for coverage of specific drugs.

This policy does not guarantee or approve benefits. Coverage depends on the specific benefit plan. Drug Determination Policies are not recommendations for treatment and should not be used as treatment guidelines.

2.0 Background or Purpose:

Third generation anticonvulsants are specialty drugs indicated for a number of types of epilepsy and are associated with significant side effects. These criteria were developed and implemented to ensure appropriate use for the intended diagnose and severity...

3.0 Clinical Determination Guidelines:

Document the following with chart notes:

I. Partial Onset Seizures.

A.. Adjunct and monotherapy of partial-onset seizures [must meet both listed below]:

1. Age [must meet one listed below]:

a. Aptiom (eslicarbazepine): at least four years.

b. Gabitril (tiagabine): at least 12 years.

c. Fycompa (perampanel): at least four years.

d. Briviact oral, intravenous (brivaracetam): at least four years.

e. Xcorpi (cenobamate): at least 18 years.

f. Onfi (clobazam) and Sympazan film (clobazam): at least two years old

2. Other therapies: contraindicated, inadequate response after four months or significant adverse effects to two formulary anti-epileptic drugs.

B. Refractory complex partial seizures [must meet both listed below]:

1. Age: Sabril (vigabatrin): at least ten years.

2. Other therapies: contraindicated, inadequate response after four months or significant adverse effects to two formulary anti-epileptic drugs.

II. Primary generalized tonic-clonic seizures [must meet both listed below]:

A. Age:

1. Fycompa (perampanel): at least 12 years.

2. Onfi (clobazam) and Sympazan film (clobazam): at least two years old

B. Other therapies [must meet both listed below]

1. Contraindicated, inadequate response after four months or had significant adverse effects with two formulary anti-epileptic drugs.

2. Concomitant use with other anti-epileptic drug(s).

III. Infantile spasm monotherapy [must meet all listed below]:

A. Age: Sabril (vigabatrin): one month to two years.

B. Prescriber: pediatric neurologist.

C. Other therapies: contraindicated, inadequate response after four months or significant adverse effects to two formulary anti-epileptic drugs.

D. Potential benefits out-weighs risk of vision loss.

IV. Syndrome or complex related epilepsy:

A. Age [must meet one listed below]:

1. Lennox-Gastaut Syndrome

a. Onfi tablet and suspension (clobazam) and Sympazan film (clobazam): at least two years

b. Epidiolex oral solution (cannabidiol): at least two years.

c. Fintepla oral solution (fenfluramine): at least two years

2. Dravet Syndrome

a. Epidiolex oral solution (cannabidiol): at least two years.

b. Diacomit capsules, packets (stiripentol): at least one year

c. Fintepla oral solution (fenfluramine): at least two years

d. Onfi (clobazam) and Sympazan film (clobazam): at least two years

3. Tuberous Sclerosis Complex

a. Epidiolex oral solution (cannabidiol): at least two years.

B. Prescriber: neurologist.

C. Other therapies: contraindicated, inadequate response after four months or significant adverse effects to two formulary anti-epileptic drugs.

V. Dosage Regimen (see Appendix I).

VI. Approval.

A. Initial.

1. All except Sabril: six months.

2. Sabril.

a. Partial onset seizure: three months.

b. Infantile spasm: two to four weeks.

2. Re-approval: auto authorization off filled claim within 1 month; if authorization required -one year duration.

4.0 Coding:

AFFECTED CODES				
HP Code	**Brand Name**	**Generic Name**	**Billing (1 unit)**	**Prior Approval**
C9254	Vimpat	lacosamide	1mg	Y

5.0 References, Citations & Resources:

1. Epilepsia. 2006 Jul;47(7):1094-120.
2. Epilepsia. 2007, 48(7): 1308-17.
3. Neurology. 2011 May 3;76(18): 1555-63.
4. Lexicomp Online®, Lexi-Drugs®, Hudson, Ohio: Lexi-Comp, Inc.; Vimpat, Fycompa, Potiga, Aptiom Sabril, Gavitril, Briviact, Epidiolex, Diacomit, Onfi, Sympazan, Xcorpi accessed April 2023
5. Consensus guidelines for therapeutic drug monitoring in neuropsychopharmacology: update 2017. Pharmacopsychiatry. 2018;51(1-02):9-62. doi:10.1055/s-0043-116492[PubMed 28910830]
6. Practice guideline update summary: Efficacy and tolerability of the new antiepileptic drugs I: Treatment of new-onset epilepsy Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology and the American Epilepsy Society Neurology 2018;91(2)

6.0 Appendices:

See pages 5-8.

7.0 Revision History:

Original Effective Date: 08/26/2010

Next Review Date: 07/01/2024

Revision Date	Reason for Revision
8/19	Moved to new format,
9/19	Replaced abbreviations, modified billing table, added clobazam
4/20	Annual review; added Xcorpi, replaced abbreviations, clarified dose table, relabeled partial seizure type and meds to treat, modified instruction and other therapies language, updated ages, approved at June P&PT Committee meeting.
9/20	Off cycle review, added drug Fintepla, clarified instructions, added duration of other therapies, approved by P&T Committee 12/9/20
5/21	Annual review, reformatted, replaced abbreviations, added Vimpat for tonic-clonic seizures
4/22	Annual review ; removed Vimpat oral (PA removed) and IV (hospital use); added reapproval by fill history
4/23	Annual review; removed Ptiga (discontinued), Added Onfi to to partial, generalized and Dravets, formatting of Syndrome or complex seizure added Tuberous sclerosis

Appendix I: Dosing of Anticonvulsants

Drug	Initial	Titration	Target/Max	Adjustment
Fycompa perampanel	Adult/Pediatric: • 2mg daily • Enzyme-inducing antiepileptic drugs (AED): 4mg daily	Adult/Pediatric: Raise by 2mg daily every week	Adult/Pediatric: 8-12mg	• Reduce dose with serious psychiatric or behavioral reactions • Severe Renal Impairment: (creatinine clearance ≤ 30ml/min): not recommended • Hepatic Impairment: mild - 6mg daily; moderate -4mg daily
Aptiom eslicarbaze-pine	Pediatric: 11-21Kg: 200mg 22-31Kg:il300mg 32-38Kg: 300mg >38Kg: 400mg Adult: 400mg daily	Pediatric: 11-21kg: raise by 200mg weekly 22-31Kg: raise by 300mg weekly 32-38Kg: raise by 300mg weekly >38Kg: raise by 400mg weekly Adult: Raise by 400mg weekly	Pediatric: 11-21Kg: 600mg daily 22-31 Kg: 800mg daily 32-38 Kg 900mg daily >38Kg 1,200mg daily Adult: 1,600mg daily	• Renal Impairment: creatinine clearance <50mL: 200mg; raise by 200mg to maximum 600mg • Hepatic Impairment : mild to moderate - no adjustment; severe - not recommended
Sabril vigabatrin POS	• ≤ 60kg: 250mg twice daily • >60Kg: 500mg twice daily	Raise by 500mg weekly to 1.5gms twice daily	• ≤60Kg: 2gms daily • >60Kg: 3gms daily	• Renal Impairment: mild (creatinine clearance [CrCl]: 50-80ml/min) reduce dose 25%; moderate (CrCl 30-50ml/min) reduce dose 50%; severe (CrCl 10-30ml/min): reduce dose 75% • Hepatic Impairment: no adjustment
Sabril vigabatrin Inf. spasms	150mg/Kg daily	Raise by 25-50mg/Kg daily every 3-4 days	150mg/Kg daily (in 2 doses)	• Renal Impairment: mild (creatinine clearance [CrCl]: 50-80ml/min) reduce dose 25%; moderate (CrCl 30-50ml/min) reduce dose 50%; severe (CrCl 10-30ml/min): reduce dose 75% • Hepatic Impairment: no adjustment
Gabitril tigabine	AED: 4mg/day No AED: 2mg daily	Raise 4-8mg weekly divided into 2-4 doses daily	32-56mg daily	• Pediatric: maximum 32mg daily • Hepatic Impairment may need to reduce dose
Briviact oral, IV brivaracetam	Pediatric: 11-50Kg 0.5 to 1.25mg/kg twice daily Adult: 50mg twice daily	Titrate up or down depending on response	Pediatric: 2.5mg/Kg twice daily Adult: 50-100mg twice daily	• Renal Impairment: end stage - not recommended • Hepatic Impairment: mild to severe - 50-150mg daily
Epidiolex oral	2.5mg/Kg twice	Raise to 5mg/kg	Max: 10mg/Kg	• Renal Impairment: no

Drug	Initial	Titration	Target/Max	Adjustment
solution (cannabidiol)	daily	twice daily at 1 week.	twice daily	adjustment • Hepatic impairment: mod.1.25- 5mg/kg twice daily
Diacomit oral stripentol	Pediatric/Adult: 50mg/Kg daily in 2-3 doses	NA	Pediatric/Adult: 3gms daily	• Renal Impairment: moderate to severe - avoid use • Hepatic Impairment: moderate to severe - avoid use
Onfi/Sympazan oral clobazam	Pediatric/Adult: ≤30Kg: 5mg daily >30Kg: 5mg twice daily	Pediatric/Adult: ≤30Kg: raise 5mg twice daily for 1 week, then 10mg 2 times weekly. >30Kg: raise 10mg twice daily at 1 week, then 20mg twice daily	Pediatric/Adult: ≤30Kg: 20mg daily >30Kg: 40mg daily	• Hepatic Impairment: mild to moderate - start with 5mg daily
Xcorpi cenobamate	Weeks 1 and 2: 2.5mg daily	Weeks 3 and 4: 25mg daily Weeks 5 and 6: 50mg daily Weeks 7 and 8: 100mg daily Weeks 9 and 10: 150mg daily Week 11 and on: 200mg daily; then raise 50mg every 2 weeks	400mg daily	• Renal Impairment: creatinine clearance <90 - consider reduced dose • Hepatic Impairment: mild to moderate: maximum dose 200mg; severe: avoid use
Fintepla fenfluramine	Pediatric/Adult: 1mg/Kg/dose twice daily	Pediatric/Adult: Week 2 may increase to 0.2mg/kg twice daily	Pediatric/Adult: 13mg/Kg/dose twice daily	• Renal Impairment: moderate to severe: not recommended • Hepatic Impairment: use not recommended

Appendix II: Monitoring & Patient Safety

Drug	Adverse Reactions*	Monitoring	REMS
Fycompa oral perampanel	• Central Nervous System: dizziness (16-47%), vertigo (3-47%), hostility (12-20%), aggressive behavior (2-20%), drowsiness (9-18%), abnormal gait (4-16%), fatigue (8-15%), headache (13%) Irritability (2-12%), falling (5-10%)	• Central Nervous System: seizure frequency, suicidality ≤ 1 post • Miscellaneous: enzyme-inducing AEDs start or DC, weight	Medication Guide
Aptiom oral Eslicarbaze-pine	• Central Nervous System: dizziness (20-28%), drowsiness (16-28%), headache (13-5%) • Gastrointestinal: nausea (10-16%), vomiting (6-10%) • Ophthalmic: diplopia (9-11%)	• Central Nervous System: seizure frequency, depression suicidality • Labs: liver function tests, sodium, chloride • Ophthalmic: visual changes • Hypersensitivity Reactions	Medication Guide
Sabril oral vigabatrin	• Central Nervous System: somnolence (17-45%), headache (33%), fatigue (23-28%), dizziness (21-24%), irritability (10-23%), sedation (inf. 17-19%), insomnia (10-12%), tremor (14-15%) • Gastrointestinal: vomiting/constipation (14%-20%), diarrhea (10-13%) • Ophthalmic: decreased vision field (30%), nystagmus (13-15%), blurred vision (11-13%) • Miscellaneous: otitis media (inf. 10-44%), fever (29%), infection (7-51%)	• CNS: sedation, suicidality • Labs: hemoglobin and hematocrit • Ophthalmic: dilated indirect exam pre, 4 weeks during, 3-6 weeks post • Miscellaneous: weight gain/edema	REMS Purpose: Awareness of vision loss
Gabitril oral tiagabine	• Central Nervous System: dizziness (27-31%), drowsiness (18-21%), nervous (10-14%) • Gastrointestinal: nausea (11%) • Infection (19%) • Musculoskeletal: weak (20%), tremor (9-21%)	• Central Nervous System: seizure activity • Therapeutic range (tentative): 50-250nmol/L	Medication guide
Briviact oral, IV brivaracetam	• Central Nervous System: fatigue, hypersomnia, lethargy or malaise (20-27%); drowsiness/sedation (16-27%), dizziness (12-16%); abnormal gait, ataxia or vertigo (16%) psyche abnormality (13%) • Musculoskeletal: weakness (20-27%) • Ophthalmic: nystagmus (16%)	• Central Nervous System: depression, suicidality • Labs: CBC with differential, liver/renal function	Medication guide
Epidiolex oral solution cannabidiol	• Central Nervous System: drowsy/lethargy/sedation (≤32%), • Dermatological: skin rash (7-13%) • Gastrointestinal: reduced appetite (16-22%), diarrhea (9-20%) • Hematology/Oncology: anemia (30%) • Hepatic: increased liver function tests • Infection: 25-40%)	• Labs: liver function tests (pre. and 1, 3, 6 months post)	None
Diacomit oral stripentol	• Central Nervous System: drowsy (67%), agitation (27%), ataxia (27%), hypotonia (18-24%, dysarthria (12%), insomnia (12%) • Endocrine/Metabolism: weight loss (27%) • Gastrointestinal: reduced appetite (46%), nausea (15%) • Hematology/Oncology: reduced platelets (13%), neutropenia (13%) • Musculoskeletal: tremor (15%) • Pregnancy: adverse effects in animal reproduction studies	• Labs: CBC (pre, every 6 months post), weight, growth rate in pediatrics	Medication guide

Drug	Adverse Reactions*	Monitoring	REMS
Onfi and Sympazan oral clobazam	• Central Nervous System: drowsiness (16-25%), lethargy (10-15%), drooling (13-14%), aggressive behavior (8-14%), irritability (11%) • Respiratory: upper respiratory infection (13-14%) • Miscellaneous: fever (10-17%)	• Central Nervous System: mental status/suicidality • Dermatological: serious skin reaction • Respiratory: status	None needed
Xcorpi cenobamate	• Cardiovascular: ECG abnormalities (QT shortening: 31-66%) • Central Nervous System: hypersomnia (57%), lethargy (57%), malaise (57%), drowsiness (19-37%), dizziness (18-33%), fatigue (12-24%), headache (10-12%) • Endocrine/Metabolism: increased potassium (8-17%) • Ophthalmic: visual disturbances (9-18%), diplopia ((6-15%) • Pregnancy: adverse effects in animal reproduction studies	• Labs: liver function tests, potassium • Hypersensitivity: drug reaction with eosinophilia and systemic symptoms • Psychological: suicidal ideation	
Fintepla fenfluramine	• Cardiovascular: aortic/mitral valve insufficiency (23%), increased blood pressure (8-13%) • Endocrine/Metabolism: weight loss (5-13%) • Gastrointestinal: decreased appetite (23-38%), diarrhea (15-31%), sialorhea (13%) • Central Nervous System: drooling (13%), drowsiness (26% fatigue (15%), lethargy (26%), malaise (15%), sedated state (26%) • Neuromuscular & Skeletal: asthenia (15%) • Respiratory: upper respiratory tract infection (5% to 21%) • Miscellaneous: fever (5%-15%)	• Cardiovascular: echocardiogram (prior, every 6 months, 3 months after), blood pressure (prior, then regularly) • Endocrine/Metabolism: weight (prior, then regularly, growth in pediatrics (regularly)	Med guide