

DRUG DETERMINATION POLICY

Title: DDP-36 Third Generation Anticonvulsants

Effective Date: 11/05/2019



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:

A. Partial Onset Seizures.

1. Adjunctive/refractory partial onset seizures:

a. Age:

- i. Potiga oral (ezogabine): at least 18 years.
- ii. Sabril oral (vigabatrin): at least 10 years.
- iii. Gabitril oral (tiagabine): at least 12 years.

b. Other therapies (both below):

- i. Contraindication, failed or had significant adverse effects with two formulary anti-epileptic drugs.

- ii. Concomitant use with other anti-epileptic drug(s).
- 2. Monotherapy partial-onset seizures (can also be used as an adjuvant).
 - a. Age.
 - i. Vimpat oral, IV (lacosamide): at least 4 years.
 - ii. Aptiom oral (eslicarbazepine): at least 4 years.
 - iii. Fycompa oral (perampanel): at least 4 years.
 - iv. Briviact oral, IV (brivaracetam): at least 16 years.
 - b. Other therapies: contraindication, failed or significant adverse effects with at least two formulary anti-epileptic drugs.
- B. Primary generalized tonic-clonic seizures.
 - 1. Age: Fycompa (perampanel) – at least 12 years.
 - 2. Other therapies (both below):
 - a. Contraindication, failed or had significant adverse effects with at least two formulary anti-epileptic drugs.
 - b. Concomitant use with other anti-epileptic drug(s).
- C. Infantile Spasm Monotherapy.
 - 1. Age: Sabril (vigabatrin) - 1 month to 2 years.
 - 2. Prescriber: pediatric neurologist.
 - 3. Other therapies: contraindication, failed or had significant adverse effects with at least two formulary anti-epileptic drugs.
 - 4. Potential benefits out-weighs risk of vision loss.
- D. Lennox-Gastaut syndrome and Dravet syndrome
 - 1. Age:
 - a. Epidiolex oral solution (cannabidiol): at least 2 years.
 - b. Diacomit capsules, packets (stiripentol): at least 3 years (only indicated for Dravet syndrome). syndrome
 - c. Onfi tablet and suspension (clobazam) and Sympazan film (clobazam): at least two years (only indicated for Lennox-Gastaut syndrome).
 - 2. Prescriber: neurologist.
 - 3. Other therapies: contraindication, treatment failure or significant adverse effects with at least two formulary anti-epileptic drugs.

E. Dosage Regimen (Appendix I).

F. Approval.

1. Initial.

a. All except Sabril: six months.

b. Sabril.

i. Partial onset seizure: three months.

ii. Infantile Spasm: two to four weeks.

2. Re-approval (all): one year; reduction of seizure activity.

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 accessed September 2019.

6.0 Appendices:

Appendix I: Dosing of Anticonvulsants

Drug	Initial	Titration	Target/Max	Adjustment
Vimpat oral, IV lacosamide	<u>Pediatric</u> : 11- <50Kg: 1mg/Kg 2 times/day <u>Adults</u> : 50mg 2 times/day	<u>Pediatric</u> : 1mg/Kg 2 times/day <u>Adults</u> : 50mg 2 times/day (weekly intervals)	<u>Pediatric</u> : 2-6mg/Kg 2 times/day <u>Adults</u> : 100-200 mg 2 times/day	<ul style="list-style-type: none"> Severe renal impairment (RI) (CrCl \leq 30ml/min): peds - \downarrow 25% Adult - max 50mg 2 times/day Hepatic impairment (HI): mild/mod - pediatric \downarrow 25%; adult max 50 mg 2 times/day; severe - not recommended
Fycompa perampanel	<u>Adults/Pediatric</u> <ul style="list-style-type: none"> 2mg Enzyme-inducing AEDs: 4mg 	<u>Adults/Pediatric</u> <ul style="list-style-type: none"> \uparrow by 2mg/day every week to 4-8mg 	<u>Adults/Pediatric</u> 8-12 mg	<ul style="list-style-type: none"> \downarrow dose w serious psychiatric or behavioral reactions Severe RI (CrCl \leq 30ml/min): not recommended HI: mild-6mg/day; moderate-4mg/day
Potiga ezogabine	<ul style="list-style-type: none"> 100mg >65yrs 50mg 	<ul style="list-style-type: none"> $\uparrow \leq$ 50 mg 3x/day, at weekly intervals 	1,200mg/day	<ul style="list-style-type: none"> RI: CrCL <50mL or on dialysis: 200mg tid HI: Child-Pugh 7-9

Drug	Initial	Titration	Target/Max	Adjustment
				250 3x/day; Child-Pugh >9 200mg 3x/day
Aptiom eslicarbazepine	<u>Pediatric:</u> 11-21 Kg: 200mg 22-31 Kg: 300mg 32-38 Kg 300mg >38Kg 400mg <u>Adults</u> 400mg	<u>Pediatric</u> 11-21 kg: ↑ by 200mg weekly 22-31 Kg: ↑ by 300mg weekly 32-38 Kg ↑ by 300mg weekly >38Kg ↑ by 400mg weekly <u>Adults</u> ↑ by 400mg weekly	<u>Pediatric</u> 11-21Kg: 600mg/day 22-31 Kg: 800mg/day 32-38 Kg 900mg/day >38Kg 1,200mg/day <u>Adults</u> 1,600mg/day	<ul style="list-style-type: none"> • RI: CrCL <50mL: 200mg; ↑ by 200mg to max 600mg • HI: mild to mod - no adjustment; severe - not recommended
Sabril vigabatrin POS	<ul style="list-style-type: none"> • ≤ 60kg: 250mg • >60 Kg: 500mg 2 times/day 	<ul style="list-style-type: none"> • ↑ by 500mg weekly to 1.5gms 2 times/day 	<ul style="list-style-type: none"> • ≤60Kg - 2gms/day • >60Kg - 3 gms /day 	<ul style="list-style-type: none"> • RI: mild (CrCl: 50-80ml/min) ↓ dose 25%; Mod (CrCl 30-50ml/min) ↓ dose 50%; Severe (CrCl 10-30ml/min): ↓ dose 75% • HI: no adjustment
Sabril vigabatrin Inf. spasms	<ul style="list-style-type: none"> • 50mg/Kg/day 	<ul style="list-style-type: none"> • ↑ by 25-50mg/Kg/day every 3-4 days 	150mg/Kg/day 2 doses	<ul style="list-style-type: none"> • RI: no information • HI: no adjustment
Gabril tigabine	<ul style="list-style-type: none"> • AED: 4mg • No AED: ↓ 	<ul style="list-style-type: none"> • ↑ 4-8mg weekly into 2-4x/day 	32-56 mg/day	<ul style="list-style-type: none"> • Pediatric: max 32mg/day • HI: may need to ↓ dose
Briavact oral, IV brivarace-tam	<u>Pediatric:</u> 11-50Kg 0.5-1.25mg/kg 2 times/day <u>Adult:</u> 50mg 2 times/day	None needed	<u>Pediatric:</u> 2.5mg/Kg 2 times/day <u>Adult:</u> 50-100mg 2 times/day	<ul style="list-style-type: none"> • RI: end stage - not recommended • HI: mild-severe - 50-150mg/day
Epidiolex oral solution (cannabidiol)	2.5 mg/Kg 2 times/day	↑ to 5mg/kg 2 times/day at 1 wk.	Max: 10mg/Kg 2 times/day	<ul style="list-style-type: none"> • RI: no adjustment • HI: mod.1.25- 5mg/kg 2 times/day
Diacomit oral stripentol	<u>Pediatric/Adult</u> 50mg/Kg/day in 2-3 doses	NA	<u>Pediatric/Adult</u> 3gms/day	<ul style="list-style-type: none"> • RI: mod-severe - avoid use • HI: mod-severe - avoid use
Onfi/Sympazan oral clobazam	<u>Pediatric/Adult</u> <30Kg: 5mg 1x/day >30Kr: 5mg 2 times/day	<u>Pediatric/Adult</u> <30Kg: ↑ 5mg 2 times/day x 1wk, then 10mg 2 times/wk. >30Kr: ↑ 10mg 2 times/day x 1 wk, then 20mg 2 times/day	<u>Pediatric/Adult</u> <30Kg: 20mg/day >30Kg: 40mg/day	<ul style="list-style-type: none"> • HI: mild-mod - start with 5mg 1x/day

Appendix II: Monitoring & Patient Safety

Drug	Adverse Reactions*	Monitoring	REMS
Vimpat Oral, IV lacosamide	<ul style="list-style-type: none"> • Central Nervous System (CNS): dizziness (16-53%), fatigue (7-15%), ataxia (4-15%), HA (11-14%) • Gastro Intestinal (GI): N (7-17%), V (6-16%) • Musculoskeletal (MSK): tremor (4-12%) • Ophthalmic.: diplopia (6-16%), ↓ vision (2-16%) 	<ul style="list-style-type: none"> • CNS: suicidality • Cardiovascular (CV): ECG w conduction problems, ↑ PR interval (drugs/severe CV dx), misc: multi-organ hypersens.: DC 	Med. guide
Fycompa oral perampanel	<ul style="list-style-type: none"> • CNS: dizziness (16-47%), vertigo (3-47%), hostility (12-20%), aggressive BH (2-20%), drowsiness (9-18%), AB gait (4-16%), fatigue (8-15%), HA (13%) • Irritability (2-12%), Falling (5-10%) 	<ul style="list-style-type: none"> • CNS: seizure frequency, suicidality ≤ 1 post • Misc: enzyme-inducing AEDs start or DC, weight 	Med. guide
Potiga oral ezogabine	<ul style="list-style-type: none"> • CNS: dizziness (23%), drowsiness (22%), fatigue (15%) 	<ul style="list-style-type: none"> • Ophthalmic. exam: pre & q 6 mons. • CNS: psychological/behavioral health (BH), seizure frequency, • CV: QT interval (risk factors) • Labs: electrolytes • Urological: hepatic/renal fx 	Med guide
Aptiom oral eslicarbazepine	<ul style="list-style-type: none"> • CNS: dizziness (20-28%), drowsiness (16-28%), HA (13-15%) • GI: N (10-16%), V (6-10%) • Ophth: diplopia (9-11%) 	<ul style="list-style-type: none"> • CNS: seizure frequency, depression suicidality • Labs: LFT, Na, Cl • Ophth: visual changes • Hypersensitivity rxns 	Med guide
Sabril oral vigabatrin	<ul style="list-style-type: none"> • CNS: somnolence (17-45%), HA (33%), fatigue (23-28%), dizziness (21-24%), irritability (10-23%), sedation (inf. 17-19%), insomnia (10-12%), tremor (14-15%) • GI: vomiting/constipation (14%-20%), diarrhea (10-13%) • Ophthalmic: ↓vision field (30%), nystagmus (13-15%), blurred vision (11-13%) • Miscellaneous (Misc): otitis media (inf. 10-44%), fever (29%), infection (7-51%) 	<ul style="list-style-type: none"> • CNS: sedation, Suicidality • Lab: Hgb/Hct • Ophthalmic: dilated indirect exam Pre, 4wks during, q 3-6 post • Misc: weight gain/edema 	REMS Purpose: Aware- ness of vision loss
Gabitril oral tiagabine	<ul style="list-style-type: none"> • CNS: dizziness (27-31%), drowsiness (18-21%), nervous (10-14%) • GI: nausea (11%) • Infection (19%) • MSK: weak (20%), tremor (9-21%) 	<ul style="list-style-type: none"> • CNS: seizure activity • Therapeutic range (tentative): 50-250nmol/L 	Med guide
Briviact oral, IV brivaracetam	<ul style="list-style-type: none"> • CNS: fatigue, hypersomnia, lethargy or malaise (20-27%); drowsiness/sedation (16-27%), dizziness (12-16%); AB gait, ataxia or vertigo (16%) psyche AB (13%) • MSK: weakness (20-27%) • Ophthalmic: nystagmus (16%) 	<ul style="list-style-type: none"> • CNS: depression, suicidality • Labs: CBC w diff, liver renal fx 	Med guide

Drug	Adverse Reactions*	Monitoring	REMS
Epidiolex oral solution cannabidiol	<ul style="list-style-type: none"> • CNS: drowsy/lethargy/sedation ($\leq 32\%$), • Derm: skin rash (7-13%) • GI: \downarrow appetite (16-22%), diarrhea (9-20%) • Hematology/oncology: anemia (30%) • Hepatic: \uparrowLFTs • Infection: 25-40%) 	<ul style="list-style-type: none"> • Lab: ALT, AST, bili (pre. & 1,3, 6 mons post) 	None
Diacomit oral striptentol	<ul style="list-style-type: none"> • CNS: drowsy (67%), agitation (27%), ataxia (27%), hypotonia (18-24%, dysarthria (12%), insomnia (12%) • Endocrine/metabolism: weight. loss (27%) • GI: \downarrow appetite (46%), nausea (15%) • Hem/Onc:\downarrow plts (13%), neutropenia (13%) • MSK: tremor (15%) • Preg: Ae's in animal repro studies 	<ul style="list-style-type: none"> • Lab: CBC (pre, q 6 mons.), weight, growth rate in peds 	Med guide
Onfi/Sympazan oral clobazam	<ul style="list-style-type: none"> • CNS: drowsiness(16-25%), lethargy (10-15%), drooling (13-14%), aggressive behavior (8-14%), irritability (11%) • Resp.: URI (13-14%) • Misc.: fever (10-17%) 	<ul style="list-style-type: none"> • CNS: mental status/suicidality • Derm.: serious skin reaction • Resp: status 	None needed

7.0 Revision History:

Original Effective Date: 08/26/2010

Next Review Date: 11/05/2020

Revision Date	Reason for Revision
8/19	Moved to new format,
9/19	Replaced abbreviations, modified billing table, added clobazam