

Pharmacy Benefit Determination Policy

Policy Subject: Third Generation Anticonvulsants	Dates:
Policy Number: SHS PBD34	Effective Date: August 23, 2012
Category: CNS Drugs	Revision Date: November 5, 2018
Policy Type: <input checked="" type="checkbox"/> Medical <input checked="" type="checkbox"/> Pharmacy	Approval Date: December 5, 2018
Department: Pharmacy	Next Review Date: June 2019
Product (check all that apply):	Clinical Approval By:
<input checked="" type="checkbox"/> Group HMO/POS	Medical Directors
<input checked="" type="checkbox"/> Individual HMO/POS	PHP: Peter Graham, MD
<input checked="" type="checkbox"/> PPO	Pharmacy and Therapeutics Committee
<input checked="" type="checkbox"/> ASO	PHP: Peter Graham, MD;

Policy Statement:
Physicians Health Plan, PHP Insurance & Service Company, and Sparrow PHP will cover third generation Anticonvulsants through the Pharmacy Benefit based on approval by the Clinical Pharmacist or Medical Director using the following determination guidelines

Drugs and Applicable Coding:
C-Code: Vimpat - C9254 (lu = 1mg)

Clinical Determination Guidelines:
<p>Document the following with chart notes</p> <p>A. Partial Onset Seizures</p> <ol style="list-style-type: none"> 1. Adjunctive/refractory partial onset seizures (POS): <ol style="list-style-type: none"> a. Age: <ul style="list-style-type: none"> • Potiga (Ezogabine): ≥ 18 years • Sabril (vigabatrin): ≥ 10 years • Gabitril (tiagabine): ≥ 12 years . b. Other therapies (both below) <ul style="list-style-type: none"> • Treatment failure or significant adverse effects with ≥ 2 formulary anti-epileptic drugs. • Concomitant use with other anti-epileptic drug(s) 2. Monotherapy partial-onset seizures (POS) <ol style="list-style-type: none"> a. Age <ul style="list-style-type: none"> • Vimpat (lacosamide Oral, IV): ≥ 4 years • Aptiom (eslicarbazepine): ≥ 18 years • Fycompa (perampanel): ≥ 12 years • Briviact (brivaracetam Oral, IV): ≥ 16 years b. Other therapies: Treatment failure or significant adverse effects with ≥ 2 formulary anti-epileptic drugs:

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- B. Primary generalized tonic-clonic seizures
 - 1. Age: Fycompa (perampanel) - \geq 12years
 - 2. Other therapies (both below)
 - a. Treatment failure or significant adverse effects with \geq 2 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: Treatment failure or significant Adverse effects with \geq 2 formulary anti-epileptic drugs
 - 4. Potential benefits out-weighs risk of vision loss
- D. Lennox-Gastaut syndrome and Dravet syndrome
 - 1. Age: Epidiolex oral solution (cannabidiol) - \geq 2 years
 - 2. Prescriber: Neurologist
 - 3. Other therapies: Treatment failure or significant Adverse effects with \geq 2 formulary anti-epileptic drugs
- E. Dosage Regimen (Appendix I)
- F. Approval
 - 1. Initial
 - a. All except Sabril: 6 months
 - b. Sabril:
 - Partial onset seizure: 3months
 - Infantile Spasm: 2-4 weeks
 - 2. Re-approval (all): 1 year; reduction of seizure activity

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Appendix I: Dosing of Anticonvulsants

Drug	Initial	Titration	Target/Max	Adjustment
Vimpat oral, IV lacosamide	<u>Peds:</u> 11- <50Kg: 1mg/Kg 2x/day <u>Adults:</u> 50mg 2x/day	<u>Peds:</u> 1mg/Kg 2x/day <u>Adults:</u> 50mg 2x/day (wkly intervals)	<u>Peds:</u> 2- 6mg/Kg 2x/day <u>Adults:</u> 100-200 mg 2x/day	<ul style="list-style-type: none"> Severe renal impairment (RI) (CrCl \leq 30ml/min): Peds - \downarrow 25% Adult - max 50mg 2x/day Hepatic Impairment (HI): Mild to mod - Peds \downarrow 25%; Adult max 50 mg 2x/day; Severe - Not recommended
Fycompa perampanel	<ul style="list-style-type: none"> 2mg HS Enzyme-inducing AEDs: 4mg 	\uparrow by 2mg/day every wk to 4-8mg	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; mod-4mg/day
Potiga ezogabine	<ul style="list-style-type: none"> 100mg >65yrs 50mg 	$\uparrow \leq$ 50 mg 3x/day, at wkly intervals	1,200mg /day	<ul style="list-style-type: none"> RI: CrCL <50mL or on dialysis: 200mg tid HI: Child-Pugh 7-9 250 3x/day; Child-Pugh >9 200mg 3x/day
Aptiom eslicarbazepine	<ul style="list-style-type: none"> 400mg daily 	\uparrow by 400mg wkly to 1,200mg max.	800mg	<ul style="list-style-type: none"> RI: CrCL <50mL: 200mg; \uparrow by 200mg to max 600mg HI: Mild to mod - No adjustment; Severe - Not recommended
Sabril vigabatrin POS	<ul style="list-style-type: none"> \leq 60kg: 250mg >60 Kg: 500mg 2x/day 	\uparrow by 500mg wkly to 1.5gms 2x/day	<ul style="list-style-type: none"> \leq60Kg - 2gms/day) >60Kg - 3 gms /day 	<ul style="list-style-type: none"> RI: Mild (CrCl: 50-80ml/min) \downarrow dose 25%; Mod (CrCl 30-50ml/min) \downarrow dose 50%; Severe (CrCl 10-30ml/min): \downarrow dose 75% HI: No adjustment
Sabril vigabatrin Inf. spasms	<ul style="list-style-type: none"> 50mg/Kg/day 	\uparrow 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
Gabitril tigabine	<ul style="list-style-type: none"> AED: 4mg No AED: \downarrow 	\uparrow 4-8mg wkly into 2-4x/day	32-56 mg/day	<ul style="list-style-type: none"> Peds: Max 32mg/day HI: May need to \downarrow dose
Briviact oral, IV brivarace-tam	<u>Peds:</u> 11-50Kg 0.5-1.25mg/kg 2x/day <u>Adult:</u> 50mg 2x/day	None needed	<u>Peds:</u> 2.5mg/Kg 2x/day <u>Adult:</u> 50- 100mg 2x/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 2x/day	\uparrow to 5mg/kg 2x/day at 1 wk.	Max: 10mg/Kg 2x/day	<ul style="list-style-type: none"> RI: No adjustment HI: Mod.1.25- 5mg/kg 2x/day

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Appendix I: Monitoring & Patient Safety

Drug	Adverse Reactions*	Monitoring	REMS
Vimpat Oral, IV lacosamide	<ul style="list-style-type: none"> • CNS: Dizziness (16-53%), fatigue (7-15%), ataxia (4-15%), HA (11-14%) • GI: N (7-17%), V (6-16%) • MSK: tremor (4-12%) • Ophth.: diplopia (6-16%), ↓ vision (2-16%) 	<ul style="list-style-type: none"> • CNS: Suicidality • 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"> • Ophth. Exam: pre & q 6 mons. • CNS: Psych/BH rx, 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%) • Ophth.: ↓ vision field (30%), nystagmus (13-15%), blurred vision (11-13%) • Misc: Otitis media (inf. 10-44%), fever (29%), infection (7-51%) 	<ul style="list-style-type: none"> • CNS: Sedation, Suicidality • Lab: Hgb/Hct • Ophth: Dilated indirect exam Pre, 4wks during, q 3-6 post • Misc: Weight gain/edema 	REMS Purpose: Awareness 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%) • MS: 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%) • Ophth: Nystagmus (16%) 	<ul style="list-style-type: none"> • CNS: depression, suicidality • Labs: CBC w diff, liver renal fx 	Med guide
Epidiolex oral solution cannabidiol	<ul style="list-style-type: none"> • CNS: Drowsy/lethargy/sedation (≤32%), • Derm: Skin rash (7-13%) • GI: ↓ appetite (16-22%), diarrhea (9-20%) • Hem/Onc: Anemia (30%) • Hepatic: ↑LFTs • Infection: 25-40%) 	<ul style="list-style-type: none"> • Lab: ALT, AST, bili (pre. & 1,3, 6 mons post) 	None

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References and Resources:

1. Epilepsia. 2006 Jul;47(7):1094-120.
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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 accessed November 2018.

Approved By:



12/5/18

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12/5/18

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