Clinical Policy: Valproate Sodium for Intravenous Injection (Depacon)

Reference Number: CP.PHAR.429
Effective Date: 06.04.19
Last Review Date: 08.20
Line of Business: Commercial, Medicaid, HIM-Medical Benefit

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Valproate sodium (Depacon®) for intravenous injection is an anticonvulsant agent.

FDA Approved Indication(s)

Epilepsy:

Depacon is indicated as an intravenous alternative in patients for whom oral administration of valproate products is temporarily not feasible in the following conditions:

- As monotherapy and adjunctive therapy in the treatment of patients with complex partial seizures that occur either in isolation or in association with other types of seizures.
- As sole and adjunctive therapy in the treatment of patients with simple and complex absence seizures, and adjunctively in patients with multiple seizure types that include absence seizures.*

**Simple absence is defined as very brief clouding of the sensorium or loss of consciousness accompanied by certain generalized epileptic discharges without other detectable clinical signs. Complex absence is the term used when other signs are also present.*

Limitation(s) of use:

- Because of the risk to the fetus of decreased IQ, neurodevelopmental disorders, neural tube defects, and other major congenital malformations, which may occur very early in pregnancy, valproate should not be used to treat women with epilepsy or bipolar disorder who are pregnant or who plan to become pregnant unless other medications have failed to provide adequate symptom control or are otherwise unacceptable.
- Valproate should not be administered to a woman of childbearing potential unless other medications have failed to provide adequate symptom control or are otherwise unacceptable.
- For prophylaxis of migraine headaches, valproate is contraindicated in women who are pregnant and in women of childbearing potential who are not using effective contraception.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Depacon is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Epilepsy (must meet all)**:**

1. Diagnosis of epilepsy;
2. Age ≥ 2 years;
3. Prescribed by or in consultation with a neurologist;
4. Oral valproate* administration *(Appendix B)* is temporarily not feasible (e.g., status epilepticus, reliance on gastrostomy tube, recent oral or neck surgery, esophageal condition or intraoral infection, myasthenia gravis or other neuromuscular condition);
   **May require prior authorization.*
5. At the time of request, member does not have any of the following contraindications:
   a. Mitochondrial disorder (e.g., Alpers Huttenlocher syndrome) caused by a mutation in mitochondrial DNA polymerase gamma (POLG);
   b. Urea cycle disorder (UCD) *(see Appendix D)*;
6. Dose does not exceed 60 mg/kg per day.

Approval duration: 1 month

B. Acute Migraine (off-label) (must meet all)**:**

1. Diagnosis of migraine;
2. Prescribed by or in consultation with a neurologist;
3. Age ≥ 18 years;
4. Oral administration of migraine medication is not feasible (e.g., due to migraine-associated nausea);
5. Failure of at least 2 non-oral migraine medications* from 2 different therapeutic classes unless clinically adverse effects are experienced or all are contraindicated *(see Appendix B)*;
   **May require prior authorization.*
6. At the time of request, member does not have any of the following contraindications:
   a. Mitochondrial disorder (e.g., Alpers Huttenlocher syndrome) caused by a mutation in mitochondrial DNA POLG;
   b. UCD *(see Appendix D)*;
7. Dose does not exceed 1,200 mg per infusion.

Approval duration: 1 infusion

C. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid and HIM-Medical Benefit.

II. Continued Therapy

A. Epilepsy (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Depacon for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. Dose does not exceed 60 mg/kg per day.

Approval duration: 1 month

B. Acute Migraine (must meet all)**:**
1. Re-authorization is not permitted. Members must meet the initial approval criteria.
Approval duration: Not applicable

C. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid and HIM-Medical Benefit.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial and CP.PMN.53 for Medicaid and HIM-Medical Benefit, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AED: antiepileptic drug
FDA: Food and Drug Administration
POLG: polymerase gamma
UCD: urea cycle disorder

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Epilepsy: Oral Valproate Formulations valproic acid (Depakene®): capsule divalproex sodium (Depakote® Sprinkles): capsule DR sprinkle valproate sodium (Depakene®): oral solution divalproex sodium (Depakote®): tablet DR divalproex sodium (Depakote® ER): tablet 24 hr ER	Varies	Varies

Acute Migraine: Non-Oral Medications *(evidence levels A and B - American Headache Society, 2019, 2015)*
<u>Nonsteroidal anti-inflammatory drugs (NSAIDs)</u>
• IM, IV
  ○ ketoralac
• Intranasal
  ○ Sprix® (tromethamine)
<u>Triptans</u>
• Intranasal
	Varies	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
○ sumatriptan nasal spray (Imitrex®) ○ Zomig® nasal spray (zolmitriptan) • Exhaler powder ○ sumatriptan nasal powder (Onzetra®, Xsail®) • SC ○ sumatriptan succinate injection (Imitrex®) sumatriptan needle-free delivery system (Sumavel® DosePro) ○ sumatriptan auto-injector (Zembrace®, SymTouch®) <u>Ergotamine derivatives</u> • SC, IM, IV ○ dihydroergotamine (D.H.E. 45®) • Intranasal ○ dihydroergotamine (Migranal®) <u>Antiemetics</u> • IV ○ metoclopramide • IM, IV ○ chlorpromazine ○ promethazine (Phenergan®) ○ droperidol ○ prochlorperazine • Rectal suppository ○ prochlorperazine (Compro®) ○ promethazine (Phenadoz®, Promethegan®)		

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Hepatic disease or significant hepatic dysfunction
  - Known mitochondrial disorders caused by mutations in mitochondrial DNA POLG
  - Suspected POLG-related disorder in children under two years of age
  - Known hypersensitivity to the drug
  - UCDs
  - Prophylaxis of migraine headaches: Pregnant women, women of childbearing potential not using effective contraception
- Boxed warning(s):
  - Hepatotoxicity, including fatalities, usually during the first 6 months of treatment
  - Fetal Risk, particularly neural tube defects, other major malformations, and decreased IQ
  - Pancreatitis, including fatal hemorrhagic cases

Appendix D: Examples of Urea Cycle Disorders

- N-acetyl glutamate synthetase deficiency
- Carbamoylphosphate synthetase I deficiency
- Ornithine transcarbamylase deficiency
- Argininosuccinate synthetase deficiency
- Argininosuccinate lyase deficiency
- Arginase deficiency
- Ornithin translocase deficiency
- Citrin deficiency

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Epilepsy	Initial dose: 10 to 15 mg/kg/day IV, increasing at 1 week intervals by 5 to 10 mg/kg/day IV to achieve optimal clinical response.* *Depacon has not been systematically studied for use in epilepsy; accordingly, the dosing information provided was obtained from studies utilizing oral divalproex sodium products for complex partial seizures in adults and children 10 years of age or older, and for simple and complex absence seizures (Depacon Package Insert).	60 mg/kg/day
Migraine - acute treatment (off-label)	Peer reviewed literature cites single doses, per IV infusion, from 300 mg to 1,200 mg.	1,200 mg/infusion

VI. Product Availability

Single-dose vials: 100 mg/mL (5 mL)

VII. References

1. Depacon Prescribing Information. November 2019. North Chicago, IL: AbbVie Inc.; February 2019. Available at Accessed May 4, 2020.
2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2019. Available at: http://www.clinicalpharmacology-ip.com/. Accessed May 4, 2020.

Epilepsy

3. Andres M. Kanner, MD, Eric Ashman, MD, et al. 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;91:74-81. doi:10.1212/WNL.0000000000005755
4. Andres M. Kanner, MD, Eric Ashman, MD, et al. Practice guideline update summary: Efficacy and tolerability of the new antiepileptic drugs II: Treatment-resistant epilepsy. Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology and the American Epilepsy Society. Neurology 2018;91:82-90. doi:10.1212/WNL.0000000000005756

5. Epilepsies: diagnosis and management. National Institute for Health and Care Excellence (NICE) website. https://www.nice.org.uk/guidance/CG137/chapter/Appendix-E-Pharmacological-treatment. Updated April 2018. Accessed April 26, 2019.
6. Glauser T, Ben-Menachem E, Bourgeois B. Special report: Updated ILAE evidence review of antiepileptic drug efficacy and effectiveness as initial monotherapy for epileptic seizures and syndromes. Epilepsia, 2013; 54(3):551-563.

Acute Migraine

7. AHS Consensus Statement: The American Headache Society position statement on integrating new migraine treatments into clinical practice. Headache 2019;59:1-18.
8. Orr SL, Friedman BW, Christie S, et al. Management of adults with acute migraine in the emergency department: The American Headache Society evidence assessment of parenteral pharmacotherapies. Headache 2016;56:911-940.
9. Marmura MJ, Silberstein SD, Schwedt TJ. The acute treatment of migraine in adults: the American Headache Society evidence assessment of migraine pharmacotherapies. Headache. 2015;55(1):3-20.
10. Mayans L, Walling A. Acute migraine headache: treatment strategies. American Family Physician, February 15, 2018; 97(4): 243-251.
11. Gelfant AA, Goadsby PJ. A neurologist's guide to acute migraine therapy in the emergency room. The Neurohospitalist 2012; 2(2): 51-59.

Urea Cycle Disorders

12. Online Mendelian Inheritance in Man (OMIM). An online catelog of human genes and genetic disorders. Updated March 25, 2019. Available at https://www.omim.org/. Accessed March 26, 2019.
13. Urea cycle disorders overview. GeneReviews [Internet]. Last updated: June 22, 2017. Available at https://www.ncbi.nlm.nih.gov/books/NBK1217/. Accessed March 26, 2019.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J3490	Unclassified drugs

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	06.04.19	08.19
3Q 2020 annual review: no significant changes; references reviewed and updated.	05.04.20	08.20

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program

approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

Note:

For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.