

## Clinical Policy: Valproate Sodium for Intravenous Injection (Depacon)

Reference Number: LA.PHAR.429

Effective Date:

Last Review Date: 01.21

Line of Business: Medicaid

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

Prior authorization is required. 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 Louisiana Healthcare Connections 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  $\geq$  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  $\geq$  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 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): LA.PMN.53 for Medicaid.

**II. Continued Therapy**

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

1. Currently receiving medication via Louisiana Healthcare Connections 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 Louisiana Healthcare Connections 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 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): LA.PMN.53 for.

**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 –LAP.PMN.53 for Medicaid, or evidence of coverage documents.

**IV. Appendices/General Information**

Appendix A: Abbreviation/Acronym Key

AED: antiepileptic drug

POLG: polymerase gamma

FDA: Food and Drug Administration

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 may require prior authorization.*

<u>Drug Name</u>	<u>Dosing Regimen</u>	<u>Dose Limit/Maximum Dose</u>
<u>Epilepsy: Oral Valproate Formulations</u> <u>valproic acid (Depakene®): capsule</u> <u>divalproex sodium (Depakote® Sprinkles): capsule DR</u> <u>sprinkle</u> <u>valproate sodium (Depakene®): oral solution</u> <u>divalproex sodium (Depakote®): tablet DR</u> <u>divalproex sodium (Depakote® ER): tablet 24 hr ER</u>	<u>Varies</u>	<u>Varies</u>
<u>Acute Migraine: Non-Oral Medications (evidence levels A and B - American Headache Society, 2019, 2015)</u> <u>Nonsteroidal anti-inflammatory drugs (NSAIDs)</u>	<u>Varies</u>	<u>Varies</u>

**CLINICAL POLICY**  
Valproate Sodium for Intravenous Injection



<u>Drug Name</u>	<u>Dosing Regimen</u>	<u>Dose Limit/Maximum Dose</u>
<ul style="list-style-type: none"> <li>• <u>IM, IV</u> <ul style="list-style-type: none"> <li>○ <u>ketoralac</u></li> </ul> </li> <li>• <u>Intranasal</u> <ul style="list-style-type: none"> <li>○ <u>Sprix® (tromethamine)</u></li> </ul> </li> </ul>		
<b>Triptans</b>		
<ul style="list-style-type: none"> <li>• <u>Intranasal</u> <ul style="list-style-type: none"> <li>○ <u>sumatriptan nasal spray (Imitrex®)</u></li> <li>○ <u>Zomig® nasal spray (zolmitriptan)</u></li> </ul> </li> <li>• <u>Exhaler powder</u> <ul style="list-style-type: none"> <li>○ <u>sumatriptan nasal powder (Onzetra®, Xsail®)</u></li> </ul> </li> <li>• <u>SC</u> <ul style="list-style-type: none"> <li>○ <u>sumatriptan succinate injection (Imitrex®)</u></li> <li><u>sumatriptan needle-free delivery system (Sumavel® DosePro)</u></li> <li>○ <u>sumatriptan auto-injector (Zembrace®, SymTouch®)</u></li> </ul> </li> </ul>		
<b>Ergotamine derivatives</b>		
<ul style="list-style-type: none"> <li>• <u>SC, IM, IV</u> <ul style="list-style-type: none"> <li>○ <u>dihydroergotamine (D.H.E. 45®)</u></li> </ul> </li> <li>• <u>Intranasal</u> <ul style="list-style-type: none"> <li>○ <u>dihydroergotamine (Migranal®)</u></li> </ul> </li> </ul>		
<b>Antiemetics</b>		
<ul style="list-style-type: none"> <li>• <u>IV</u> <ul style="list-style-type: none"> <li>○ <u>metoclopramide</u></li> </ul> </li> <li>• <u>IM, IV</u> <ul style="list-style-type: none"> <li>○ <u>chlorpromazine</u></li> <li>○ <u>promethazine (Phenergan®)</u></li> <li>○ <u>droperidol</u></li> <li>○ <u>prochlorperazine</u></li> </ul> </li> <li>• <u>Rectal suppository</u> <ul style="list-style-type: none"> <li>○ <u>prochlorperazine (Compro®)</u></li> <li>○ <u>promethazine (Phenadoz®, Promethegan®)</u></li> </ul> </li> </ul>		

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
- Ornithine translocase deficiency
- Citrin deficiency

**V. Dosage and Administration**

<u>Indication</u>	<u>Dosing Regimen</u>	<u>Maximum Dose</u>
<u>Epilepsy</u>	<u>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.*</u>  <u>*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).</u>	<u>60 mg/kg/day</u>
<u>Migraine - acute treatment (off-label)</u>	<u>Peer reviewed literature cites single doses, per IV infusion, from 300 mg to 1,200 mg.</u>	<u>1,200 mg/infusion</u>

**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.
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.00000000000005755

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.00000000000005756
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 catalog 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.**

<u><b>HCPCS Codes</b></u>	<u><b>Description</b></u>
<u><b>J3490</b></u>	<u><b>Unclassified drugs</b></u>

<u><b>Reviews, Revisions, and Approvals</b></u>	<u><b>Date</b></u>
<u><b>Converted corporate to local policy.</b></u>	<u><b>1/2021</b></u>

**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.**

**LHCC 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.**

**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 LHCC administrative policies and procedures.**

**This clinical policy is effective as of the date determined by LHCC. 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. LHCC 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 LHCC has no control or right of control. Providers are not agents or employees of LHCC.**

**This clinical policy is the property of LHCC. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and**

**conditions by providing services to members and/or submitting claims for payment for such services.**

**©2020 Louisiana Healthcare Connections. All rights reserved. All materials are exclusively owned by Louisiana Healthcare Connections and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Louisiana Healthcare Connections. You may not alter or remove any trademark, copyright or other notice contained herein. Louisiana Healthcare Connections is a registered trademark exclusively owned by Louisiana Healthcare Connections.**