Preemptive policy: This is a P&T approved policy and can be used after the drug is FDA approved until it is superseded by an updated policy

CENTENE® Corporation

Clinical Policy: Encaleret (CLTX-305)

Reference Number: CP.PHAR.801
Effective Date: FDA Approval Date
Last Review Date: 11.26
Line of Business: Commercial, HIM/ICHRA, Medicaid

Revision Log

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

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Description

Encaleret (CLTX-305®/™) is calcium-sensing receptor (CaSR) antagonist.

FDA Approved Indication(s) [Pending]

CLTX-305 is indicated for the treatment of autosomal dominant hypocalcemia type 1 (ADH1).

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 CLTX-305 is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria*

**Criteria will mirror the clinical information from the prescribing information once FDA-approved*

A. Autosomal Dominant Hypocalcemia (must meet all)**:**

1. Diagnosis of ADH1 as evidenced by both of the following (a and b):
   a. Genetic test confirming activating variant of the CaSR gene;
   b. Member has history of symptoms or signs of ADH1 (e.g., hypercalciuria, *see Appendix D for additional examples*);
2. Prescribed by or in consultation with an endocrinologist;
3. Age ≥ 16 years;*
4. If age 16 to < 18 years, epiphyseal growth plates have closed;
5. Recent (dated within the last 30 days) albumin-corrected blood calcium < 8.6 mg/dL;
6. Recent (dated within the last 30 days) lab result shows sufficient 25-hydroxyvitamin D stores ≥ 25 ng/mL;
7. Failure of a 12-week trial of calcium supplements and active forms of vitamin D (e.g., calcitriol) at up to maximally indicated doses, unless contraindicated or clinically significant adverse events are experienced;*^
   **Prescriber must indicate that the hypocalcemia is not well controlled with calcium supplements and active forms of vitamin D (see examples in Appendix B below)*
   ^For Illinois HIM requests, the step therapy requirements above do not apply per IL HB 5395
8. Dose does not exceed both of the following (a and b):*
   a. 360 mg per day;
   b. 6 tablets per day.

Approval duration: 6 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid.

II. Continued Therapy*

**Criteria will mirror the clinical information from the prescribing information once FDA-approved*

A. Autosomal Dominant Hypocalcemia (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B)*;
2. Member is responding positively to therapy as evidenced by, including but not limited to, improvement in any of the following parameters (a, b, c, or d):
   a. Improvement in albumin-corrected serum calcium (e.g., 8.3 to 10.6 mg/dL [2.08-2.68 mmol/L]);
   b. Improvement in urinary calcium (e.g., 24-hour urinary calcium < 300 mg/day for men [7.5 mmol/day], 24-hour urinary calcium < 250 mg/day for women [6.25 mmol/day]);
   c. Improvement in intact parathyroid hormone (iPTH) levels;
   d. Independence from conventional therapy due to adequate disease control with CLTX-305 (e.g., no active vitamin D and elemental calcium supplementation ≤ 600 mg/day);
3. If request is for a dose increase, new dose does not exceed both of the following (a and b):*
   a. 360 mg per day;
   b. 6 tablets per day.

Approval duration: 12 months

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B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid.

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, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ADH1: autosomal dominant hypocalcemia type 1
CaSR: calcium-sensing receptor
FDA: Food and Drug Administration
iPTH: intact parathyroid hormone

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
calcitriol (Rocaltrol®)	0.25 mcg PO QD initially; dose may be increased at 2- to 4-wk intervals	2 mcg/day
calcium carbonate (Caltrate®, OsCal®, Tums®)	1-3 g PO QD in divided dose	3 g/day
calcium citrate (Cal-Citrate®, Cal-C-Caps®)	1-3 g PO QD in divided doses	3 g/day

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 [Pending]

- Contraindication(s): pending

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- Boxed warning(s): pending

Appendix D: General Information

- Signs and symptoms of hypocalcemia include hypercalciuria, basal ganglia or other cerebral calcification, Chvostek sign, nephrocalcinosis, papilledema, premature cataracts, prolonged QT interval on ECG, pseudotumor cerebri, Trousseau sign, agitation, anxiety, back pain, brain fog, bronchospasm, blepharospasm, cardiac failure, cognitive impairment, difficulty focusing/concentration, esophageal spasm, facial spasm, headaches, hypoesthesia (including facial and oral), irritability, laryngospasm, muscle cramping, muscle fatigue, muscle spasms, muscle tightness, muscle twitching, musculoskeletal pain, musculoskeletal stiffness, myalgia, nephrolithiasis, nervousness, paresthesia (including oral), polydipsia, polyuria, seizure, tetany, throat tightness, or tremor.
- Corrected calcium (cCa) = measured total calcium (mg/dL) + 0.8(4–albumin (g/dL))
- Examples of a "failure" of calcium and vitamin D supplementation can include: large swings in calcium levels, calcium phosphate product cannot be maintained within an acceptable range, high risk of renal complications due to hypercalciuria or calcium containing stones, evidence of renal complications such as nephrolithiasis or having a condition causing poor calcium and vitamin D absorption.

V. Dosage and Administration [Pending]

Indication	Dosing Regimen	Maximum Dose
ADH1*	Pending*	Pending*

VI. Product Availability [Pending]

Tablets: 10 mg, 30 mg, 60 mg*

VII. References

1. Encaleret Prescribing Information.
2. Clinicalstudies.info.nih.gov. CALIBRATE: A phase 3, randomized, open-label study evaluating the efficacy and safety of encaleret compared to standard of care in participants with Autosomal Dominant Hypocalcemia Type 1 (ADH1) Available at: https://clinicalstudies.info.nih.gov/protocoldetails.aspx?id=001521-D. Accessed August 17, 2026.
3. De Coster T, David K, Breckpot J, Decallonne B. Management of autosomal dominant hypocalcemia type 1: Literature review and clinical practice recommendations. *J Endocrinol Invest*. 2025 Apr;48(4):831-844. doi: 10.1007/s40618-024-02496-y.
4. Brandi ML, Bilezikian JP, Shoback D, et al. Management of Hypoparathyroidism: Summary Statement and Guidelines. J Clin Endocrinol Metab. 2016 Jun;101(6):2273-83. doi: 10.1210/jc.2015-3907.
5. Khan AA, Bilezikian JP, Brandi ML, et al. Evaluation and management of hypoparathyroidism summary statement and guidelines from the second international workshop. *J Bone and Mineral Research*. December 2022;37(12):2568-85.
6. Khan AA, Ali DS, Bilezikian JP, et al. Best practice recommendations for the diagnosis and treatment of hypoparathyroidism. *Metabolism*. October 2025;171:156335. doi: 10.1016/j.metabol.2025.156335.

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively	08.25.26	11.26

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.

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This clinical policy is the property of the Health Plan. 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.

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.

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