Clinical Policy: Crinecerfont (Crenessity)

Reference Number: CP.PHAR.692
Effective Date: 12.13.24
Last Review Date: 11.25
Line of Business: Commercial, HIM, Medicaid Revision Log

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

Description

Crinecerfont (Crenessity™) is a corticotropin-releasing factor type 1 (CRF1) receptor antagonist.

FDA Approved Indication(s)

Crenessity is indicated as adjunctive treatment to glucocorticoid replacement to control androgens in adults and pediatric patients 4 years of age and older with classic congenital adrenal hyperplasia (CAH).

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 Crenessity is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Congenital Adrenal Hyperplasia (must meet all)**:**

1. Diagnosis of classic CAH;
2. Prescribed by or in consultation with an endocrinologist;
3. Age ≥ 4 years;
4. Medically confirmed diagnosis of classic 21-hydroxylase deficiency CAH based on one of the following (a, b, c, or d):
   a. Elevated 17-hydroxyprogesterone (17-OHP) level;
   b. Confirmed CYP21A2 genotype;
   c. Positive newborn screening with confirmatory second-tier testing (e.g., liquid chromatography – tandem mass spectrometry);
   d. Cosyntropin stimulation test;
5. Member is currently receiving chronic glucocorticoid treatment for CAH (e.g., hydrocortisone, prednisone, prednisolone, methylprednisolone, dexamethasone);*
   **For Illinois HIM requests, the step therapy requirements above do not apply as of 1/1/2026 per IL HB 5395*
6. Crenessity is prescribed in combination with glucocorticoid treatment;
7. Request meets one of the following (a, b, or c):
   a. Dose does not exceed both of the following (a and b):
      i. 200 mg per day (*see Section V for dosing based on weight*);
      ii. 2 capsules per day or 4 bottles per month;

b. If prescribed concomitantly with a strong CYP3A4 inducer (e.g., phenytoin, carbamazepine, rifampin, rifabutin, rifapentine, and phenobarbital): Dose does not exceed both of the following (i and ii):
   i. 400 mg per day (*see Section V for dosing based on weight*);
   ii. 4 capsules per day or 8 bottles per month;
c. If prescribed concomitantly with a moderate CYP3A4 inducer (e.g., bosentan, efavirenz, etravirine, and primidone): Dose does not exceed both of the following (i and ii):
   i. 300 mg per day (*see Section V for dosing based on weight*);
   ii. 3 capsules per day or 6 bottles per month.

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) 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, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) 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, 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, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Congenital Adrenal Hyperplasia (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 <u>any</u> of the following parameters:
   a. Reduction in glucocorticoid dose;
   b. Reduction in serum androstenedione (A4);
3. If request is for a dose increase, request meets one of the following (a, b, or c):
   a. New dose does not exceed both of the following (a and b):
      i. 200 mg per day (*see Section V for dosing based on weight*);
      ii. 2 capsules per day or 4 bottles per month;

b. If prescribed concomitantly with a strong CYP3A4 inducer (e.g., phenytoin, carbamazepine, rifampin, rifabutin, rifapentine, and phenobarbital): New dose does not exceed both of the following (i and ii):
   i. 400 mg per day (*see Section V for dosing based on weight*);
   ii. 4 capsules per day or 8 bottles per month;
c. If prescribed concomitantly with a moderate CYP3A4 inducer (e.g., bosentan, efavirenz, etravirine, and primidone): New dose does not exceed both of the following (i and ii):
   i. 300 mg per day (*see Section V for dosing based on weight*);
   ii. 3 capsules per day or 6 bottles per month.

Approval duration: 12 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) 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, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) 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, 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, 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, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
CAH: congenital adrenal hyperplasia
CRF1: corticotropin-releasing factor type 1
FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives
Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): hypersensitivity to crinecerfont or any excipients of Crenessity
- Boxed warning(s): none reported

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
CAH	Adults*: 100 mg PO BID Pediatric (age 4 to 17) by body weight*: 10 kg to 19 kg: 25 mg PO BID 20 kg to 54 kg: 50 mg PO BID ≥ 55 kg: 100 mg PO BID *If taking strong CYP3A4 inducer both morning and evening doses should be increased 2-fold; if taking moderate CYP3A4 inducer only the evening dose should be increased 2-fold	Adults: 200 mg/day; 400 mg/day if taking a strong CYP3A4 inducer; 300 mg/day if taking a moderate CYP3A4 inducer Pediatric: See weight based dosing regimen

VI. Product Availability

- Capsules: 25 mg, 50 mg, 100 mg
- Oral solution: 50 mg/mL (30 mL bottle)

VII. References

1. Crenessity Prescribing Information. Neurocrine Biosciences, Inc.: San Diego, CA; December 2024. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/218808s000,218820s000lbl.pdf. Accessed July 16, 2025.
2. Sarafoglou K, Kim MS, Lodish M, et al.; CAHtalyst Pediatric Trial Investigators. Phase 3 trial of crinecerfont in pediatric congenital adrenal hyperplasia. N Engl J Med. 2024 Aug 8;391(6):493-503.
3. Auchus RJ, Hamidi O, Pivonello R, et al.; CAHtalyst Adult Trial Investigators. Phase 3 trial of crinecerfont in adult congenital adrenal hyperplasia. N Engl J Med. 2024 Aug 8;391(6):504-514.
4. ClinicalTrials.gov. Global safety and efficacy registration study of crinecerfont for congenital adrenal hyperplasia (CAHtalyst). Available at: https://www.clinicaltrials.gov/study/NCT04490915. Accessed July 17, 2025.
5. ClinicalTrials.gov. Global safety and efficacy registration study of crinecerfont in pediatric patients with classic congenital adrenal hyperplasia (CAHtalyst Pediatric Study). Available at: https://clinicaltrials.gov/study/NCT04806451. Accessed July 17, 2025.
6. Speiser PW, Arlt W, Auchus RJ, et al. Congenital Adrenal Hyperplasia Due to Steroid 21-Hydroxylase Deficiency: An Endocrine Society Clinical Practice Guideline. J Clinical Endocrinol Metab. November 2018; 103(11): 4043-4088.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively.	08.27.24	11.24
RT4: converted PEPP to post-FDA-approved status; revised age from 2 to 4 years; updated maximum dosing and added quantity limit per prescribing information dosing; references reviewed and updated.	01.07.25	
4Q 2025 annual review: added step therapy bypass for IL HIM per IL HB 5395; extended continued approval duration from 6 to 12 months for this chronic condition; references reviewed and updated.	07.17.25	11.25

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.

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.