Clinical Policy: Crinecerfont (Crenessity)

Reference Number: PA.CP.PHAR.692
Effective Date: 02/2025
Last Review Date: 10/2025

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 PA Health & Wellness® 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);
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 (i and ii):
      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

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): PA.CP.PMN.53

II. Continued Therapy

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

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
2. Member is responding positively to therapy as evidenced by, including but not limited to, improvement in any 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 (i and ii):
      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. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.
   Approval duration: Duration of request or 12 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): PA.CP.PMN.53

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 – PA.CP.PMN.53

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
Policy created	01/2025
4Q 2025 annual review: extended continued approval duration from 6 to 12 months for this chronic condition; references reviewed and updated.	10/2025