Generic Name: Crinecerfont

Therapeutic Class or Brand Name: Crenessity

Applicable Drugs: N/A

Preferred: N/A

Non-preferred: N/A

Date of Origin: 6/2/2025

Date Last Reviewed / Revised: N/A

PRIOR AUTHORIZATION CRITERIA

(May be considered medically necessary when criteria I through VIII are met)

I. Documented diagnosis of classic Congenital Adrenal Hyperplasia (CAH) due to 21-hydroxylase deficiency (21-OHD) as confirmed with one of the following:
   A. Elevated 17-hydroxyprogesterone (17-OHP) level
   B. Genetic test confirming CYP21A2 genotype
   C. Positive newborn screening with confirmatory second-tier testing
   D. Diagnostic results after cosyntropin (ACTH) stimulation

II. Documented stable regimen of glucocorticoid (GC) dose for at least 4 weeks and one of the following A or B:
   A. Uncontrolled androgen levels despite maximally tolerated glucocorticoid (GC) dose
   B. Requirement for supraphysiologic GC daily doses for disease control (i or ii):
      i. Pediatric (≥4 to 17 years): Total GC dose >12 mg/m^2/day in hydrocortisone dose equivalents
      ii. Adult (≥18 years): Total GC dose >13 mg/m^2/day in hydrocortisone dose equivalents

III. Crenessity (crinecerfont) will be used as an adjunct to systemic glucocorticoid (GC) replacement therapy (e.g., hydrocortisone, prednisone, prednisolone, or dexamethasone).

IV. For pediatric patients weighing ≥55 kg or patients weighing ≥20 kg requiring CYP3A4 dose adjustment: request is for capsule formulation or there must be documentation of inability to swallow capsules whole.

V. Minimum age requirement: 4 years old.

VI. Treatment must be prescribed by or in consultation with an endocrinologist or physician who specializes in the treatment of adrenal hyperplasia.

VII. Request is for a medication with the appropriate FDA labeling, or its use is supported by current clinical practice guidelines.

VIII. Refer to the plan document for the list of preferred products. If the requested agent is not listed as a preferred product, must have documented treatment failure or contraindication to the preferred product(s).

Exclusion Criteria

- Diagnosis of any other forms of classic CAH (e.g., 11-beta-hydroxylase deficiency, 17-alpha-hydroxylase deficiency).
- History of bilateral adrenalectomy, hypopituitarism, or other conditions requiring chronic GC therapy.
- History of severe renal impairment (eGFR <44 mL/min/1.73 m^2) or end-stage renal disease.

Other Criteria

- N/A

Quantity / Days Supply Restrictions

- 50 mg Capsule: 60 capsules per 30 days
- 100 mg Capsule: 60 capsules per 30 days
- 50 mg/mL Solution: 120 mL per 30 days

Approval Length

- **Authorization:** 6 months
- **Re-Authorization:** 1 year. An updated letter of medical necessity or progress notes showing positive clinical response, as confirmed with a reduction in daily GC dose or improved androgen control.

Appendix

Recommended Dosage for Adults

- 100 mg orally, twice daily with a meal in the morning and evening
- 200 mg orally, twice daily with a meal in the morning and evening when used concomitantly with strong CYP3A4 inducers
- 100 mg orally with the morning meal and 200 mg orally with the evening meal when used concomitantly with moderate CYP3A4 inducers

Table 1. Recommended CRENESSITY Weight-Based Dosage for Pediatric Patients 4 Years of Age and Older

Weight	Dosage Regimen with a Meal
10 kg to less than 20 kg	25 mg orally twice daily
20 kg to less than 55 kg	50 mg orally twice daily
Greater than or equal to 55 kg	100 mg orally twice daily

Table 2. Dosage Increase of CRENESSITY for Use with Strong CYP3A4 Inducers in Pediatric Patients 4 Years of Age and Older

Weight	Dosage Regimen with a Meal
10 kg to less than 20 kg	50 mg orally twice daily
20 kg to less than 55 kg	100 mg orally twice daily
Greater than or equal to 55 kg	200 mg orally twice daily

Table 3. Dosage Increase of CRENESSITY for Use with Moderate CYP3A4 Inducers in Pediatric Patients 4 Years of Age and Older

	Dosage Regimen with a Meal	
Weight	**Morning Dose**	**Evening Dose**
10 kg to less than 20 kg	25 mg orally	50 mg orally
20 kg to less than 55 kg	50 mg orally	100 mg orally
Greater than or equal to 55 kg	100 mg orally	200 mg orally

REFERENCES

1. Crenessity [Prescribing Information], San Diego, CA; Neurocrine Biosciences, Inc; 2024. Accessed April 21, 2025.

   https://pi.neurocrine.com/crenessity/CRENESSITY-Full-US-Prescribing-Information.pdf

2. Auchus RJ, Hamidi O, Pivonello R, et al. Phase 3 Trial of Crinecerfont in Adult Congenital Adrenal Hyperplasia. N Engl J Med. 2024;391(6):504-514. doi:10.1056/NEJMoa2404656. Accessed April 21, 2025.

   https://pubmed.ncbi.nlm.nih.gov/38828955/

3. Sarafoglou K, Kim MS, Lodish M, et al. Phase 3 Trial of Crinecerfont in Pediatric Congenital Adrenal Hyperplasia. N Engl J Med. 2024;391(6):493-503. doi:10.1056/NEJMoa2404655. Accessed April 21, 2025.

   https://pubmed.ncbi.nlm.nih.gov/38828945/

4. Speiser PW, Arlt W, Auchus RJ, et al. Congenital Adrenal Hyperplasia Due to Steroid 21-Hydroxylase Deficiency: An Endocrine Society Clinical Practice Guideline [published correction appears in J Clin Endocrinol Metab. 2019 Jan 1;104(1):39-40. doi: 10.1210/jc.2018-02371.]. J Clin Endocrinol Metab. 2018;103(11):4043-4088. doi:10.1210/jc.2018-01865. Accessed April 21, 2025.

   https://pubmed.ncbi.nlm.nih.gov/30272171/