PRIOR AUTHORIZATION POLICY

POLICY: Adrenal Hyperplasia – Crenessity Prior Authorization Policy
- Crenessity™ (crinecerfont capsules and oral solution – Neurocrine Biosciences)

REVIEW DATE: 12/18/2024

OVERVIEW
Crenessity, a corticotropin-releasing factor type 1 receptor antagonist, is indicated for the treatment of classic congenital adrenal hyperplasia (CAH) as adjunctive treatment to glucocorticoid replacement to control androgens in adults and pediatric patients ≥ 4 years of age.[1]

Disease Overview
Classic CAH due to 21-hydroxalase deficiency is the most common cause of primary adrenal insufficiency in children.[2] The prevalence of classic CAH is 1 in 10,000 to 1 in 15,000 live births. However, the prevalence of classic CAH is lower in Black and Asian populations. CAH typically presents during the newborn screening or by presentation of atypical genitalia in females. Early detection can prevent salt wasting adrenal crisis and decrease neonatal mortality. A diagnosis of CAH is most often confirmed during the newborn screenings which tests for elevated 17-hydroxyprogesterone levels. Other tests that are used in the diagnosis of CAH include cosyntropin stimulation tests and genetic testing with confirmed cytochrome (CYP)21A2 genotype. Management of classic CAH requires adequate glucocorticoid replacement with hydrocortisone at supraphysiological doses.

Clinical Efficacy
The efficacy of Crenessity for the treatment of classic CAH has been evaluated in two pivotal studies.[1,3,4] One study included pediatric patients and the other included adults. Both studies required the patients to have a confirmed diagnosis of CAH and to receive a stable dose of glucocorticoid of > 12 mg/m^2/day in hydrocortisone dose equivalents. In both studies, compared with placebo, Crenessity significantly decreased serum androstenedione levels from baseline at Week 4. In addition, compared with placebo, the total glucocorticoid dose while androstenedione was controlled (≤ 120% of baseline or ≤ upper limit of normal) was significantly reduced in the Crenessity group at Week 24.

POLICY STATEMENT
Prior Authorization is recommended for prescription benefit coverage of Crenessity. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Crenessity as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Crenessity to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA
Coverage of Crenessity is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Classic Congenital Adrenal Hyperplasia (CAH).** Approve for the duration noted if the patient meets ONE of the following (A and B):
   - **A)** Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, and iii):
     - **i.** Patient is ≥ 4 years of age; AND
     - **ii.** Patient meets BOTH of the following (a and b):
       - **a)** The medication will be taken in combination with a systemic glucocorticoid; AND
       Note: Examples of glucocorticoids include hydrocortisone, prednisone, prednisolone, or dexamethasone.
       - **b)** Patients has a diagnosis of 21-hydroxylase deficiency CAH confirmed by ONE of the following [(1), (2), (3), or (4)]:
         - **(1)** Elevated 17-hydroxyprogesterone level; OR
         - **(2)** Confirmed cytochrome (CYP)21A2 genotype; OR
         - **(3)** Positive newborn screening with confirmatory second-tier testing; OR
         - **(4)** Diagnostic results after cosyntropin stimulation; AND
     - **iii.** The medication is prescribed by or in consultation with an endocrinologist, urologist, or a physician who specializes in the treatment of adrenal hyperplasia.
   - **B)** Patient is Currently Receiving Crenessity. Approve for 1 year if, according to the prescriber, the patient is continuing to derive benefit from Crenessity.
   Note: Examples of responses to Crenessity therapy are reduced androstenedione levels, decreased 17-hydroxyprogesterone levels, or reduction in glucocorticoid dose from baseline (i.e., prior to Crenessity therapy) or improved or stabilized clinical signs/symptoms of classic Congenital Adrenal Hyperplasia (e.g., decrease in body mass index standard deviation scores, improved insulin resistance, reduction of hirsutism, or improvement in androstenedione-to-testosterone ratio).

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Crenessity is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Crenessity™ capsules and oral solution [prescribing information]. San Diago, CA: Neurocrine Biosciences, December 2024.
2. Fraga NR, Minaeian N, Kim MS. Congenital adrenal hyperplasia. *Pediatr Rev*. 2024;45(2):74-84.
3. 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.
4. 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.