Original Effective Date: 06/28/2025
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Last P&T Approval/Version: 04/30/2025
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Policy Number: C29356-A

Crenessity (crinecerfont)

PRODUCTS AFFECTED

Crenessity (crinecerfont)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Classic congenital adrenal hyperplasia (CAH)

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by-case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. CLASSIC CONGENITAL ADRENAL HYPERPLASIA (CAH):
   1. Documentation of a confirmed diagnosis of classic congenital adrenal hyperplasia due to 21-hydroxylase deficiency (21-OHD) [DOCUMENTATION REQUIRED]
      AND

2. Documentation that crinecerfont will be used as an adjunctive treatment with glucocorticoid replacement
   AND
3. Documentation that member currently requires supraphysiologic glucocorticoid dosing to control their condition AND that the dose is currently stable, defined as [DOCUMENTATION REQUIRED]:
   a. Pediatric patients: Glucocorticoid dose >12 mg/m2/day in hydrocortisone dose equivalents (see Appendix)
      OR
   b. Adult patients: Glucocorticoid dose >13 mg/m2/day in hydrocortisone dose equivalents (see Appendix)

   AND
4. For requests for the oral solution, Members must meet one of the following:
   a. Member is a pediatric patient weighing less than 55kg
      OR
   b. Documentation has been provided to support that Member is unable to swallow tablets

CONTINUATION OF THERAPY:

A. CLASSIC CONGENITAL ADRENAL HYPERPLASIA (CAH):
1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
   AND
2. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity
   AND
3. Documentation of positive clinical response as demonstrated by reduction in daily glucocorticoid dose [DOCUMENTATION REQUIRED]
   AND
4. Documentation that Member continues to use crinecerfont adjunctively with glucocorticoids
   AND
5. For requests for the oral solution, Members must meet one of the following:
   a. Member is a pediatric patient weighing less than 55kg
      OR
   b. Documentation has been provided to support that Member is unable to swallow tablets

DURATION OF APPROVAL:

Initial authorization: 6 months, Continuation of Therapy: 12 months

PRESCRIBER REQUIREMENTS:

Prescribed by or in consultation with a board-certified endocrinologist. [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:

4 years of age and older

QUANTITY:

Adults: 100 mg twice daily
Pediatric Weight Based Dosing:
10 kg to less than 20 kg: 25 mg orally twice daily
20 kg to less than 55 kg: 50 mg orally twice daily
≥55 kg: 100 mg orally twice daily

Maximum Quantity Limits – 200 mg twice daily (Concomitant CYP3A4 inducer required)

PLACE OF ADMINISTRATION:
The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Oral

DRUG CLASS:
Corticotropin-Releasing Factor (CRF) Receptor Type 1 Antag

FDA-APPROVED USES:
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).

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:

Pediatric Weight Based Dosing:

Weight	Dosage Regimen with a Meal
≥55 kg	100 mg orally twice daily
20 kg to <55 kg	50 mg orally twice daily
10 kg to <20 kg	25 mg orally twice daily

Dosing modifications for concomitant use with Strong and Moderate CYP3A4 Inducers:
Adults: Increase dose to 200 mg, twice daily with a meal in the morning and the evening
Pediatric Weigh Based Modification:

Weight	Dosage Regimen with a Meal
≥55 kg	200 mg orally twice daily
20 kg to <55 kg	100 mg orally twice daily
10 kg to <20 kg	50 mg orally twice daily

Glucocorticoid Dose Relationships (only applicable to oral or IV administration routes):
Cortisone: 25 mg
Hydrocortisone: 20 mg
Prednisolone: 5 mg
Prednisone: 5 mg
Methylprednisolone:4 mg
Triamcinolone:4 mg
Dexamethasone: 0.75 mg
Betamethasone: 0.75 mg

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:

Congenital adrenal hyperplasia (CAH) is a group of autosomal recessive disorders which result in impaired cortisol synthesis. In the majority of cases (approximately 95%), CAH is caused by mutation of the CYP212A2 gene. CAH is an autosomal recessive disease, which means that both parents must be carriers of the recessive gene. This gene encodes for the enzyme 21-hydroxylase, which converts 17-hydroxyprogesterone to 11-deoxycortisol and progesterone to deoxycorticosterone. 11-deoxycortisol and deoxycorticosterone are both necessary for the production of aldosterone and cortisol, with the deficiency resulting in a loss of negative feedback within the hypothalamic-pituitary-adrenal (HPA) axis.

CAH has two forms, classic and nonclassic; classic is the more severe form and is usually diagnosed in infants. Classic CAH is characterized by impairment in the synthesis of cortisol and aldosterone. Classic CAH is a rare condition affecting approximately 15,000-25,000 patients in the US. Newborn screening programs in the United States screen for CAH due to 21-hydroxylase deficiency (21OHD). Mineralocorticoid deficiency can result in adrenal crisis. In infants, this can result in failure to thrive, hypovolemia and shock. Newborn screenings aim to reduce this risk.

In classic CAH, the impaired negative feedback inhibition in the HPA axis, leads to increased adrenal gland stimulation and resultant excess production of adrenal androgens. The increase in adrenal androgens in childhood can result in early puberty, virilization and growth acceleration with resultant adult short stature. Males with classic CAH can have testicular adrenal rest tumors (TARTs) and females can have oligomenorrhea or amenorrhea.

Current treatment guidelines recommend classic CAH treatment with glucocorticoids. In patients that are growing, maintenance therapy with hydrocortisone is recommended. In adults with classic CAH, guidelines recommend daily hydrocortisone and/or long-acting glucocorticoids, along with mineralocorticoids if needed. While glucocorticoids are the standard of care, doses are typically supraphysiological. Long term chronic exposure can result in decreased bone density and fracture risk, insulin resistance and diabetes, obesity, and hypertension.

Crinecerfont is a corticotropin-releasing factor type 1 (CRF1) receptor antagonist which is intended to control adrenal androgen levels utilizing a non-glucocorticoid mechanism. By blocking CRF from binding to CRF1 receptor, crinecerfont reduces adrenocorticotropic hormone (ACTH) and the production of androgens. Crinecerfont was studied in two phase three trials, CAHtalyst Adult Study (NCT04490915) and CAHtalyst Pediatric Study (NCT04806451). Both were randomized, double-blind, placebo-controlled studies in patients with classic CAH. Patients in both studies were treated with glucocorticoids, which is the standard of care, at supraphysiological doses.

In the CAHtalyst Adult Study, adult patients (n=182) were randomized to crinecerfont (n=122) or placebo (n=60) for 24 weeks of treatment. For inclusion, participants were required to have CAH, be 18 years of age or older, and be receiving a daily dose of hydrocortisone equivalence greater than 13 mg/m^2. The glucocorticoid dose was required to be stable for at least 1 month. Key exclusion criteria included the presence of any history of another condition that also required chronic glucocorticoid treatment (e.g., bilateral adrenalectomy or hypopituitarism). The primary endpoint was a percent change from baseline in glucocorticoid dose while maintaining androstenedione control. At twenty-four weeks, the crinecerfont arm had a statistically significant greater percentage of participants achieve a reduction in glucocorticoid

daily dose while controlling androstenedione levels (A4) compared to placebo.

In the CAHtalyst Pediatric Study, participants (n=103) included children ages 2 to 17 years with CAH. A stable daily glucocorticoid dose of at least 12 mg/m^2 hydrocortisone equivalence, which was stable for at least 4 weeks, was required. Baseline laboratory measures of an androstenedione level greater than the midpoint of the reference range and a 17-hydroxyprogesterone level more than two times the upper limit of the normal range were required. In this pediatric study, the primary end point was a change in androstenedione level from baseline to week 4 and the secondary end point was a change in the 17-hydroxyprogesterone level from baseline to week 4. Treatment with crinecerfont was found show a reduction of -197 mg/dL androstenedione (A4) levels, while the placebo group showed an increase of 71 ng/dL (least-squares mean difference [LSMD], −268 ng per deciliter, P<0.001). Participants were also found to have decreases in their glucocorticoid dosing to physiologic levels.

In the CAHtalyst adult trial, the most commonly observed adverse reactions, reported in greater than or equal to 4 percent of the participants were fatigue, headache, dizziness, arthralgias, back pain, decreased appetite and myalgia. Three percent of the crinecerfont treated adult patients discontinued treatment due to treatment emergent adverse effects (TEAEs). These TEAS were assessed and determined to not likely be due to crinecerfont. In the CAHtalyst pediatric trial, the most commonly observed adverse reactions, reported in greater than or equal to 4 percent of the participants were headache, abdominal pain, fatigue, nasal congestion and epitaxis. Three percent of the crinecerfont treated pediatric patients discontinued treatment due to abdominal pain, myalgia, and dizziness.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Crenessity (crinecerfont) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Crenessity (crinecerfont) include: hypersensitivity to crinecerfont or any excipients of Crenessity.

OTHER SPECIAL CONSIDERATIONS:
Crinecerfont should be taken with a meal. The oral solution should be stored and dispensed in the oringal container in an upright postion. The oral solution should be stored in the refrigerator until opened. Once it is opened, it may be stored in the refrigerator or at room temperature and should be discarded 30 days after opening. The capsules should be swallowed whole, with liquid, and should not be opened, chewed or broken. Dosing modifications are required when concomitantly used with a strong or moderate CYP3A4 inducer.

CODING/BILLING INFORMATION

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not be all-inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.*

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:
Crenessity CAPS 50MG
Crenessity CAPS 100MG
Crenessity SOLN 50MG/ML

REFERENCES

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7. Solu-Cortef (hydrocortisone sodium succinate for injection, USP) [prescribing information], New York, NY, Pharmacia & Upjohn Company LLC, July 2024

SUMMARY OF REVIEW/REVISIONS	DATE
NEW CRITERIA CREATION	Q2 2025