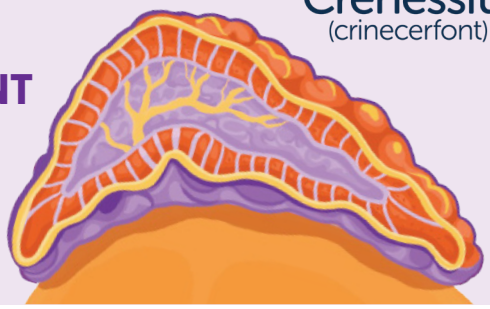
CAHNGE ANDROGEN MANAGEMENT

Crenessity™ (crinecerfont)

CRENESSITY is the first-ever medication that controls adrenal androgens *and* enables GC dose reductions, making it a breakthrough for treating classic CAH.[1,2]



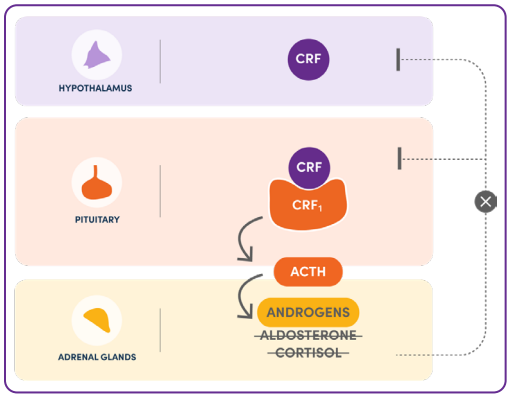
Cortisol deficiency in CAH leads to androgen excess[3,4]

In the HPA axis, loss of negative feedback due to lack of cortisol leads to[3,4]:

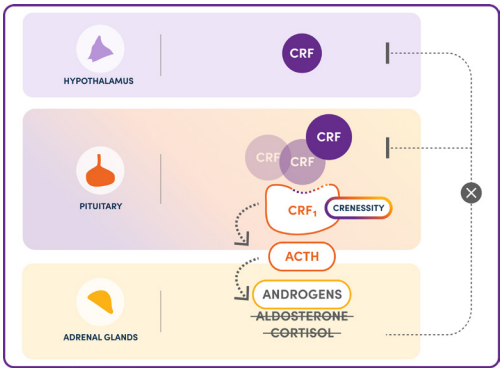
- Increase in **CRF** secretion
- Increase in **CRF_1** receptor activation
- Increase in **ACTH** release
- Overproduction of **adrenal androgens**

95% of CAH cases are caused by 21-OH deficiency.[5,6]

Because of the 21-OH deficiency, the adrenal glands cannot make enough cortisol and, in many cases, aldosterone. Instead, they make excess androgens.[3]



CRENESSITY inhibits secretion at the source[1]



CRENESSITY is a potent and selective CRF_1 receptor antagonist.[7,8] **By selectively blocking CRF binding to CRF_1 receptors in the pituitary gland, CRENESSITY[1]:**

- Directly reduces **ACTH**
- Reduces downstream production of **androgens**

CRF has been identified as a primary regulator of the HPA axis, including production of adrenal cortisol, aldosterone, and androgens.[2,3]

CRENESSITY improves androgen control and allows for GC dose reductions, enabling a transformational approach to managing CAH.[1]

Learn more about the MOA at **CRENESSITY.com/HCP**

CAH=congenital adrenal hyperplasia; ACTH=adrenocorticotropic hormone; GC=glucocorticoid; CRF=corticotropin-releasing factor; CRF_1=corticotropin-releasing factor type 1; 21-OH=21-hydroxylase; MOA=mechanism of action; HPA=hypothalamic-pituitary-adrenal.

INDICATION

CRENESSITY (crinecerfont) 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).

SELECT IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

CRENESSITY is contraindicated in patients with hypersensitivity to crinecerfont or any excipients of CRENESSITY.

Please see additional Important Safety Information and full Prescribing Information.

TRANSFORM CAH MANAGEMENT

Breakthrough Treatment

The first and only FDA-approved classic CAH treatment that targets ACTH and the downstream production of androgens[1,2]

Twice-Daily Dosing

Ensures reduction of ACTH and androgens throughout the day. CRENESSITY must be taken with meals and is available as capsules or oral solution.[1]

Demonstrated Safety Profile

The most common side effects of CRENESSITY in adults include tiredness, headache, dizziness, joint pain, back pain, decreased appetite, and muscle pain. The most common side effects of CRENESSITY in children include headache, stomach pain, tiredness, nasal congestion, and nosebleeds.[1]

Multiple Treatment Effects

Significantly reduces androgens, allows for lower GC doses, or both[1,9,10]

Prescribe Confidently

Personalized support at every step to ensure timely access, with most patients paying $10 or less per month for CRENESSITY*

*Additional terms and conditions apply.

Learn more about CRENESSITY and what it can mean for your patients at **CRENESSITY.com/HCP**

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WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions. A hypersensitivity reaction, including throat tightness, angioedema, and generalized rash, occurred in a subject after 3 days of treatment with CRENESSITY. If a clinically significant hypersensitivity reaction occurs, initiate appropriate therapy and discontinue CRENESSITY.

Risk of Acute Adrenal Insufficiency or Adrenal Crisis with Inadequate Concomitant Glucocorticoid Therapy. Acute adrenal insufficiency or adrenal crisis, which is potentially life-threatening, can occur in patients with underlying adrenal insufficiency who are on inadequate daily glucocorticoid doses, especially in situations associated with increased cortisol need, such as acute intercurrent illness, serious trauma, or surgical procedures. Continue glucocorticoids upon initiation of and during treatment with CRENESSITY. Do not reduce the glucocorticoid dose below the dose required for cortisol replacement. Patients should continue to use stress dosing of glucocorticoids in cases of increased cortisol need.

ADVERSE REACTIONS

In adult patients, the most common adverse reactions (at least 4% for CRENESSITY and greater than placebo) are fatigue, headache, dizziness, arthralgia, back pain, decreased appetite, and myalgia.

In pediatric patients, the most common adverse reactions (at least 4% for CRENESSITY and greater than placebo) are headache, abdominal pain, fatigue, nasal congestion, and epistaxis.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit MedWatch at www.fda.gov/medwatch or call 1-800-FDA-1088.

Dosage Forms and Strengths:

CRENESSITY is available in 50 mg and 100 mg capsules, and as an oral solution of 50 mg/mL.

Please see full Prescribing Information.

REFERENCES: 1. CRENESSITY Package Insert. Neurocrine Biosciences, Inc. **2.** Neurocrine Biosciences announces FDA approval of CRENESSITY (crinecerfont), a first-in-class treatment for children and adults with classic congenital adrenal hyperplasia. News release. Neurocrine Biosciences. December 13, 2024. Accessed December 13, 2024. https://neurocrine.gcs-web.com/news-releases/news-release-details/neurocrine-biosciences-announces-fda-approval-crenessitytm. **3.** Mallappa A, Merke DP. Management challenges and therapeutic advances in congenital adrenal hyperplasia. *Nat Rev.* 2022;18(6):337-352. doi:10.1038/s41574-022-00655-w **4.** Schroder MAM, Claahsen-van der Grinten HL. Novel treatments for congenital adrenal hyperplasia. *Rev Endocr Metab Disord.* 2022;23(3):631-645. doi:10.1007/s11154-022-09717-w **5.** Speiser PW, Arlt W, Auchus RJ, et al. Congenital adrenal hyperplasia due to steroid 21-hydroxylase deficiency: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab.* 2018;103(11):4043-4088. doi:10.1210/jc.2018-01865 **6.** Auer MK, Nordenstrom A, Lajic S, Reisch N. Congenital adrenal hyperplasia. *Lancet.* 2023;401(10372):227-244. doi:10.1016/S0140-6736(22)01330-7 **7.** Gully D, Geslin M, Serva L, et al. 4-(2-Chloro-4-methoxy-5-methylphenyl)-N-[(1S)-2-cyclopropyl-1-(3-fluoro-4-methylphenyl)ethyl]5-methyl-N-(2-propynyl)-1,3-thiazol-2-amine hydrochloride (SSR125543A): a potent and selective corticotrophin-releasing factor(1) receptor antagonist. I. Biochemical and pharmacological characterization. *J Pharmacol Exp Ther.* 2002;301(1):322-332. doi:10.1124/jpet.301.1.322 **8.** Fleck BA, Hoare SR, Pick RR, Bradbury MJ, Grigoriadis DE. Binding kinetics redefine the antagonist pharmacology of the corticotropin-releasing factor type 1 receptor. *J Pharmacol Exp Ther.* 2012;341(2):518-531. doi:10.1124/jpet.111.188714 **9.** 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 **10.** 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

NEUROCRINE® BIOSCIENCES