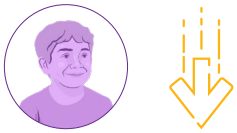
Crenessity®
(crinecerfont)

Achieving CAH Treatment Goals

Explore how 4 patients with classic CAH reached the treatment goals that matter[1-3]*

DAMON

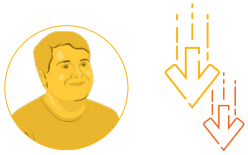


Reduce androgens

KIERRA

Reduce high GC doses†

AARON



Reduce androgens and reduce high GC doses†

OLIVIA

Maintain androgens and reduce high GC doses†

Patients with androstenedione >ULN

Patient with androstenedione ≤ULN

In CAHtalyst™ Pediatric (103 participants)[1,2]:

- After 4 weeks, androstenedione levels were reduced by 197 ng/dL with CRENESSITY vs a 71 ng/dL increase with placebo
- After 4 weeks, 17-OHP levels were reduced by 5865 ng/dL vs a 556 ng/dL increase with placebo
- After 28 weeks, GC doses were reduced by 18% with CRENESSITY vs a 6% increase with placebo

In CAHtalyst™ Adult (182 participants)[1,3]:

- After 4 weeks, androstenedione levels were reduced by 299 ng/dL with CRENESSITY vs a 46 ng/dL increase with placebo
- After 4 weeks, 17-OHP levels were reduced by 5994 ng/dL vs 156 ng/dL with placebo
- After 24 weeks, GC doses were reduced by 27% with CRENESSITY vs 10% with placebo

Androstenedione levels can be assessed beginning 4 weeks after CRENESSITY initiation to inform reduction in GC dosage as clinically indicated.[1]

*Based on real experiences of patients with classic CAH who were participants in the CAHtalyst™ clinical studies. Names and personal details have been changed.
†In the CAHtalyst™ Pediatric clinical trial, high GC doses were defined as >11 mg/m²/day in hydrocortisone equivalents, based on an equivalency factor of 4 times for prednisolone and prednisone. In the CAHtalyst™ Adult clinical trial, high GC doses were defined as >20 mg/day in hydrocortisone equivalents, based on an equivalency factor of 4 times for methylprednisolone, prednisolone, and prednisone and 60 times for dexamethasone and BSA of 1.84 m². The CAHtalyst™ clinical trials were phase 3, randomized, double-blind, placebo-controlled studies in children and adults. Androstenedione levels were evaluated at week 4, and GC dose reductions occurred from week 4 through the end of the study period (week 28 for children and week 24 for adults).[2,4]
17-OHP=17-hydroxyprogesterone; BSA=body surface area; CAH=congenital adrenal hyperplasia; GC=glucocorticoid; ULN=upper limit of normal.

INDICATION

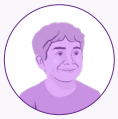
CRENESSITY (crinecerfont) is indicated as adjunctive treatment to glucocorticoid replacement to control androgens in adults and pediatric patients 4 years of age and older with classic congenital adrenal hyperplasia (CAH).

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 on page 4 and full Prescribing Information.



DAMON*

10-year-old with classic CAH

TREATMENT GOAL: Reduce Androgens
Damon's family, together with their endocrinologist, decided to focus on lowering his androgens, knowing that androgen control is important for achieving growth targets. He wasn't able to achieve this goal with GCs alone, but 4 weeks after starting CRENESSITY® (crinecerfont), his androstenedione levels were reduced below his baseline level.

At baseline[5†]:

- Androstenedione: 179 ng/dL (above the upper limit of normal for his age)
- 17-OHP: 2830 ng/dL
- GC dose: 17.5 mg/day hydrocortisone (~13 mg/m²/day based on his BSA)

What changed after 6 months of CRENESSITY[5]:

- Androstenedione: **dropped ~18%** to 147 ng/dL†
- 17-OHP: dropped to 2122 ng/dL†
- GC dose: **remained stable**

	Dose 1	Dose 2	Dose 3	Total GC‡
Before CRENESSITY	7.5 mg	2.5 mg	7.5 mg	17.5 mg/day (13.3 mg/m²/day)
With CRENESSITY	7.5 mg	2.5 mg	7.5 mg	17.5 mg/day (13.3 mg/m²/day)

KIERRA*

35-year-old with classic CAH

TREATMENT GOAL: Reduce High GC Doses
Although Kierra's androstenedione levels were above the upper limit of normal, she wanted to focus on lowering her GC dose to reduce her risk of comorbidities associated with high GC doses, such as obesity and diabetes. After 4 weeks on CRENESSITY, Kierra's androstenedione levels declined, which allowed her HCP to begin reducing her GC dose.

At baseline[5†]:

- GC dose: 30 mg/day hydrocortisone (15.3 mg/m²/day based on her BSA)
- Androstenedione: 361 ng/dL (above the upper limit of normal for her age)
- 17-OHP: 2201 ng/dL

What changed after 6 months of CRENESSITY[5]:

- GC dose: **lowered by ~34%** to 20 mg/day (10.2 mg/m²/day)
- Androstenedione: **remained stable** at 365 ng/dL†
- 17-OHP: dropped to 1800 ng/dL†

	Dose 1	Dose 2	Total GC‡
Before CRENESSITY	20 mg	10 mg	30 mg/day (15.3 mg/m²/day)
With CRENESSITY 1st reduction	**15 mg**	10 mg	25 mg/day (12.8 mg/m²/day)
With CRENESSITY 2nd reduction	15 mg	**5 mg**	20 mg/day (10.2 mg/m²/day)

Kierra's path to lower GC doses
Kierra's doctor began reducing her morning hydrocortisone dose by 5 mg to assess whether this step was manageable for her. The next step was lowering her evening dose by 5 mg for a **total reduction of 10 mg.**

Setting expectations can help your patients manage GC withdrawal symptoms. Let patients know that withdrawal symptoms like fatigue, nausea, and mood changes are common and usually improve within a few weeks. A pause in down-titration or a temporary GC increase may ease withdrawal symptoms.[6]

*Based on real experiences of patients with classic CAH who were participants in the CAHtalyst™ clinical studies. Names and personal details have been changed. Damon is based on a patient from the double-blind period. Kierra is based on a patient from the open-label period. GC reductions for adults were approached differently in the open-label period relative to the double-blind period of CAHtalyst™ Adult.
†Damon's androstenedione and 17-OHP measurements were taken before his morning GC dose. Kierra's were taken after her morning GC dose.
‡In hydrocortisone equivalents based on patient's BSA.

SELECT IMPORTANT SAFETY INFORMATION (continued)

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.

Please see additional Important Safety Information on page 4 and full Prescribing Information.

AARON[§]

18-year-old with classic CAH

TREATMENT GOAL: Reduce Androgens and Reduce High GC Doses
Aaron's androstenedione levels were elevated despite the high dose of dexamethasone he was taking. He wanted to try to reduce the risks associated with high androgen levels (eg, infertility) and high GC doses (eg, osteoporosis, insomnia), so his goal was to reduce both. Aaron's androstenedione levels were reduced after 4 weeks of CRENESSITY, enabling reduction of his GC dose.

At baseline[5¶]:

- GC dose: 0.5 mg/day dexamethasone (17.9 mg/m^2/day hydrocortisone equivalents based on his BSA)
- Androstenedione: 390 ng/dL (above the upper limit of normal for his age)
- 17-OHP: 4222 ng/dL

What changed after 7 months of CRENESSITY[5]:

- GC dose: **lowered by 30%** to 0.35 mg/day
- Androstenedione: **dropped ~78%** to 85 ng/dL[¶]
- 17-OHP: dropped to 760 ng/dL[¶]

	Dose 1	Total GC[‖]
Before CRENESSITY	0.5 mg/day	30 mg/day (17.9 mg/m^2/day)
With CRENESSITY 1st reduction	**0.4 mg/day**	24 mg/day (13 mg/m^2/day)
With CRENESSITY 2nd reduction	**0.35 mg/day**	21 mg/day (11 mg/m^2/day)

Aaron's path to lower GC doses
Aaron wanted to maintain a once-daily steroid, so his doctor **tapered his dexamethasone dose** in a stepwise manner while monitoring him for any adverse events including GC withdrawal symptoms.

OLIVIA[§]

5-year-old with classic CAH

TREATMENT GOAL: Maintain Androgens and Reduce High GC Doses
Olivia's androstenedione levels were within the limits of normal for her age, so her physician and caregivers wanted to maintain her androgen control and lower her high GC dose to reduce the risk of associated comorbidities. Androstenedione measurement 4 weeks after CRENESSITY initiation confirmed her androgen control was maintained, thereby enabling reduction of her GC dose.

At baseline[5¶]:

- GC dose: 15 mg/day hydrocortisone (15.3 mg/m^2/day based on her BSA)
- Androstenedione: 12 ng/dL (within the limits of normal for her age)
- 17-OHP: 1429 ng/dL

What changed after 6 months of CRENESSITY[5]:

- GC dose: **lowered by ~35%** to 9.9 mg/m^2/day
- Androstenedione: **remained within the limits of normal** at 23 ng/dL[¶]
- 17-OHP: dropped to 872 ng/dL[¶]

	Dose 1	Dose 2	Dose 3	Total GC[‖]
Before CRENESSITY	5 mg	5 mg	5 mg	15 mg/day (15.3 mg/m^2/day)
With CRENESSITY 1st reduction	5 mg	5 mg	**2.5 mg**	12.5 mg/day (12.5 mg/m^2/day)
With CRENESSITY 2nd reduction	5 mg	5 mg	**0 mg**	10 mg/day (9.9 mg/m^2/day)

Olivia's path to lower GC doses
Olivia's doctor gradually reduced her nighttime hydrocortisone dose in 2.5 mg increments. Eventually they **eliminated her nighttime dose** altogether, achieving more circadian GC dosing.

As patients reduce their daily GC dose, it's important to reassess stress dosing protocols. Despite lower maintenance doses, stress dosing remains necessary and should reflect absolute cortisol needs. Reevaluate the appropriate dose, frequency, and threshold for initiating stress dosing.[6]

[§]Both Aaron and Olivia are based on patients from the open-label period. GC reductions for adults were approached differently in the open-label period relative to the double-blind period of CAHtalyst™ Adult.
[¶]Aaron's androstenedione and 17-OHP measurements were taken after his morning GC dose. Olivia's were taken before her morning GC dose.
[‖]In hydrocortisone equivalents based on patient's BSA.

SELECT IMPORTANT SAFETY INFORMATION (continued)

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.

Please see additional Important Safety Information on page 4 and full Prescribing Information.

Any GC dose reduction—even a small one—could make a difference[7]

- Small reductions add up to a large cumulative reduction over a patient's life
- Any reduction can meaningfully reduce the risk of comorbidities associated with high GC doses

A Delphi panel reached 100% consensus that a GC reduction of ≥2.5 mg/day (≥1.39 mg/m^2/day) is clinically meaningful, and 70% agreed that any reduction is clinically meaningful.[5]*

*The 100% consensus reflects 24 of 24 endocrinologists surveyed. The 70% figure represents 7 of 10 endocrinologists surveyed.[5]

All patients with classic CAH need physiologic GC doses to treat their cortisol deficiency; however, controlling androgens using only GCs inherently requires supraphysiologic dosing[7]

- CRENESSITY can lower androgen levels to allow for GC dose reductions in both children and adults taking a range of different GC regimens for CAH[1]

See how CRENESSITY could fit into your patients' treatment plans.
Explore additional clinical resources on our site.

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).

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

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

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.** 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. **3.** Auchus RJ, Hamidi O, Pivonello R, et al. Phase 3 trial of crinecerfont in adult congenital adrenal hyperplasia. Supplementary appendix. *N Engl J Med.* 2024;391(6):504-514. doi:10.1056/NEJMoa2404656. **4.** 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. **5.** Data on file. Neurocrine Biosciences, Inc. **6.** *Adrenal Insufficiency: Identification and Management.* London: National Institute for Health and Care Excellence (NICE); August 28, 2024. **7.** Bancos I, Kim H, Cheng HK, et al. Glucocorticoid therapy in classic congenital adrenal hyperplasia: traditional and new treatment paradigms. *Expert Rev Endocrinol Metab.* 2025;20(1):33-49. doi:10.1080/17446651.2025.2450423

Crenessity® (crinecerfont)

CP-CFT-US-0660 12/2025

NEUROCRINE® BIOSCIENCES