Flip the switch™

on your expectations of hereditary angioedema (HAE) treatment

INDICATION

DAWNZERA™ (donidalorsen) is a prescription medicine used to prevent hereditary angioedema (HAE) attacks in adults and children 12 years of age and older.

It is not known if DAWNZERA is safe and effective in children under 12 years of age.

SELECT IMPORTANT SAFETY INFORMATION

Do not use DAWNZERA if you have had a serious allergic reaction, including anaphylaxis to donidalorsen or any of the ingredients in DAWNZERA.

Please see Important Safety Information throughout, and full Prescribing Information and Patient Information for DAWNZERA, also available at Dawnzera.com.

DAWNZERA™
(donidalorsen) 80 mg / 0.8 mL injection

It's time to REDEFINE WHAT'S "NORMAL" FOR HAE

ALMOST

9 OUT OF 10

people reported that they **frequently missed or avoided events** because of their HAE.*

Talking openly with your doctor about how HAE impacts you matters, even though it can be hard to put into words. **That's where your Angioedema Control Test (AECT) score can help.**

The AECT is a 4-question test that can help you and your doctor assess and monitor your disease control†

Your AECT results can help you talk with your doctor about your disease control and treatment goals.

If your HAE isn't well controlled, it may be time to consider something different.

†The AECT was validated in 81 patients with recurrent angioedema, including 25 with HAE or acquired angioedema due to C1-inhibitor deficiency. It was not specifically validated for HAE.

You're always allowed to ASK FOR "MORE"

Check off any statements below that ring true, and use them to guide conversations with your doctor.

- ○ **I feel dissatisfied with how my current treatment is working**
- ○ **I want the preparation of my treatment to be simple**
- ○ **I don't want to worry about taking my treatment every day**
- ○ **I want to ask my doctor whether my HAE treatment is working**
- ○ **I want more flexible dosing options**

As HAE care has evolved, treatment guidelines now emphasize strategies that help people live as normally as possible

*Online survey conducted by The Harris Poll of 150 US adults diagnosed with HAE by a health care provider and 228 board-certified allergists and immunologists practicing in the US, sponsored by Ionis.

MEET DAWNZERA™ (donidalorsen)

DAWNZERA offers:

- **Delivered through a convenient, single-use autoinjector, no mixing or syringes required**
- **At-home dosing every 4 or 8 weeks, with recommended dosing being every 4 weeks**
- **~10 seconds to inject**
- **No citric acid, which is associated with injection-site pain***
- **Refrigeration recommended, but not required for up to 6 weeks†**

*In clinical studies, injection-site reactions, including injection-site pain, were the most frequently reported adverse reactions.

†If needed, autoinjectors can be stored in their original carton at room temperature (up to 86 °F [30 °C]) for up to 6 weeks. If not used within 6 weeks, throw away DAWNZERA.

Please see Important Safety Information throughout, and full Prescribing Information and Patient Information for DAWNZERA, also available at Dawnzera.com.

PLACE, PUSH, HOLD.

How to Use DAWNZERA

Watch the training video and review the Instructions for Use at DAWNZERA.com/taking-dawnzera for step-by-step instructions on how to **place, push, and hold** the autoinjector.

SELECT IMPORTANT SAFETY INFORMATION

Before using DAWNZERA, tell your healthcare provider about all of your medical conditions, including if you: are pregnant or plan to become pregnant, are breastfeeding or plan to breastfeed. It is not known if DAWNZERA can harm your unborn baby, or if it passes into your breast milk and if it can harm your baby.

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SAFETY AND SIDE EFFECTS seen with DAWNZERA

The most common side effects of DAWNZERA were injection-site reactions.*

Redness was the most common injection-site reaction.

Adverse reaction, n (%)	DAWNZERA every 4 weeks (n=45)	DAWNZERA every 8 weeks (n=23)	Placebo (n=22)
Injection-site reactions†	11 (24)	1 (4)	1 (5)
Upper respiratory tract infection	4 (9)	2 (9)	1 (5)
Urinary tract infection	4 (9)	2 (9)	0
Abdominal discomfort	3 (7)	0	0

In clinical trials, hypersensitivity reactions, including anaphylaxis, have occurred. Symptoms included generalized rash, shortness of breath, chest pain, and swelling around the mouth.

At 1 year, no new safety concerns were identified, and most side effects were mild or moderate.

These are not the only possible side effects of DAWNZERA. Tell your doctor if you have any side effect that bothers you or that does not go away while taking DAWNZERA.

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*Injection site reactions include: erythema (redness), discoloration, pain, pruritus (itching), induration (hardening or thickening of the skin), bruising, hematoma (localized bleeding under the skin), hypersensitivity, swelling, reaction, and urticaria (hives).

†All injection-site reactions were mild, nonserious, and the majority of them resolved without receiving any treatment.

SELECT IMPORTANT SAFETY INFORMATION

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

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SIGNIFICANT REDUCTIONS in HAE attacks

Primary Study

The safety and efficacy of DAWNZERA were evaluated in the primary study. At 6 months, those who took DAWNZERA every 4 weeks saw **81% FEWER ATTACKS** on average vs placebo (primary endpoint).*

About 90% fewer moderate-to-severe HAE attacks, HAE attacks requiring rescue medication, and HAE attacks requiring ER visits†

ER=emergency room.

*Reductions in HAE attacks were measured 24 weeks after their first dose.

†Average percentage (%) observed in people using DAWNZERA every 4 weeks. Moderate-to-severe HAE attacks and rescue medication use were secondary endpoints, and ER visits due to HAE attacks were an exploratory endpoint.

‡Across both dosing groups (every 4 weeks and every 8 weeks), secondary endpoint.

SELECT IMPORTANT SAFETY INFORMATION

What are the possible side effects of DAWNZERA? DAWNZERA can cause serious side effects including allergic reactions.

Please see Important Safety Information throughout, and full Prescribing Information and Patient Information for DAWNZERA, also available at Dawnzera.com.

SUSTAINED RESULTS seen through 1 year in a long-term safety study

Long-term Safety Study

94% fewer attacks on average after 1 year vs attack rate before beginning treatment‡

DAWNZERA starts working after your 1st dose. For patients taking DAWNZERA every 4 weeks, the medicine provides substantial benefit after the 2nd dose

SELECT IMPORTANT SAFETY INFORMATION

What are the possible side effects of DAWNZERA? (cont'd) Allergic reactions can include rash, trouble breathing, chest pain, fainting, dizziness, feeling lightheaded, swelling of the face, lips or tongue, and itching. Stop using DAWNZERA and call your healthcare provider or get emergency help right away if you have any of these symptoms.

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In the open-label study,

The majority of people SWITCHED SAFELY

DAWNZERA every 4 weeks was evaluated in people who switched from **lanadelumab, berotralstat,** or a **C1-INH**.

HAE attack reduction was seen regardless of prior preventative treatment.*

people in the study who used the AECT reported being **well-controlled** after switching to DAWNZERA (exploratory endpoint interim analyses at Week 16 and Week 52)†

These are not head-to-head data. Findings are from an open-label, uncontrolled safety study in patients who wanted to switch to DAWNZERA, and was not powered for any comparisons between prior treatment groups; thus, these observations cannot be generalized to other patients on prior long-term preventative treatments.

The majority of side effects were mild to moderate and consistent with the primary study.

of people surveyed in an interim analysis after 16 weeks of treatment preferred DAWNZERA over their previous preventive treatment, citing better disease control, less time required for treatment, and reduced injection pain as reasons for their preference‡

AECT=Angioedema Control Test; C1-INH=C1-inhibitor.

*Previous on-treatment monthly HAE attack rate established in the 10-week screening period.

†The AECT is a simple, 4-question survey that helps you and your doctor understand how well your swelling symptoms have been managed over the past month.

‡More than 1 reason was permitted. Exploratory endpoint interim analysis at Week 16.

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SELECT IMPORTANT SAFETY INFORMATION

The most common side effects of DAWNZERA include injection site reactions (such as redness or pain at the injection site), upper respiratory tract infection, urinary tract infection, abdominal discomfort.

These are not all the possible side effects of DAWNZERA. Tell your healthcare provider or treatment team about any side effects you may have.

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DAWNZERA works differently

TO PREVENT HAE ATTACKS

DAWNZERA is the first treatment to use RNA technology for HAE attack prevention.

RNA technology has been used across many types of medical conditions for almost 30 years. It works by reducing, enhancing, or modifying proteins

DAWNZERA does not change DNA

DAWNZERA works by lowering plasma prekallikrein (PKK), a protein in the HAE pathway that contributes to swelling

DAWNZERA restores balance to the HAE pathway by reducing production of plasma PKK in the liver, where it's produced

DNA=deoxyribonucleic acid; mRNA=messenger RNA; RNA=ribonucleic acid.

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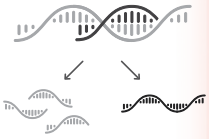
DAWNZERA is designed to work in 3 steps:

1 **DAWNZERA** is specifically targeted to the liver, where plasma PKK is made.

2 **DAWNZERA** finds and directs the breakdown of the message (called mRNA) that tells your body to make plasma PKK.



3 By targeting mRNA, **DAWNZERA** helps to control the pathway that leads to swelling.

SELECT IMPORTANT SAFETY INFORMATION

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

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IONIS EVERY STEP™ SUPPORT SERVICES

Let's take this step by step, TOGETHER

Ionis Every Step™ is here for you every step of the way, from getting your prescribed medicine to learning how to use it and ways to help follow your doctor's treatment plan.

Signing up for Ionis Every Step™ gives you access to:

A Patient Education Manager*

You'll be connected with a dedicated Patient Education Manager—your primary Ionis Every Step partner from the start and throughout your treatment journey.

Insurance Navigation†

Ionis Every Step works with you and your doctor to help get insurance approval for your medication and provide updates along the way.

Affordability Programs‡

Ionis Every Step is committed to helping you access your Ionis medication. There are many financial assistance options available regardless of your insurance.

DAWNZERA Direct

Your digital companion for managing your DAWNZERA treatment journey. Reach out to your Patient Education Manager to get started.

Take your next step with **Ionis Every Step.** Scan the QR code or visit **DAWNZERA.com/enroll**

*Patient Education Managers cannot give medical advice and do not replace your medical team. Contact your doctor for any medical concerns.
†Insurance approval is not guaranteed. Ionis Every Step offers financial assistance programs for patients who are uninsured or denied coverage for their Ionis medication.
‡Terms and conditions apply. Programs subject to change or discontinue without notice, including in specific states.

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WHY DAWNZERA?

The safety and efficacy of DAWNZERA were evaluated in the primary study. At 6 months, those who took DAWNZERA every 4 weeks saw **81% FEWER ATTACKS** on average vs placebo (primary endpoint).*

In the long-term safety study,
94% FEWER ATTACKS
on average after 1 year vs attack rate before beginning treatment†

SWITCH SAFELY
with the only treatment backed by a clinical trial that evaluated how to safely switch‡

As few as **6** doses **PER YEAR** with dosing every **4 or 8 weeks**

Visit DAWNZERA.com to access more resources about treatment

*Reductions in HAE attacks were measured 24 weeks after their first dose.
†Across both dosing groups (every 4 weeks and every 8 weeks), secondary endpoint.
‡DAWNZERA every 4 weeks was evaluated in people who switched from lanadelumab, berotralstat, or a C1-INH.

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