RNA=ribonucleic acid.

INDICATION

DAWNZERA (donidalorsen) is indicated for prophylaxis to prevent attacks of hereditary angioedema (HAE) in adult and pediatric patients 12 years of age and older.

SELECT IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

DAWNZERA is contraindicated in patients with a history of serious hypersensitivity reactions, including anaphylaxis, to donidalorsen or any of the excipients in DAWNZERA.

Please see Important Safety Information throughout and accompanying full Prescribing Information for DAWNZERA.

The physical and mental burden of BREAKTHROUGH ATTACKS may be greater than what your patients report[3-5]

In a survey of 110 patients with HAE taking long-term prophylaxis, **NEARLY HALF** said they didn't tell their physician about every attack[3]*

Many patients are still living with **undesirable trade-offs[3,6-9]:**

Burdensome dosing[8]

Breakthrough attacks[9]

GI side effects[9]

In a survey of patients with HAE,[3]*

~50% OF PATIENTS REPORTED THEY **MISS OUT** ON SOCIAL EVENTS DUE TO HAE ATTACKS

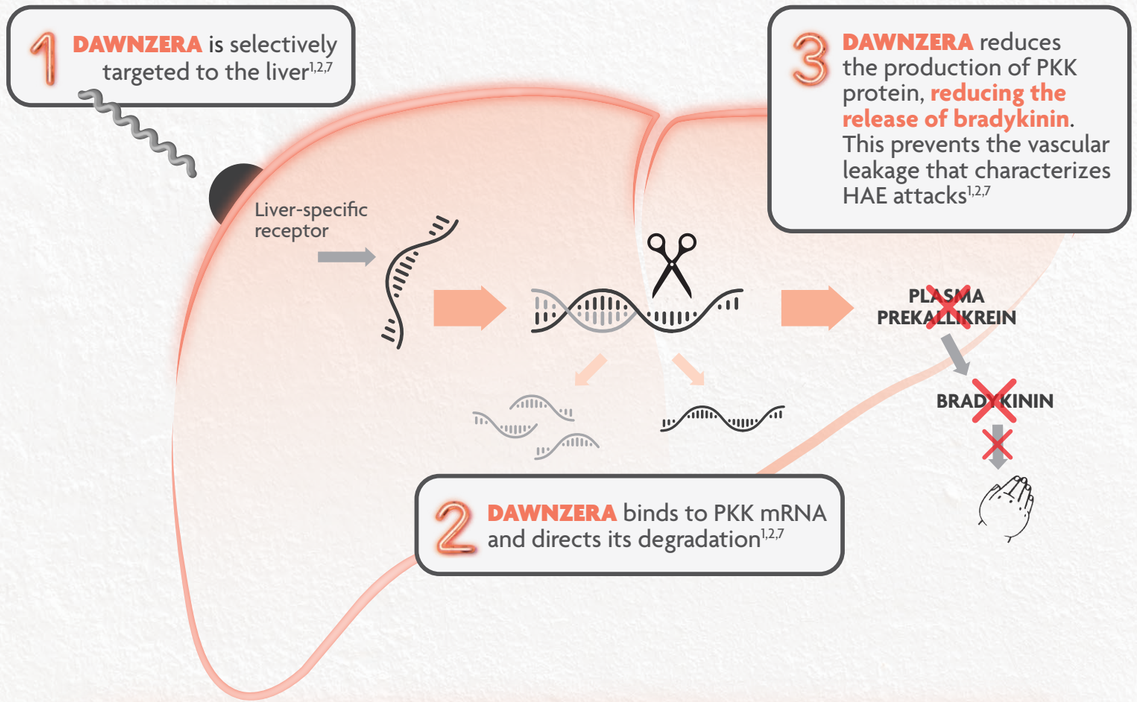
Living with trade-offs may not be the only option
Are you discussing changing HAE therapies with your patients?

GI=gastrointestinal.

***These findings are a result of an online survey conducted by the Harris Poll, sponsored by Ionis, of 150 US adults diagnosed with HAE by a health care provider.[3]**

The first and only RNA-TARGETED TREATMENT for HAE[1,2]

DAWNZERA is an **antisense oligonucleotide (ASO) that binds to prekallikrein (PKK) mRNA** to limit plasma protein production at the source—in the liver, where it's made[1,6]



DAWNZERA has the selectivity of RNA technology and does not irreversibly edit DNA[2,10]

DNA=deoxyribonucleic acid; mRNA=messenger ribonucleic acid.

SELECT IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions

Hypersensitivity reactions, including anaphylaxis, have been reported in patients treated with DAWNZERA. If signs and symptoms of serious hypersensitivity reactions occur, discontinue DAWNZERA and institute appropriate therapy.

ADVERSE REACTIONS

Most common adverse reactions (incidence ≥ 5%) are injection site reactions, upper respiratory tract infection, urinary tract infection, and abdominal discomfort.

DAWNZERA has the LONGEST DOSING OPTION for HAE[1]

DAWNZERA can give patients control without added complexity

At-home dosing every 4 or 8 weeks[1]

Recommended dose: DAWNZERA 80 mg SC every 4 weeks.

- DAWNZERA 80 mg SC every 8 weeks may also be considered

Convenient and easy-to-store autoinjector[1,11]

Refrigeration is recomended.

- Can be stored at room temperature up to 86 °F (30 °C) in the original carton for up to 6 weeks

DAWNZERA contains no citric acid—which is associated with injection-site pain[1,12*]

If a dose is missed, advise patients to take DAWNZERA as soon as possible and then take their next dose 4 or 8 weeks later, as prescribed.[1]

14-day protocol to switch to DAWNZERA[13†]

Berotralstat or C1-INH

1. Start DAWNZERA
2. Continue taking the current dose of berotralstat or the C1-INH for 14 days

Lanadelumab

1. Stop taking lanadelumab
2. Wait 14 days before starting DAWNZERA

C1-INH=C1-inhibitor; SC=subcutaneously.

*In clinical studies, injection-site reactions, including injection-site pain, were the most frequently reported adverse reactions with DAWNZERA.[1]

†Switch protocol used in the OASISplus study.[13]

Please see Important Safety Information throughout and accompanying full Prescribing Information for DAWNZERA.

DAWNZERA™ (donidalorsen) 80 mg/0.8 mL injection

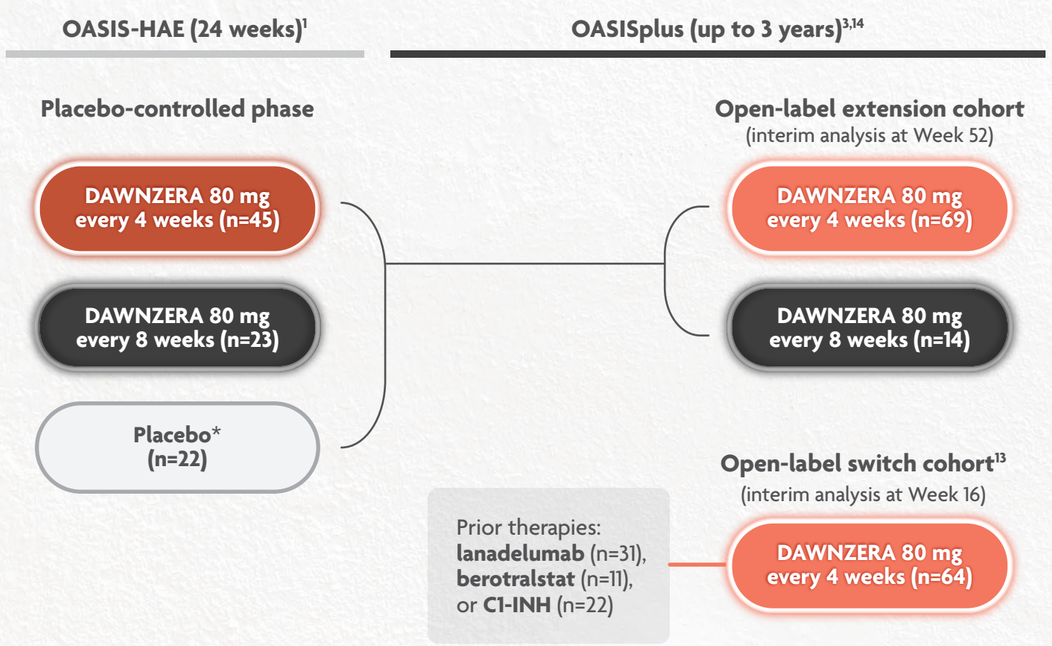
Studied in patients STARTING OR SWITCHING HAE prophylactic therapy

OASIS-HAE: Phase 3, randomized, double-blind, placebo-controlled 6-month trial of patients aged ≥12 years with HAE type 1 or 2 (N=90)[1,6]

- At baseline, 69% of patients had >2 monthly attacks[1]

OASISplus: Ongoing, open-label, long-term safety (primary endpoint) and efficacy (secondary endpoint) study of patients with HAE type 1 or 2 (N=147)[13,14]

- 94% of eligible patients opted to continue in the open-label study[14]



- Enrolled patients had to have at least two investigator-confirmed attacks during the 8-week run-in period[1]
- Enrolled patients on a stable dose of HAE prophylactic therapy for ≥12 weeks. Patients started taking DAWNZERA every 4 weeks on Day 1, following the 14-day switch protocol

*Pooled placebo every 4 and 8 weeks.[1]

SELECT IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

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WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions

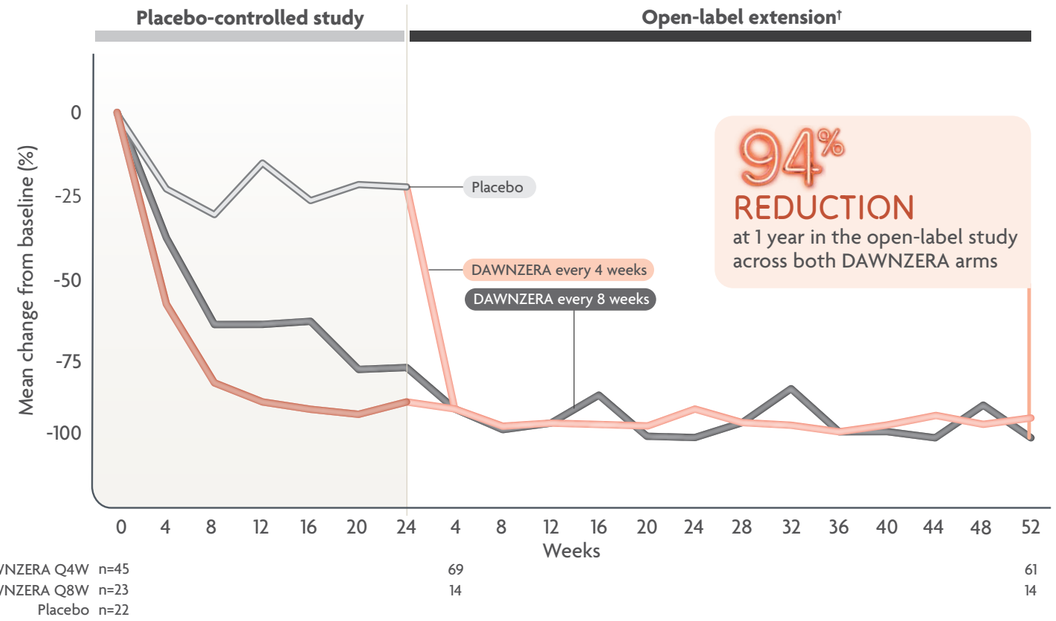
Hypersensitivity reactions, including anaphylaxis, have been reported in patients treated with DAWNZERA. If signs and symptoms of serious hypersensitivity reactions occur, discontinue DAWNZERA and institute appropriate therapy.

AN ATTACK-FREE YEAR is possible with DAWNZERA[3]

SUBSTANTIAL and **SUSTAINED** reductions in HAE attack rates[1,3,6]

- Mean monthly HAE attack rate at Week 24 with DAWNZERA every 4 weeks was 0.44 vs 2.26 for placebo, an 81% reduction (**primary endpoint**, *P*<0.001) increasing to an 87% reduction when measured from the second dose (0.30 vs 2.25 for placebo, **secondary endpoint**, *P*<0.001)[1,6]

Reductions in mean monthly HAE attack rate (investigator-confirmed) from baseline[3]



†Data cut-off: January 27, 2025.[3]

Placebo-controlled study results:

- **53% of patients were attack free** on DAWNZERA every 4 weeks (*P*=0.003 vs 9% with placebo)[1,6‡]
- DAWNZERA every 8 weeks **reduced HAE attacks by 55%** vs placebo (*P*=0.004)[1]
- **~90% fewer moderate-to-severe HAE attacks** with DAWNZERA every 4 weeks (*P*<0.001) and **41% fewer when taken every 8 weeks**[1,6‡]
- DAWNZERA **significantly reduced HAE attacks requiring acute therapy by 92% and 67%** when taken every 4 or 8 weeks, respectively (*P*<0.001 and *P*=0.004)[1,6‡]

‡Secondary endpoint.[1]

Please see Important Safety Information throughout and accompanying full Prescribing Information for DAWNZERA.

DAWNZERA™ (donidalorsen) 80 mg / 0.8 mL injection

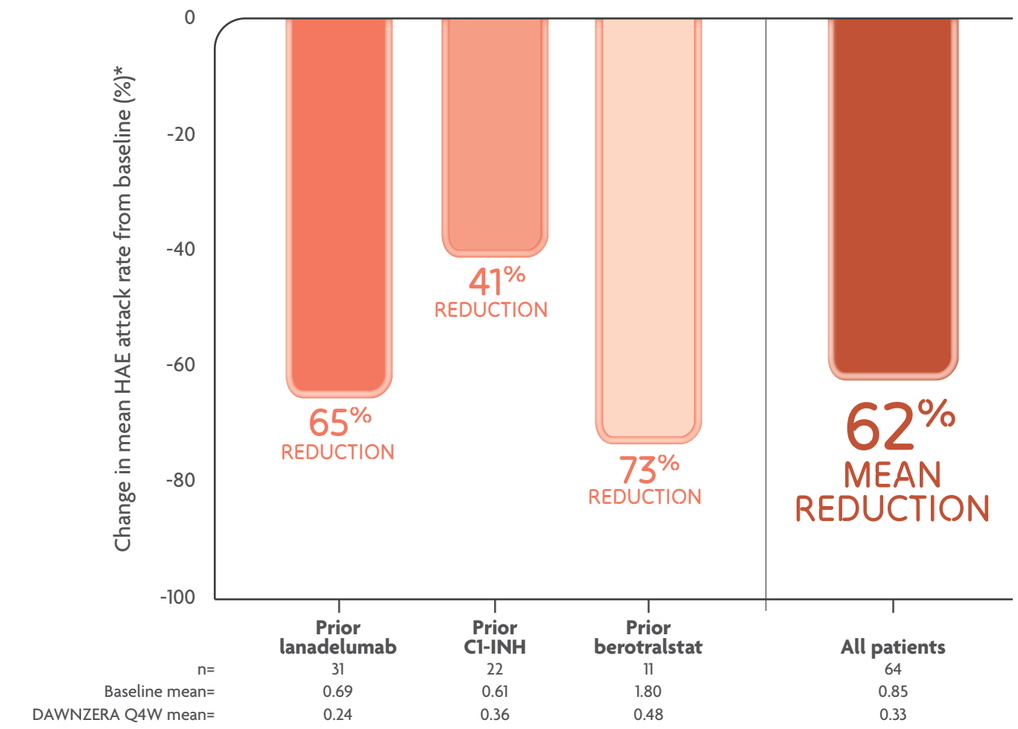
In the open-label study

SWITCHING TO DAWNZERA

reduced mean HAE attack rate by 62% from prior treatment

Results in patients who switched to DAWNZERA every 4 weeks from an interim analysis at Week 16[13]*

Exploratory endpoint: reductions in mean monthly HAE attack rate with DAWNZERA[13]



*Baseline monthly HAE attack rate established in the 10-week screening period.[13]

- 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 prophylactic treatments
- The majority of adverse events were mild to moderate and consistent with the placebo-controlled study[1,13]

In the open-label study

Majority of patients who switched reported they PREFERRED DAWNZERA

Patients successfully transitioned to DAWNZERA every 4 weeks from lanadelumab, berotralstat, or a C1-INH with no mean loss of efficacy, and no new safety signals[13]

Exploratory endpoint: patient preference in an interim analysis at Week 16 (n=55)[13]

84% of patients surveyed who switched **PREFERRED DAWNZERA**, most saying it worked better to control their HAE[13]

Reasons patients chose for preferring DAWNZERA[13†]:

- **63%** chose "it works better to control my HAE"
- **65%** chose "less time to administer"
- **50%** chose "less injection-site pain or reaction"

†More than 1 reason was permitted.[13]

SELECT IMPORTANT SAFETY INFORMATION

ADVERSE REACTIONS

Most common adverse reactions (incidence ≥ 5%) are injection site reactions, upper respiratory tract infection, urinary tract infection, and abdominal discomfort.

CONTRAINDICATIONS

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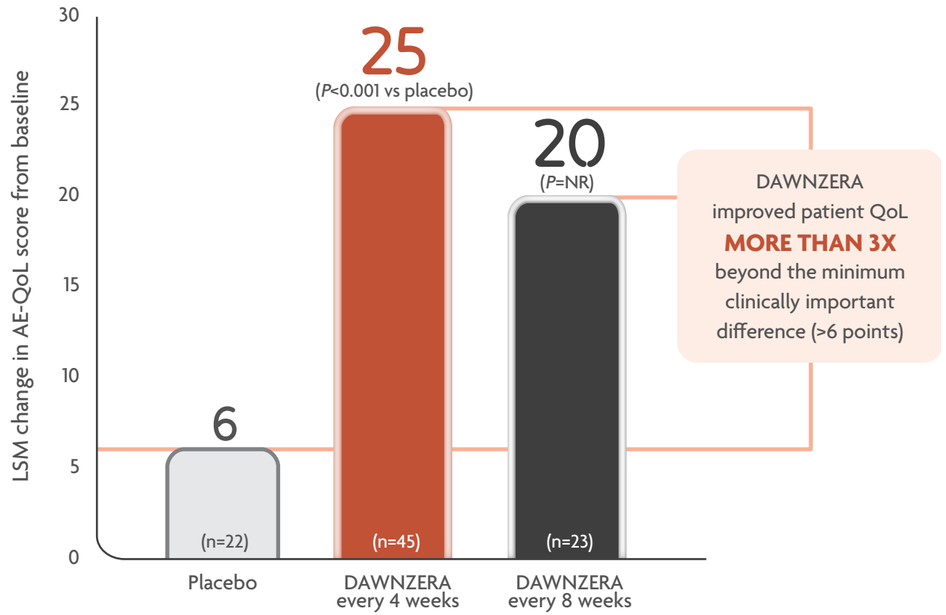
DAWNZERA™ (donidalorsen) 80 mg / 0.8 mL injection

In the 6-month placebo-controlled study

Patients reported IMPROVED QoL with DAWNZERA

DAWNZERA every 4 weeks significantly improved Angioedema Quality of Life (AE-QoL) scores—a validated measure in patients with angioedema[6,15,16]

Improvements from baseline in LS mean AE-QoL score with DAWNZERA at Week 24[6]



LSM=least squares mean; NR=not reported; QoL=quality of life.

SELECT IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions

Hypersensitivity reactions, including anaphylaxis, have been reported in patients treated with DAWNZERA. If signs and symptoms of serious hypersensitivity reactions occur, discontinue DAWNZERA and institute appropriate therapy.

ADVERSE REACTIONS

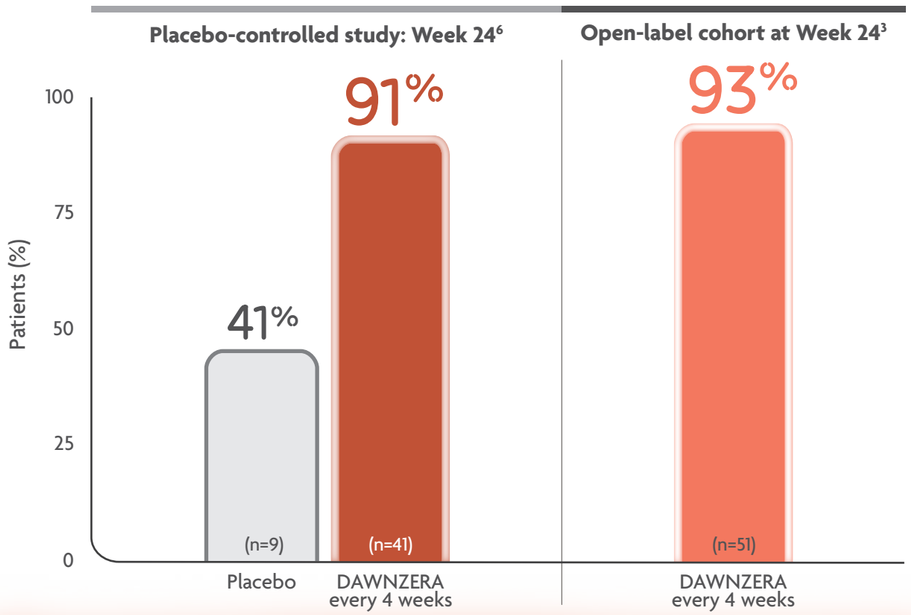
Most common adverse reactions (incidence ≥ 5%) are injection site reactions, upper respiratory tract infection, urinary tract infection, and abdominal discomfort.

>90% of patients reported they were WELL-CONTROLLED with DAWNZERA

Disease control was self-reported by patients using the Angioedema Control Test (AECT)[15]

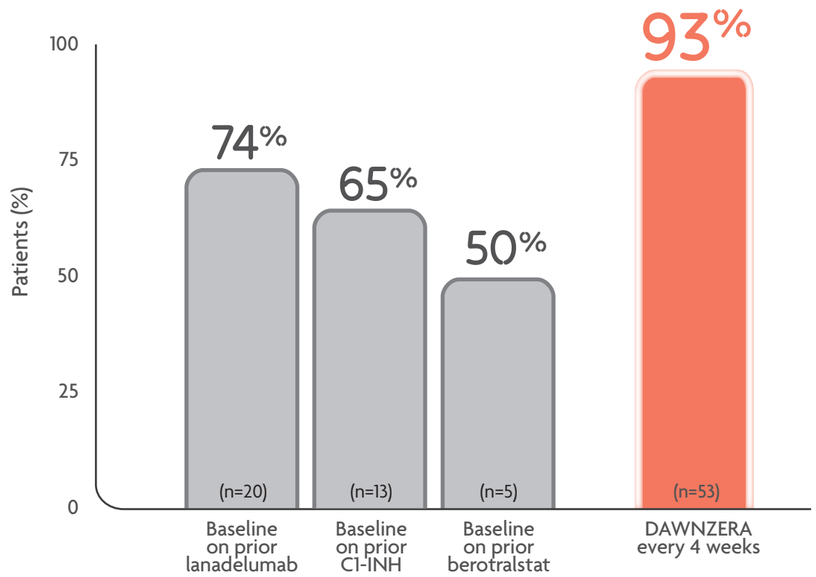
In the open-label study, **93% of patients** who switched to DAWNZERA reported they were **well-controlled**[13]

Mean proportion of patients well-controlled on DAWNZERA (AECT)



Well-controlled was defined as ≥10 out of 16 possible points on the AECT.*
Scores of 0 to 9 equated to poorly-controlled angioedema[17]

Mean proportion of patients well-controlled on DAWNZERA (AECT)[13]



AECT: patients answer 4 questions about their disease control over the past 4 weeks[18]:

1. How often have you had angioedema?
2. How much has your quality of life been affected by angioedema?
3. How much has the unpredictability of your angioedema bothered you?
4. How well has your angioedema been controlled by your therapy?

*The AECT was validated in 81 patients with recurrent angioedema, including 25 with HAE or acquired angioedema due to C1-INH deficiency. It was not specifically validated for HAE.[17]

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 prophylactic treatments.

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CONTRAINDICATIONS
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WARNINGS AND PRECAUTIONS
Hypersensitivity Reactions
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DAWNZERA™ (donidalorsen) 80 mg / 0.8 mL injection

SAFETY AND TOLERABILITY
established in clinical trials

The safety of DAWNZERA reflects an average duration of exposure of 14 months in 171 adult and pediatric patients aged ≥12 across 3 clinical trials[1]

Adverse reactions (≥5% with DAWNZERA and more common than placebo) in OASIS-HAE at Week 24[1]

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

*Injection-site reactions: erythema, discoloration, pain, pruritus, induration, bruising, hematoma, hypersensitivity, swelling, reaction, and urticaria.[1]

- All injection-site reactions were mild and nonserious, and the majority resolved without receiving any treatment[1]
  - Erythema was the most common injection-site reaction[6]

In clinical trials, hypersensitivity reactions, including anaphylaxis, have occurred. Symptoms included generalized rash, dyspnea, chest pain, and peri-oral swelling.[1]

The majority of adverse reactions with DAWNZERA were mild to moderate[6]

References: 1. DAWNZERA. Prescribing information. Ionis Pharmaceuticals. **2.** Riedl MA, Bordone L, Revenko A, et al. Clinical progress in hepatic targeting for novel prophylactic therapies in hereditary angioedema. *J Allergy Clin Immunol Pract*. 2024;12(4):911-918. doi:10.1016/j.jaip.2023.12.025 **3.** Data on file. Ionis Pharmaceuticals. **4.** Busse PJ, Christiansen SC, Riedl MA, et al. US HAEA Medical Advisory Board 2020 Guidelines for the Management of Hereditary Angioedema. *J Allergy Clin Immunol Pract*. 2021;9(1):132-150.e3. doi:10.1016/j.jaip.2020.08.046 **5.** Jain G, Walter L, Reed C, et al. How do patients and physicians communicate about hereditary angioedema in the United States? *PLoS One*. 2021;16(12):e0260805. doi:10.1371/journal.pone.0260805 **6.** Riedl MA, Tachdjian R, Lumry WR, et al. Efficacy and safety of donidalorsen for hereditary angioedema. *N Engl J Med*. 2024;391(1):21-31. doi:10.1056/NEJMoa2402478 **7.** Smith TD, Riedl MA. The future of therapeutic options for hereditary angioedema. *Ann Allergy Asthma Immunol*. 2024;133(4):380-390. doi:10.1016/j.anai.2024.04.029 **8.** Haegarda. Prescribing information. CSL Behring. **9.** Orladeyo. Prescribing information. BioCryst Pharmaceuticals Inc. **10.** Ferrone JD, Bhattacharjee G, Revenko AS, et al. IONIS-PKK$_{Rx}$ a novel antisense inhibitor of prekallikrein and bradykinin production. *Nucleic Acid Ther*. 2019;29(2):82-91. doi:10.1089/nat.2018.0754 **11.** Khatri H, Estepa P, Cummings B. Participant reported ease-of-use with a prefilled, single-dose, disposable autoinjector for the treatment of hereditary angioedema. *J Allergy Clin Immunol*. 2025;155(2 suppl):AB228. Abstract 699. **12.** Junker S, Ebert O, Bartsch R. A systematic literature review of injection site pain perception in adult patients treated with citrate-free and citrate-containing biologic agents. *Curr Rheumatol Rev*. 2023;19(3):303-313. doi:10.2174/1573397118666220829123713 **13.** Riedl MA, Bernstein JA, Jacobs JS, et al. Donidalorsen treatment of hereditary angioedema in patients previously on long-term prophylaxis. *J Allergy Clin Immunol Pract*. Published online July 17, 2025. doi:10.1016/j.jaip.2025.06.018 **14.** Tachdjian R, Riedl MA, Bordone L, et al. Long-term safety of donidalorsen for the treatment of hereditary angioedema: Results from the phase 3 open-label extension OASISplus study. Lecture presented: at EAACI Congress; May 31-June 3, 2024; Valencia, Spain. **15.** Riedl MA, Yarlas A, Bordone L, et al. Patient-reported outcomes in the Phase III OASIS-HAE Study of Donidalorsen for Hereditary Angioedema. *Allergy*. Published online April 19, 2025. doi:10.1111/all.16563 **16.** Weller K, Magerl M, Peveling-Oberhag A, et al. The Angioedema Quality of Life Questionnaire (AE-QoL) - assessment of sensitivity to change and minimal clinically important difference. *Allergy*. 2016;71(8):1203-1209. doi:10.1111/all.12900 **17.** Weller K, Donoso T, Magerl M, et al. Validation of the Angioedema Control Test (AECT)—a patient-reported outcome instrument for assessing angioedema control. *J Allergy Clin Immunol Pract*. 2020;8(6):2050-2057.e4. doi:10.1016/j.jaip.2020.02.038 **18.** Weller K, Donoso T, Magerl M, et al. Development of the Angioedema Control Test—a patient-reported outcome measure that assesses disease control in patients with recurrent angioedema. *Allergy*. 2020;75(5):1165-1177. doi:10.1111/all.14144

STEP BY STEP,
together with your patient

IONIS EVERY STEP™ SUPPORT SERVICES

Ionis Every Step™ is a support program dedicated to help your patient start and follow your prescribed treatment plan with DAWNZERA.

If your patient is new to DAWNZERA, they may be eligible to receive a one-time, one-dose supply of DAWNZERA at no cost to see if DAWNZERA if right for them. Fill out the Free Trial Prescription on the enrollment form or through DAWNZERA Direct to enroll your patient. For eligibility, see terms and conditions at DAWNZERA.com/FreeTrialProgram.†

Patient Education Manager‡

Your patient is connected with a dedicated Patient Education Manager from the start so you can feel confident that they're supported at every step. Support includes how your patient receives DAWNZERA, injection training, educational resources, and keeping your office updated throughout treatment.

Insurance Navigation§

Assistance with the insurance approval process, including prior authorizations, appeals, and reauthorizations.

Affordability Programs¶

Programs to help eligible patients access their Ionis medication, regardless of their insurance.

DAWNZERA Direct

An online companion to support your patient's treatment journey.

We have several options to make signing up easier for your patient:

1 Sign the DAWNZERA Patient Authorization and Consent section of the **Patient Enrollment and Prescription Form** in your office.

2 Visit **DAWNZERA.com/Enroll.**

3 Call Ionis Every Step at **1-844-444-4305**, Monday to Friday, 8 AM to 8 PM ET.

†The Free Trial Program is meant to help your patient evaluate the tolerability of DAWNZERA and to assess the administration process prior to prescription. See full terms and conditions at DAWNZERA.com/FreeTrialProgram. May not be billed back to the third-party payer or resold. Participating in the program does not impose an obligation to purchase in the future. Terms and conditions apply. Programs subject to change or discontinue without notice, including in specific states.

‡Patient Education Managers do not provide clinical recommendations and will refer patients back to their health care providers as necessary.

§Insurance approval is not guaranteed. Ionis Every Step offers affordability programs for people prescribed DAWNZERA.

¶Terms and conditions apply. Programs subject to change or discontinue without notice, including in specific states.

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DAWNZERA™ (donidalorsen) 80 mg / 0.8 mL injection

When your patients need long-term prevention,

SWITCH TO DAWNZERA™ (donidalorsen)

Flip the switch on your expectations of HAE prophylaxis

- **First-in-class mechanism of action selectively targets PKK**[1,2]
- **The longest dosing option approved to prevent HAE attacks up to every 8 weeks**[1]
- **Well-tolerated safety profile**[1]

DAWNZERA every 4 weeks:

- **Reduced HAE attack rate** at 6 months **by 81% from the first dose, 87% when measured from the second dose, and 94% at 1 year** in an open-label study[3,6]

Switching to DAWNZERA every 4 weeks*:

- **Reduced mean HAE attack rate by 62% from prior therapy baseline**[13]
- **Preferred by 84% of patients surveyed, including those switching from oral therapy**[13]
  - 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 prophylactic treatments

*Exploratory endpoint.[13]

INDICATION

DAWNZERA (donidalorsen) is indicated for prophylaxis to prevent attacks of hereditary angioedema (HAE) in adult and pediatric patients 12 years of age and older.

SELECT IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

DAWNZERA is contraindicated in patients with a history of serious hypersensitivity reactions, including anaphylaxis, to donidalorsen or any of the excipients in DAWNZERA.

ADVERSE REACTIONS

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IONIS

DAWNZERA™ (donidalorsen) 80 mg / 0.8 mL injection