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RESEARCH**

APPLICATION NUMBER:

219407Orig1s000

LABELING

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use DAWNZERA™ (donidalorsen) safely and effectively. See full prescribing information for DAWNZERA.

DAWNZERA™ (donidalorsen) injection, for subcutaneous use
Initial U.S. Approval: 2025

INDICATIONS AND USAGE
DAWNZERA is a prekallikrein-directed antisense oligonucleotide indicated for prophylaxis to prevent attacks of hereditary angioedema (HAE) in adult and pediatric patients 12 years of age and older. (1)

DOSAGE AND ADMINISTRATION
The recommended dosage of DAWNZERA is 80 mg administered subcutaneously every 4 weeks.
• A dosage of 80 mg every 8 weeks may also be considered. (2.1)
• See full prescribing information for administration instructions. (2.2)

DOSAGE FORMS AND STRENGTHS
Injection: 80 mg/0.8 mL solution in a single-dose autoinjector. (3)

CONTRAINDICATIONS
History of serious hypersensitivity reactions, including anaphylaxis, to donidalorsen or any of the excipients in DAWNZERA. (4)

WARNINGS AND PRECAUTIONS
Hypersensitivity reactions including anaphylaxis have been reported following use of DAWNZERA. Advise patients to discontinue DAWNZERA and seek immediate medical attention if serious hypersensitivity reactions occur. (5.1)

ADVERSE REACTIONS
Most common adverse reactions (incidence ≥ 5%) are injection site reactions, upper respiratory tract infection, urinary tract infection, and abdominal discomfort. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Ionis Pharmaceuticals at 1-833-644-6647 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

USE IN SPECIFIC POPULATIONS
Hepatic Impairment: Use in patients with moderate and severe hepatic impairment is not recommended (8.7)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 8/2025

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

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

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage

The recommended dosage of DAWNZERA is 80 mg administered subcutaneously every 4 weeks.

- A dosage of 80 mg administered subcutaneously every 8 weeks may be considered.

Missed Dose(s)

If a dose of DAWNZERA is missed, administer DAWNZERA as soon as possible. Resume treatment at the recommended dosing frequency from the date of the most recently administered dose.

2.2 Administration Instructions

- For subcutaneous use.
- DAWNZERA is intended for self-administration or administration by a caregiver. Prior to treatment initiation, train patients and/or caregivers on proper preparation and subcutaneous administration technique of DAWNZERA autoinjector [see [Instructions for Use](#)].
- Remove the single-dose autoinjector from the refrigerator 30 minutes prior to the injection and allow to warm to room temperature. Do not use other warming methods.
- Inspect DAWNZERA visually for particulate matter and discoloration prior to administration. The solution should appear clear and colorless to yellow. Do not use if cloudiness, particulate matter, or discoloration is observed prior to administration.
- Administer DAWNZERA subcutaneously into the abdomen or upper thigh region. The back of the upper arm can also be used as an injection site if a caregiver or healthcare provider administers the injection.

3 DOSAGE FORMS AND STRENGTHS

Injection: 80 mg/0.8 mL of donidalorsen as a sterile, clear, colorless to yellow solution in a single-dose autoinjector.

4 CONTRAINDICATIONS

DAWNZERA is contraindicated in patients with a history of serious hypersensitivity reactions, including anaphylaxis, to donidalorsen or any of the excipients in DAWNZERA [see [Warnings and Precautions \(5.1\)](#) and [Adverse Reactions \(6\)](#)].

5 WARNINGS AND PRECAUTIONS

5.1 Risk of Hypersensitivity Reactions, Including Anaphylaxis

Hypersensitivity reactions, including anaphylaxis, have been reported in patients treated with DAWNZERA [see [Adverse Reactions \(6.1\)](#)]. If signs and symptoms of serious hypersensitivity reactions occur, discontinue DAWNZERA and institute appropriate therapy.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are discussed elsewhere in the labeling:

- Risk of Hypersensitivity Reactions, Including Anaphylaxis [see [Warnings and Precautions \(5.1\)](#)]

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of DAWNZERA reflects the exposure in a total of 171 adult and pediatric patients 12 years and older with hereditary angioedema (HAE) from a placebo-controlled trial (OASIS-HAE) [see [Clinical Studies \(14\)](#)], and 2 other clinical studies. The average duration of DAWNZERA treatment exposure across the 3 clinical studies was 14 months.

The safety data below is based on the 24-week multicenter, randomized, double-blind, placebo-controlled trial (OASIS-HAE), in which patients received at least one subcutaneous dose of DAWNZERA 80 mg once every 4 weeks (n=45), DAWNZERA 80 mg once every 8 weeks (n=23), or matching placebo (n=22). Demographics of the patients in OASIS-HAE are summarized in Clinical Studies [see [Clinical Studies \(14\)](#)].

Table 1 provides the most common adverse reactions with DAWNZERA with incidence $\geq 5\%$ and more common than placebo.

Table 1: Adverse Reactions with DAWNZERA with Incidence $\geq 5\%$ and More Common than Placebo in Patients with HAE (OASIS-HAE)

Adverse Reaction	DAWNZERA		Placebo (N=22) n (%)
	80 mg q4wks (N=45)	80 mg q8wks (N=23)	
	n (%)	n (%)	
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

N = number of patients; n = number of patients experiencing the event; q4wks = every 4 weeks; q8wks = every 8 weeks.

* Injection site reactions include: erythema, discoloration, pain, pruritus, induration, bruising, haematoma, hypersensitivity, swelling, reaction, and urticaria.

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

Specific Adverse Reactions

Hypersensitivity Reactions, Including Anaphylaxis

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

Laboratory Tests

Decrease in Platelet Count: DAWNZERA can cause reductions in platelet count. In OASIS-HAE, the mean platelet count at baseline was 266,000/mm³ for the DAWNZERA 80 mg every 4 weeks group,

265,000/mm³ for the DAWNZERO 80 mg every 8 weeks group, and 245,000/mm³ for the placebo group. The mean percent change in platelet count at Week 25 was -9.6% for the DAWNZERO 80 mg every 4 weeks group, -7.9% for the DAWNZERO 80 mg every 8 weeks group, and -1.4% for the placebo group. In OASIS-HAE and 2 other clinical studies no DAWNZERO-treated patient had a platelet count of <50,000/mm³, and there were no major bleeding events associated with a low platelet count.

Increase in Liver Function Tests: Increases from baseline in liver enzymes (alanine aminotransferase, aspartate aminotransferase, and gamma-glutamyl transferase) were observed with DAWNZERO use. The increased levels were generally below 3 times the upper limit of normal and stabilized. Discontinuations due to liver function test increases were infrequent.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no available data on DAWNZERO use in pregnant women to evaluate for a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes.

In animal reproduction studies, subcutaneous administration of donidalorsen or a pharmacologically active mouse-specific surrogate in a combined fertility and embryo-fetal development study in mice and a pre- and postnatal development study in mice with F0 parental doses up to 5 times the maximum recommended human dose (MRHD, 80 mg) on a body surface area (BSA, mg/m²) basis did not result in any adverse effects on embryofetal development, or behavioral, fertility, and reproductive development in the F1 offspring. Donidalorsen does not cross the placental barrier (see *Data*).

The estimated background risk of major birth defects and miscarriage for the indicated population(s) is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data

Animal Data

In reproductive toxicity studies with donidalorsen, the unconjugated form was not detected (below the limit of quantitation) in fetal tissues. Donidalorsen does not cross the placental barrier.

In a combined fertility and embryofetal development study, subcutaneous administration of donidalorsen (up to 10 mg/kg/week [2.5-times the MRHD on a BSA basis]) or a mouse-specific surrogate (4 mg/kg/week) to male and female F0 mice weekly, prior to and during mating, and continuing every other day in females throughout the periods of implantation and organogenesis (Gestation Days 0 to 16), resulted in no adverse effects on embryofetal development. There was no evidence of maternal toxicity with doses up to 10 mg/kg/week.

In a pre- and postnatal development study, subcutaneous administration of donidalorsen (up to 20 mg/kg/week [5-times the MRHD on a BSA basis]) or a mouse-specific surrogate (5 mg/kg/week) to F0 female mice every other day throughout pregnancy (from Gestation Day 6 to 18) and weekly throughout lactation (from Lactation Day 1 to 20) produced no adverse effects on behavioral, fertility,

and reproductive development in the F1 offspring. There was no evidence of maternal toxicity with doses up to 20 mg/kg/week.

8.2 Lactation

Risk Summary

There are no data on the presence of donidalorsen in human milk, the effects on the breast-fed infant, or the effects on milk production. Donidalorsen was excreted into the milk of lactating mice; however, due to species-specific differences in lactation physiology, animal lactation data may not reliably predict levels in human milk (*see Data*). The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for DAWNZERA and any potential adverse effects on the breast-fed infant from DAWNZERA or from the underlying maternal condition.

Data

Animal Data

In the mouse pre- and postnatal development study, the concentrations of donidalorsen in breast milk from lactating mice on Lactation Day 15 increased in a dose-dependent manner at doses ≥ 10 mg/kg/week, but these concentrations of donidalorsen in breast milk were lower than the observed concentrations in the liver where the drug is preferentially taken up. Even though donidalorsen was detected in the maternal mouse milk, systemic exposure in pups was not expected due to the lack of oral absorption of donidalorsen.

8.4 Pediatric Use

The safety and effectiveness of DAWNZERA for prophylaxis to prevent attacks of HAE have been established in pediatric patients aged 12 years and older. Use of DAWNZERA for this indication is supported by evidence from an adequate and well-controlled trial (OASIS-HAE) that included 7 pediatric patients (aged 12 to 17 years) who received DAWNZERA 80 mg subcutaneously every 4 weeks (n=4) or every 8 weeks (n=3). The safety and effectiveness of DAWNZERA in pediatric patients aged 12 years and older is extrapolated from adults from OASIS-HAE with support from pharmacokinetic analysis and pharmacodynamic response [see [Clinical Pharmacology \(12.2, 12.3\)](#) and [Clinical Studies \(14\)](#)]. No new safety signals were identified in pediatric patients aged 12 years and older who received DAWNZERA [see [Adverse Reactions \(6.1\)](#)].

The safety and effectiveness of DAWNZERA have not been established in pediatric patients younger than 12 years of age.

8.5 Geriatric Use

Clinical studies of DAWNZERA did not include sufficient numbers of patients 65 years of age and older to determine whether they respond differently from younger adult patients.

8.6 Renal Impairment

No dosage adjustment of DAWNZERA is recommended for patients with mild renal impairment (estimated glomerular filtration rate [eGFR] ≥ 60 to <90 mL/min/1.73 m²) [see [Clinical Pharmacology \(12.3\)](#)].

DAWNZERA has not been studied in patients with moderate or severe renal impairment or end-stage renal disease.

8.7 Hepatic Impairment

No dosage adjustment of DAWNZERA is required for patients with mild hepatic impairment (defined by National Cancer Institute Organ Dysfunction Working Group [NCI-ODWG] Criteria: total bilirubin $\leq 1 \times$ upper limit of normal [ULN] and aspartate aminotransferase [AST] $> 1 \times$ ULN, or total bilirubin > 1 to $1.5 \times$ ULN and any AST level) [see [Clinical Pharmacology \(12.3\)](#)].

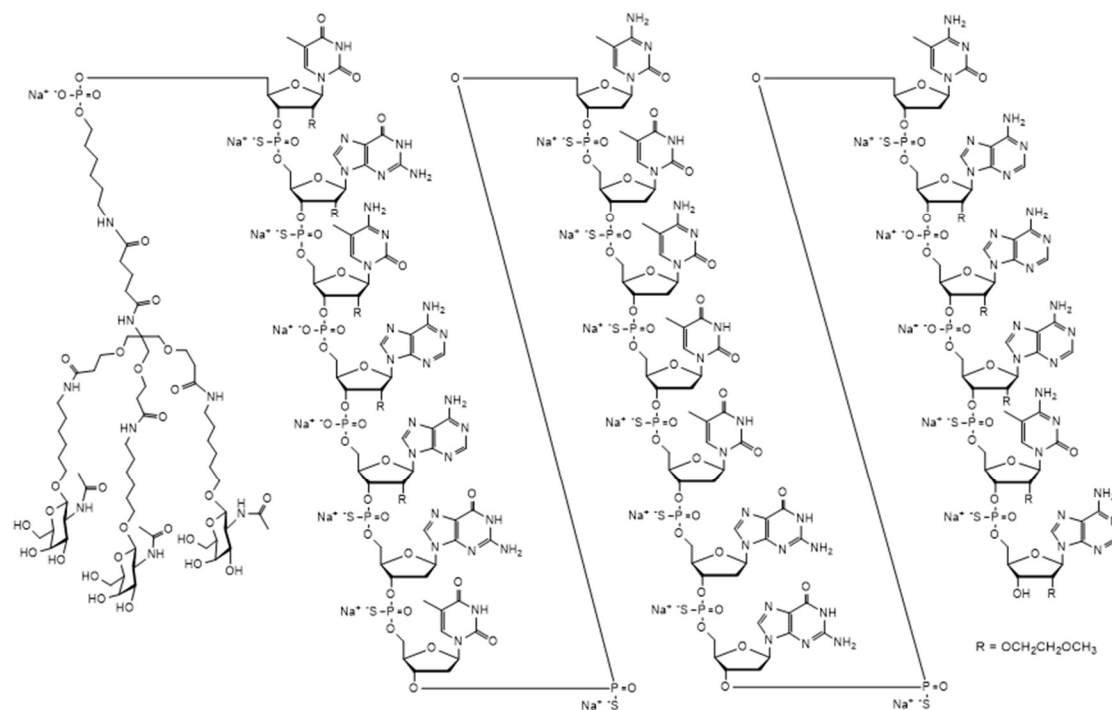
DAWNZERA has not been studied in patients with moderate or severe hepatic impairment. Use of DAWNZERA is not recommended in patients with moderate or severe hepatic impairment (defined by NCI-ODWG Criteria: total bilirubin $> 1.5 \times$ ULN regardless of AST level).

11 DESCRIPTION

Donidalorsen is a prekallikrein-directed antisense oligonucleotide (ASO) covalently linked to a ligand containing three *N*-acetyl galactosamine (GalNAc) residues to facilitate delivery of the ASO to hepatocytes.

DAWNZERA contains donidalorsen sodium as the active ingredient. Donidalorsen sodium is a white to yellow solid and it is freely soluble in water and in sodium phosphate buffer. The molecular formula of donidalorsen sodium is $C_{296}H_{415}N_{83}O_{151}P_{20}S_{15}Na_{20}$ and the molecular weight is 9112.27 daltons. The chemical name of donidalorsen is DNA, d([2'-O-(2-methoxyethyl)]m⁵rU-s^p-[2'-O-(2-methoxyethyl)]rG-s^p-[2'-O-(2-methoxyethyl)]m⁵rC-[2'-O-(2-methoxyethyl)]rA-[2'-O-(2-methoxyethyl)]rA-s^p-G-s^p-T-s^p-m⁵C-s^p-T-s^p-m⁵C-s^p-T-s^p-T-s^p-G-s^p-G-s^p-m⁵C-s^p-[2'-O-(2-methoxyethyl)]rA-[2'-O-(2-methoxyethyl)]rA-[2'-O-(2-methoxyethyl)]rA-s^p-[2'-O-(2-methoxyethyl)]m⁵rC-s^p-[2'-O-(2-methoxyethyl)]rA), 5'-[26-[[2-(acetylamino)-2-deoxy-β-D-galactopyranosyl]oxy]-14,14-bis[[3-[[6-[[2-(acetylamino)-2-deoxy-β-D-galactopyranosyl]oxy]hexyl]amino]-3-oxopropoxy]methyl]-8,12,19-trioxo-16-oxa-7,13,20-triazahexacos-1-yl hydrogen phosphate], sodium salt (1:20).

The chemical structure of donidalorsen sodium is presented below:



DAWNZERA (donidalorsen) injection is a sterile, preservative-free solution for subcutaneous injection supplied as a single-dose autoinjector. Each single-dose autoinjector contains 80 mg of donidalorsen (equivalent to 84 mg donidalorsen sodium) in 0.8 mL of solution. The solution also contains disodium hydrogen phosphate; sodium chloride; sodium dihydrogen phosphate; water for injection; and may include hydrochloric acid and/or sodium hydroxide for pH adjustment between 6.9 to 7.9. Each dose of DAWNZERA injection contains 6 mg of phosphorous and 5 mg of sodium.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Donidalorsen is an ASO-GalNAc conjugate that causes ribonuclease H1 (RNase H1)-mediated degradation of PKK mRNA through binding to PKK mRNA, which results in reduced production of PKK protein. PKK is a pro-enzyme for plasma kallikrein, which results in the release of bradykinin, a potent vasodilator causing swelling and pain in HAE. In patients with HAE, C1-inhibitor (C1-INH) deficiency or dysfunction leads to excessive plasma kallikrein activity, bradykinin generation, and angioedema attacks. Donidalorsen lowers PKK concentration, preventing excessive bradykinin production in patients with HAE.

12.2 Pharmacodynamics

In OASIS-HAE in adult and pediatric patients (≥ 12 years) with HAE-1 or HAE-2 [see [Clinical Studies \(14\)](#)], a decrease in plasma PKK concentrations was observed at the first assessment (Week 4) following treatment with DAWNZERA 80 mg. The mean percentage reduction from baseline at Week 4 across both treatment groups was 48%. The mean percentage change from baseline to Week 24 in trough plasma PKK concentrations indicated reductions of 73% and 47% following

treatment with DAWNZERA 80 mg every 4 weeks and every 8 weeks, respectively, compared with a slight increase (2%) observed in the placebo group.

Cardiac Electrophysiology

At the maximum recommended dose of DAWNZERA 80 mg every 4 weeks, clinically significant QTc interval prolongation was not observed.

12.3 Pharmacokinetics

The pharmacokinetic properties of DAWNZERA were evaluated following subcutaneous administration of multiple doses every 4 weeks in healthy subjects and every 4 weeks or every 8 weeks in patients with HAE. The pharmacokinetics of DAWNZERA were similar between healthy subjects and patients with HAE.

Donidalorsen exposure (area under the plasma concentration-time curve [AUC]) at steady state following subcutaneous administration in healthy subjects increased in a greater than dose-proportional manner over the dose range of 0.25 times the maximum recommended dosage to 80 mg every 4 weeks.

Geometric Mean (Coefficient of Variation (CV%)) of steady-state maximum plasma concentration ($C_{max,ss}$), trough plasma concentration ($C_{trough,ss}$), and area under the plasma concentration-time curve over the dosing interval ($AUC_{\tau,ss}$) are presented in Table 2. No accumulation of donidalorsen C_{max} and AUC was observed in plasma after repeated dosing every 4 weeks. However, a 2-fold increase of plasma donidalorsen C_{trough} was observed following repeated dosing every 4 weeks.

Table 2: Summary of Geometric Mean (CV%) Steady-State Donidalorsen Pharmacokinetic Parameters Following Dosage of DAWNZERA 80 mg Every 4 Weeks or 80 mg Every 8 Weeks in Patients with HAE

Pharmacokinetic Parameters (Geometric Mean)	DAWNZERA	
	80 mg q4wks	80 mg q8wks
$C_{max,ss}$ (ng/mL)	417 (81%)	416 (78%)
$C_{trough,ss}$ (ng/mL)	0.755 (63%)	0.255 (73%)
$AUC_{\tau,ss}$ (ng·h/mL)	5240 (52%)	5210 (52%)

$AUC_{\tau,ss}$ = area under the plasma concentration-time curve over each dosing interval at steady-state; $C_{max,ss}$ = maximum plasma concentration at steady-state; $C_{trough,ss}$ = trough plasma concentration at steady-state; q4wks = every 4 weeks; q8wks = every 8 weeks.

Absorption

Following subcutaneous administration, donidalorsen is absorbed with the median (range) time to maximum plasma concentration of approximately 2 (0.25, 8) hours post dose.

Distribution

Donidalorsen is expected to distribute primarily to the liver and kidney cortex after subcutaneous dosing. The apparent volume of distribution for the central (V_c/F) and peripheral (V_p/F) compartment

were 69.8 L and 1840 L, respectively. Donidalorsen is highly bound to human plasma proteins (>98% bound) *in vitro*.

Elimination

The terminal plasma elimination half-life of donidalorsen in a typical patient with HAE is approximately 1 month. The half-life of the initial rapid clearance phase, reflecting tissue distribution, was approximately 5 hours.

Metabolism

The oligonucleotide moiety of donidalorsen is expected to be metabolized by endo- and exonucleases to short oligonucleotide fragments of varying sizes within the liver. Based on *in vitro* studies, donidalorsen is not a substrate of cytochrome P450 (CYP) enzymes.

The linker that covalently connects the ASO to the GalNAc residues is cleaved via hydrolysis and undergoes dephosphorylation and subsequent oxidative metabolism to form inactive metabolites, which are minimally released in circulation. The most abundant linker-related metabolite (M8) is a substrate of CYP3A4.

Excretion

The mean fraction of unchanged ASO eliminated in urine was less than 1% of the administered dose in healthy subjects within 24 hours post-dose. The renal route of elimination is minor for linker-related metabolites.

Specific Populations

No clinically meaningful differences in the pharmacokinetics or pharmacodynamics of donidalorsen were observed based on age (12 to 68 years), body weight (37 to 152 kg), sex, race (68% White, 24% Black, and 4% Asian), ethnicity, disease status (healthy subjects or subjects with HAE), mild renal impairment (eGFR ≥ 60 to < 90 mL/min/1.73 m²), or mild hepatic impairment (defined using NCI-ODWG Criteria: total bilirubin $\leq 1 \times$ ULN and AST $> 1 \times$ ULN, or total bilirubin > 1 to $1.5 \times$ ULN and any AST).

Donidalorsen has not been studied in patients with moderate or severe renal impairment, end-stage renal disease, or moderate or severe hepatic impairment.

Drug Interaction Studies

No clinical drug-drug interaction studies have been performed with donidalorsen. *In vitro* studies show that donidalorsen is not a substrate or inhibitor of transporters, does not interact with highly plasma protein bound drugs, and is not an inhibitor/inducer of CYP enzymes. *In vitro* studies show that linker-related metabolite M8 is not an inhibitor or inducer of CYP enzymes. M8 is a substrate of transporters bile salt export pump (BSEP) and organic anion transporting polypeptide 1B3 (OATP1B3), and is an inhibitor of multidrug and toxin extrusion protein 1 (MATE1) transporter.

12.6 Immunogenicity

The observed incidence of anti-drug antibodies (ADAs) is highly dependent on the sensitivity and specificity of the assay. Differences in assay methods preclude meaningful comparisons of the incidence of anti-drug antibodies in the studies described below with the incidence of anti-drug antibodies in other studies, including those of donidalorsen or of other donidalorsen products.

In OASIS-HAE, with a treatment duration up to 24 weeks, the incidence rate of treatment-emergent ADAs in adult and pediatric patients (≥ 12 years of age) with HAE was 20% (9 of 45 patients) in the DAWNZERA 80 mg every 4 weeks group and 22% (5 of 23 patients) in the DAWNZERA 80 mg every 8 weeks group. In an open-label extension trial, patients that rolled over from OASIS-HAE continued treatment with DAWNZERA in the 80 mg every 4 weeks or every 8 weeks groups for up to 3 years (median exposure duration of 227 days). The incidence rate of treatment-emergent ADAs was 35% (22 of 63 patients) in the DAWNZERA 80 mg every 4 weeks group, including patients initially randomized to DAWNZERA 80 mg every 4 weeks in OASIS-HAE (36%, 16/44) and patients initially randomized to placebo in OASIS-HAE (32%, 6/19). The incidence rate of treatment-emergent ADAs was 21% (3 of 14 patients) among patients who received DAWNZERA 80 mg every 8 weeks in OASIS-HAE and open-label extension.

In general, the development of ADAs was not found to affect the pharmacodynamics, safety, or efficacy of DAWNZERA. An increase in donidalorsen plasma C_{trough} was observed in ADA-positive patients with high titers. Because of small sample size, the effect of ADA on the pharmacokinetics, pharmacodynamics, safety and effectiveness of DAWNZERA is inconclusive.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

In a 6-month carcinogenicity study in transgenic (Tg.rasH2) mice, subcutaneous administration of donidalorsen, up to the highest dose tested (20 mg/kg in males and 60 mg/kg in females) or a mouse-specific surrogate (10 mg/kg) once every 2 weeks did not result in an increase in malignant tumors.

Mutagenesis

Donidalorsen was negative for genotoxicity in the *in vitro* bacterial reverse mutation test and chromosomal aberration assay in Chinese hamster lung cells and *in vivo* mouse bone marrow micronucleus assay.

Fertility

Fertility and reproductive performance were unaffected by subcutaneous administration of donidalorsen (up to 10 mg/kg/week [2.5-times the MRHD on a BSA basis]) or a mouse-specific surrogate (4 mg/kg/week) to male and female mice weekly, prior to and during mating, and continuing every other day in females throughout the periods of implantation and organogenesis.

14 CLINICAL STUDIES

The efficacy of DAWNZERA for prophylaxis to prevent attacks of hereditary angioedema (HAE) in adult and pediatric patients 12 years of age and older was evaluated in a 24-week multicenter, randomized, double-blind, placebo-controlled trial (OASIS-HAE [NCT05139810]).

The trial (OASIS-HAE) included 90 adult and pediatric patients 12 years of age and older with Type I and Type II HAE, who had at least 2 investigator-confirmed attacks during the 8-week run-in period. Patients were randomized to receive DAWNZERA 80 mg once every 4 weeks (n=45), DAWNZERA 80 mg once every 8 weeks (n=23), or matching placebo (n=22). Patients were required to discontinue other prophylactic HAE medications, except androgens and tranexamic acid, prior to entering the trial; all patients were allowed to use rescue medications for treatment of breakthrough HAE attacks.

The demographics and baseline characteristics of OASIS-HAE trial are provided in [Table 3](#).

Table 3: Demographics and Baseline Characteristics of Patients in the OASIS-HAE Trial

	OASIS-HAE (N=90)
Female, n (%)	48 (53)
Race, n (%)	
Asian	1 (1)
Black or African American	2 (2)
White	82 (91)
American Indian or Alaskan Native Asian	3 (3)
Multiple	1(1)
Other	1(1)
Hispanic or Latino, n (%)	6 (7)
Mean age, years (SD)	37 (14)
≤ 17 years, n (%)	7 (8)
>17 years, n (%)	83 (92)
C1-INH HAE Type 1, n (%)	84 (93)
Prior HAE prophylaxis*, n (%)	16 (18)
Baseline HAE attack rate**, n (%)	
≤ 2 attacks/4 weeks	28 (31)
2 to 5 attacks/4 weeks	48 (53)
≥ 5 attacks/4 weeks	14 (16)

* Within 5 half-lives of screening (up to 10 weeks).
**Period from screening to first dose.

The primary endpoint for OASIS-HAE was the HAE attack rate (number of investigator-confirmed HAE attacks per 4 weeks) from Week 0 to Week 24. As shown in Table 4, DAWNZERO 80 mg administered subcutaneously every 4 or 8 weeks demonstrated statistically significant reductions in the HAE attack rate compared to placebo.

Table 4: HAE Attack Rate (Attacks/4 Weeks) at Week 24 in OASIS-HAE

	DAWNZERO 80 mg q4wks (N=45)	DAWNZERO 80 mg q8wks (N=23)	Placebo (N=22)
HAE Attack Rate per 4 Weeks from Week 0 to Week 24*			
LS mean (95% CI) attack rate	0.44 (0.27, 0.73)	1.02 (0.65, 1.59)	2.26 (1.66, 3.09)
% Reduction (95% CI) relative to placebo†	-81 (-89, -65)	-55 (-74, -22)	--
Wald chi-square p-value	<0.001	0.004	--

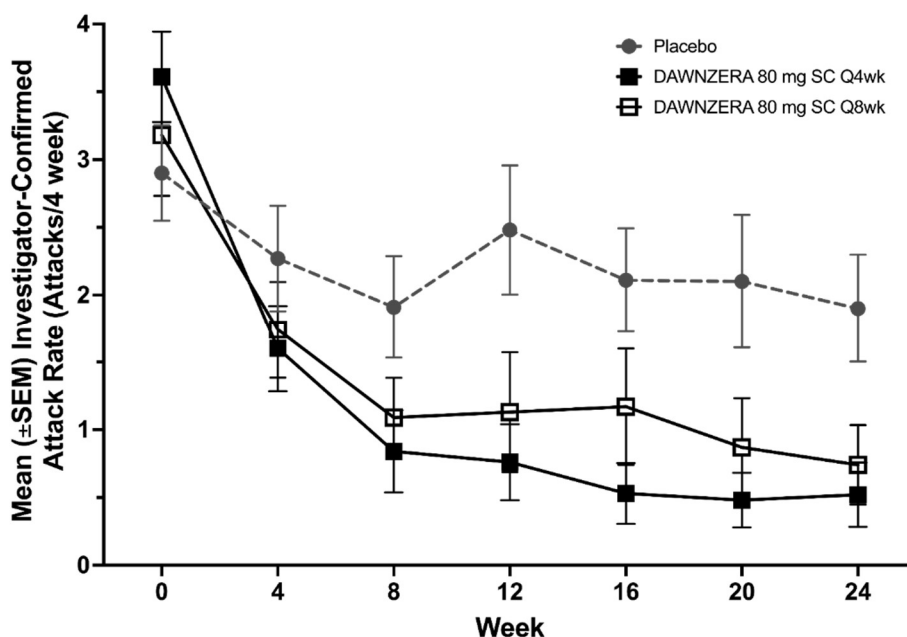
CI = confidence interval; HAE = hereditary angioedema; LS = least square; N = number of patients in the specific treatment group; q4wks = every 4 weeks; q8wks = every 8 weeks.

* Primary efficacy endpoint = comparison of the time-normalized number of investigator-confirmed HAE attacks per 4 weeks from Week 0 to Week 24 between the DAWNZERO 80 mg q4wks group and the placebo group.

† Calculated as the ratio of the model-based treatment period HAE attack rates (donidalorsen/placebo) minus 1 multiplied by 100.

The mean decreases from baseline in the HAE attack rate observed throughout the treatment period in the DAWNZERO treatment groups are shown in Figure 1.

Figure 1: Mean ($\pm$ SEM) Investigator-confirmed HAE Attack Rate (Attacks/4 Weeks) in OASIS-HAE



HAE = hereditary angioedema; q4wks = every 4 weeks; q8wks = every 8 weeks; SC = subcutaneous; SEM = standard error of the mean.

Pre-defined secondary endpoints were assessed from Week 4 to Week 24. The moderate or severe HAE attack rate was 0.12 for the DAWNZERA 80 mg every 4 weeks group, 0.68 for the DAWNZERA 80 mg every 8 weeks group, and 1.15 for the placebo group, representing a reduction of 89% (95% CI: 66, 97) and 41% (95% CI: -26, 72) in moderate or severe HAE attack rate relative to placebo, respectively. The HAE attacks requiring acute therapy was 0.15 for the DAWNZERA 80 mg every 4 weeks group, 0.59 for the DAWNZERA 80 mg every 8 weeks group, and 1.80 for the placebo group, representing a reduction of 92% (95% CI: 77, 97) and 67% (95% CI: 29, 85) in HAE attacks requiring acute therapy relative to placebo, respectively.

The proportion of patients who were attack-free from Week 4 to Week 24 were 53% in the DAWNZERA 80 mg every 4 weeks group, 35% in the DAWNZERA 80 mg every 8 weeks group, and 9% in the placebo group, representing an odds ratio of being attack-free of 11.79 (95% CI: 2.34, 59.36) and 3.23 (95% CI: 0.46, 22.85), respectively.

The proportion of patients with a $\geq 50\%$, $\geq 70\%$, and $\geq 90\%$ reduction from baseline to Week 4 through Week 24 was 93%, 82%, and 62% in the DAWNZERA 80 mg every 4 weeks group, 83%, 65%, and 48% in the DAWNZERA 80 mg every 8 weeks group, and 27%, 18%, and 9% in the placebo group, respectively.

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

DAWNZERA (donidalorsen) 80 mg/0.8 mL injection is a sterile, preservative-free, clear, colorless to yellow solution supplied in a single-dose autoinjector. Each autoinjector of DAWNZERA is filled to

deliver 0.8 mL of solution containing 80 mg of donidalorsen. Table 5 provides the presentation and strength for DAWNZERA.

Table 5: Presentation and Strength for DAWNZERA

Presentation	Strength	Unit Count	NDC
Autoinjector	80 mg/0.8 mL	1	71860-103-01

Storage and Handling

- Store the DAWNZERA autoinjector in the refrigerator between 36°F to 46°F (2°C to 8°C) in the original carton.
- The DAWNZERA autoinjector can be stored at room temperature up to 86°F (30°C) in the original carton for up to 6 weeks; if not used within the 6 weeks stored at room temperature, discard DAWNZERA.
- Do not freeze. Do not expose to heat. Protect from direct light.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information and Instructions for Use).

Administration Instructions

- Instruct patients that DAWNZERA is for subcutaneous use and intended for self-administration or administration by a caregiver.
- Instruct patients and/or caregivers on proper preparation and subcutaneous administration technique of DAWNZERA autoinjector [see [Dosage and Administration \(2.2\)](#) and [Instructions for Use](#)].
- Instruct patients to administer DAWNZERA subcutaneously into the abdomen or upper thigh region for self-administration. The back of the upper arm can be used as an injection site if a caregiver or healthcare provider administers DAWNZERA.

Missed Dose(s)

Instruct patients to use DAWNZERA as prescribed. If a dose is missed, instruct patients to administer DAWNZERA as soon as they remember. Instruct patients to resume treatment at the recommended dosing frequency (every 4 weeks or every 8 weeks) from the date of the most recently administered dose [see [Dosage and Administration \(2.1\)](#)].

Risk of Hypersensitivity Reactions, Including Anaphylaxis

Advise patients hypersensitivity reactions, including anaphylaxis, have been reported following administration of DAWNZERA. Instruct patients to immediately discontinue DAWNZERA and seek medical attention if they experience signs and symptoms of serious hypersensitivity reaction [see [Warnings and Precautions \(5.1\)](#)].

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PATIENT INFORMATION
DAWNZERA™ (dawn-ZAIR-ah)
(donidalorsen)
injection, for subcutaneous use

What is DAWNZERA?

DAWNZERA 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.

Do not use DAWNZERA if you:

- have had a serious allergic reaction, including anaphylaxis to donidalorsen or any of the ingredients in DAWNZERA. See the end of this Patient Information leaflet for a complete list of ingredients in DAWNZERA.

Before using DAWNZERA, tell your healthcare provider about all your medical conditions, including if you:

- are pregnant or plan to become pregnant. It is not known if DAWNZERA can harm your unborn baby. Tell your healthcare provider if you become pregnant during treatment with DAWNZERA.
- are breastfeeding or plan to breastfeed. It is not known if DAWNZERA passes into your breast milk. Talk to your healthcare provider about the best way to feed your baby while using DAWNZERA.

Tell your healthcare provider about any other medications you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

How should I use DAWNZERA?

- Read the detailed Instructions for Use that comes with your DAWNZERA single-dose autoinjector.
- Your healthcare provider will show you and your caregiver how to inject DAWNZERA the first time.
- DAWNZERA is injected under your skin (subcutaneous use) in your stomach area (abdomen) or the front of your upper legs (thighs). Only a healthcare provider or caregiver may give you an injection in the back of your upper arm.
- Use DAWNZERA exactly as your healthcare provider tells you to take it.
- You, your caregiver, or healthcare provider should inject DAWNZERA 1 time every 4 weeks or 1 time every 8 weeks depending on your prescribed dosing frequency.
- If you miss a dose of DAWNZERA, administer the missed dose as soon as possible. Then inject DAWNZERA on the regular dosing schedule from the date of the most recently injected dose.

What are the possible side effects of DAWNZERA?

DAWNZERA can cause serious side effects, including:

- **Allergic reactions.** DAWNZERA can cause allergic reactions. Stop using DAWNZERA and call your healthcare provider or go to your nearest emergency room right away if you have symptoms of serious allergic reaction. Symptoms of serious allergic reaction may include:
 - rash
 - trouble breathing
 - fainting, dizziness, feeling lightheaded (low blood pressure)
 - swelling of your face, lips, or tongue
 - chest pain
 - itching

The most common side effects of DAWNZERA include:

- injection site reactions
- upper respiratory tract infection
- urinary tract infection
- abdominal discomfort

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

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store DAWNZERA?

- Store DAWNZERA in the refrigerator between 36°F to 46°F (2°C to 8°C) in the original carton.
- If needed, DAWNZERA can be stored at room temperature up to 86°F (30°C) in the original carton for up to 6 weeks. If not used within 6 weeks, throw away DAWNZERA.
- Do not freeze.
- Do not expose the autoinjector to heat.
- Protect from direct light.

Keep DAWNZERA and all medicines out of the reach of children.

General information about the safe and effective use of DAWNZERA.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use DAWNZERA for a condition for which it was not prescribed. Do not give DAWNZERA to other people, even if they have the same symptoms or condition that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about DAWNZERA that is written for health professionals.

What are the ingredients in DAWNZERA?

Active ingredients: donidalorsen

Inactive ingredients: disodium hydrogen phosphate; sodium chloride; sodium dihydrogen phosphate; water for injection; and may include hydrochloric acid or sodium hydroxide. Phosphorous and sodium.

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For more information go to www.DAWNZERA.com or call 1-833-644-6647. If you still have questions, contact your healthcare provider.

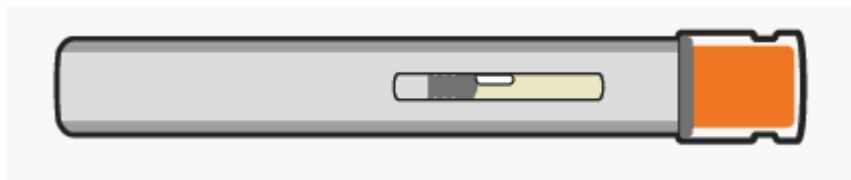
This Patient Information has been approved by the U.S. Food and Drug Administration

Issued: 08/2025

INSTRUCTIONS FOR USE
DAWNZERA™ [dawn-ZAIR-ah]
(donidalorsen)
injection, for subcutaneous use

This Instructions for Use contains information on how to inject **DAWNZERA** using the autoinjector.

Read this Instructions for Use before you start using your DAWNZERA autoinjector and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or treatment. Your healthcare provider should show you or your caregiver how to use the DAWNZERA autoinjector the right way. If you or your caregiver have any questions, talk to your healthcare provider.



Important information:

- DAWNZERA is injected under the skin (subcutaneous use) only.
- Each autoinjector contains 1 single-dose and can only be used 1 time.
- **Do not** remove the clear cap until you are ready to inject DAWNZERA (See Step 5).
- **Do not** share your autoinjector with anyone.
- **Do not** use if the autoinjector appears damaged.

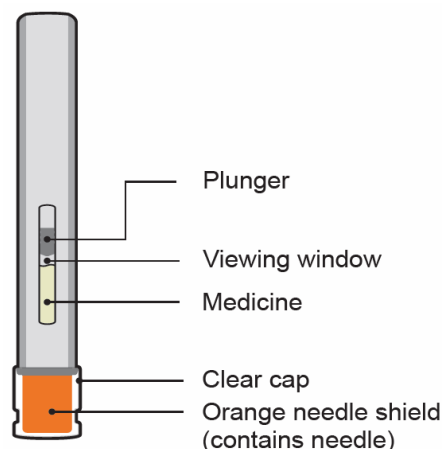
Storage information:

- Store the autoinjector in the refrigerator between 36°F to 46°F (2°C to 8°C) in the original carton.
- If needed, DAWNZERA can be stored at room temperature up to 86°F (30°C) in the original carton for up to 6 weeks.
- **Do not** store DAWNZERA at room temperatures above 86°F.
- Throw away the DAWNZERA if kept at room temperature longer than 6 weeks.
- **Do not** freeze.
- **Do not** expose the autoinjector to heat.
- Protect from direct light.
- Keep the autoinjector in the carton until ready to use.
- **Do not** store the autoinjector with the clear cap removed.

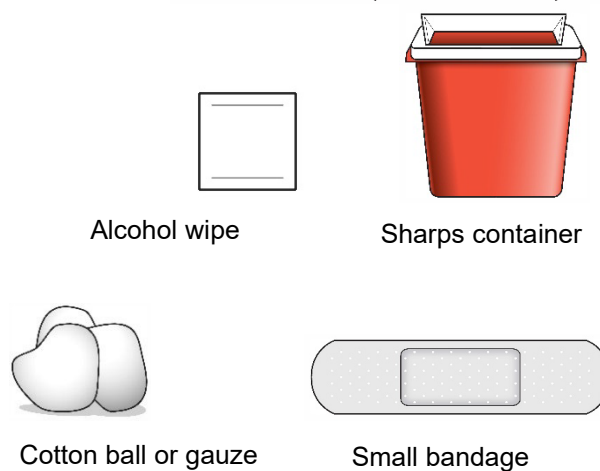
Keep DAWNZERA and all medicine out of the reach of children.

Parts of your DAWNZERA autoinjector

Single-dose autoinjector



Other supplies (not included)



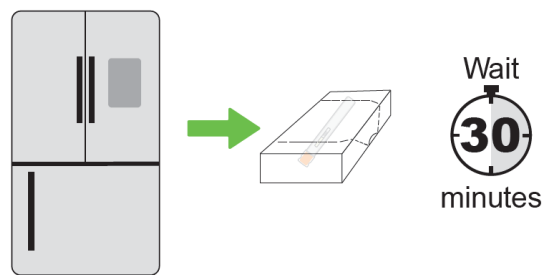
Preparing to inject DAWNZERA

Step 1 Remove from the refrigerator 30 minutes before you inject

a) Remove the autoinjector from the refrigerator.

b) **Keep the autoinjector in the original carton** and let the autoinjector come to room temperature for 30 minutes before injecting.

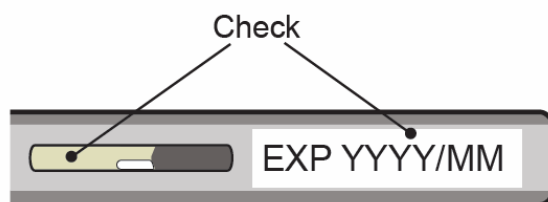
Do not try to speed up the warming process using other heat sources, such as a microwave or hot water.



Step 2 Check the medicine

a) Check the expiration (EXP) date.

b) Check the medicine through the viewing window. The DAWNZERA medicine should be clear and colorless to yellow. There should be no



particles. It is normal to see air bubbles in the solution.

Do not use the autoinjector if the:

- clear cap is missing or not attached.
- expiration (EXP) date has passed.
- medicine looks cloudy, discolored, or has particles.
- autoinjector appears damaged.

Step 3 Choose the injection site

a) Choose an injection site on the stomach or the front of the thigh.

b) Only healthcare providers or caregivers may choose the back of the upper arm.

Do not inject:

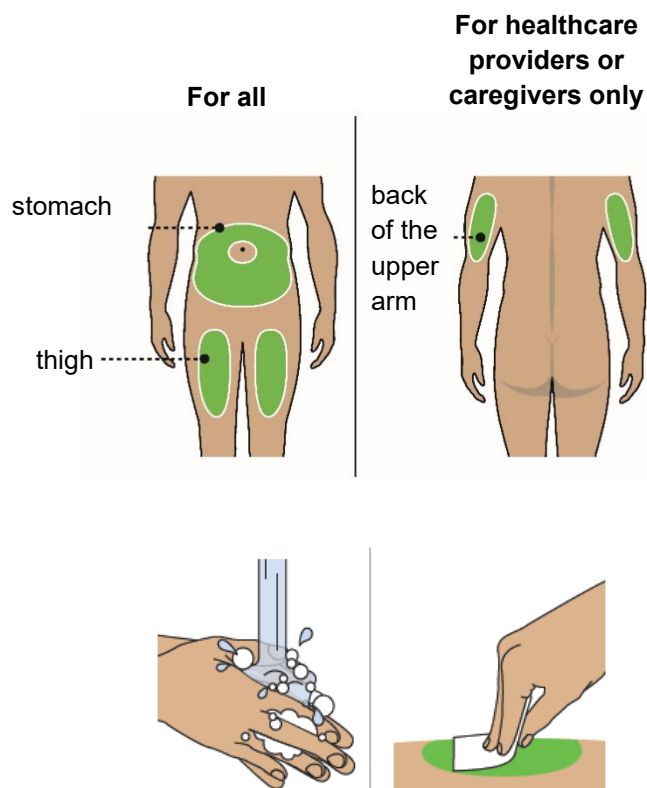
- within 2 inches of the belly button (navel).
- into skin that is bruised, tender, red, or hard.
- into scars or damaged skin.

Step 4 Wash hands and clean the injection site

a) Wash your hands with soap and water.

b) Clean the injection site with an alcohol wipe in a circular motion. Let the skin air dry.

Do not touch the cleaned skin before injecting.



Injecting DAWNZERO

Step 5 Remove and throw away the clear cap

a) Hold the autoinjector by the middle with the clear cap facing away from you.

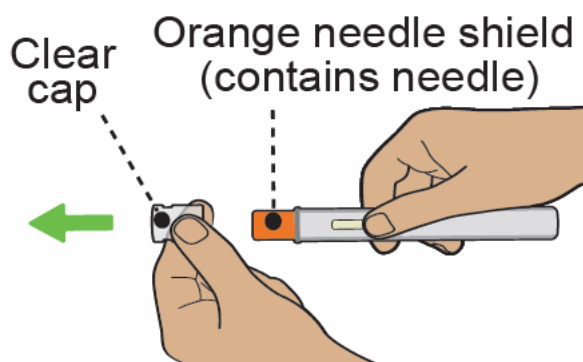
b) Remove the clear cap by pulling it straight off. **Do not** twist it off. The needle is inside the orange needle shield.

c) Throw away the clear cap in the trash or sharps container.

Do not remove the clear cap until right before you inject.

Do not recap the autoinjector.

Do not push the orange needle shield against the hand or finger.



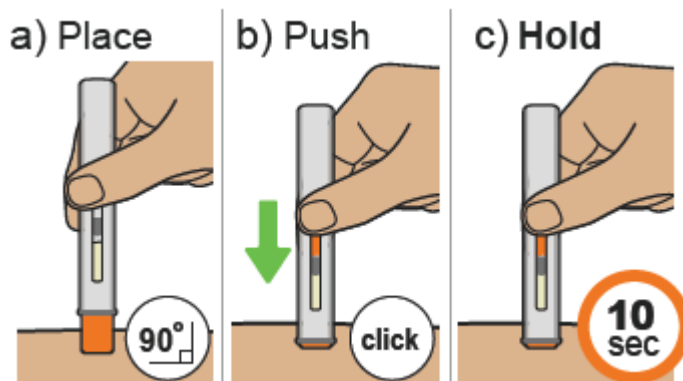
Step 6 Begin injection

a) Hold the autoinjector in 1 hand. Place the orange needle shield at a 90-degree angle against your skin. Make sure you can see the viewing window.

b) Push firmly and hold the autoinjector straight against the skin. You will hear a click as the injection starts.

You may hear a second click. This is normal. The procedure is not finished.

c) Hold the autoinjector against the skin for 10 seconds to make sure the full dose has been given.



Do not move, turn, or change the angle of the autoinjector during the injection.

Step 7 Finish injection

a) Check that the orange plunger rod has moved down to fill the entire viewing window.

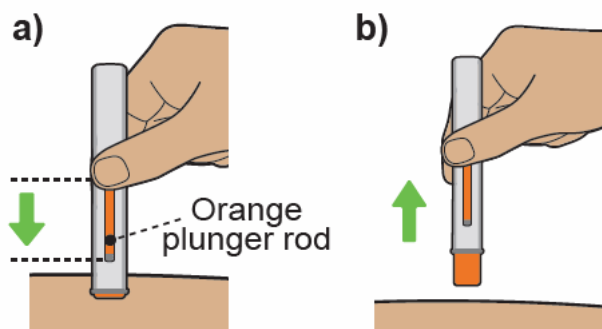
- If the orange plunger rod does not fill the viewing window, you may not have received the full dose.
- If this happens or if you have other concerns, contact your healthcare provider.

b) Remove the autoinjector by lifting it straight up. After removal from the skin, the orange needle shield locks into place and covers the needle.

c) There may be a small amount of blood or liquid where you injected. This is normal.

If needed, press a cotton ball or gauze on the area and apply a small bandage.

The autoinjector contains 1 dose. **Do not** reuse the autoinjector.



Throwing away DAWNZERA

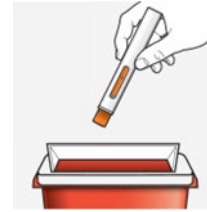
Step 8 Throw away autoinjector

a) Put the used autoinjector in a sharps container right away after use.

Do not throw away the autoinjector in your household trash.

Do not recycle your used sharps disposal container.

Do not reuse the autoinjector or clear cap.



If you do not have an FDA-cleared sharps container, you may use a household container that is:

- made of a heavy-duty plastic,
- can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
- upright and stable during use,
- leak-resistant, and
- properly labelled to warn of hazardous waste inside the container.

When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used autoinjectors.

For more information about safe sharps disposal, and specific information about sharps disposal in the state that you live in, go to the FDA's website at: <http://www.fda.gov/safesharpsdisposal>.

Do not throw away your used sharps disposal container in your household trash unless your community guidelines permit this. **Do not** recycle your used sharps disposal container.

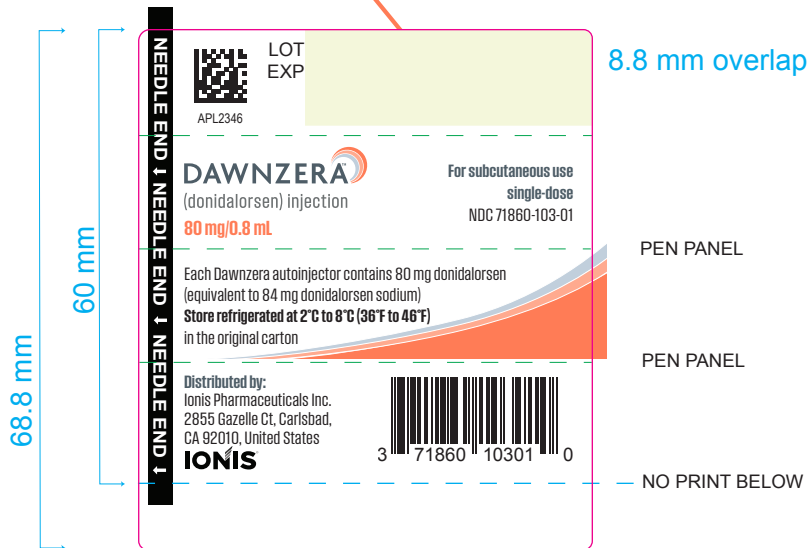
For more information, go to <https://www.DAWNZERA.com> or call 1-833-644-6647. If you still have questions, contact your healthcare provider.

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Approved: 08/2025

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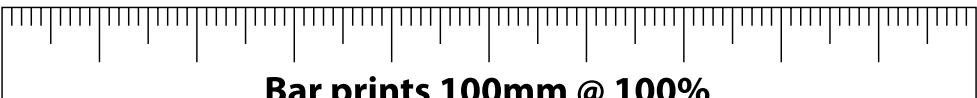
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