CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

219407Orig1s000

PRODUCT QUALITY REVIEW(S)

MEMORANDUM: DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: 10-Jun-2025

TO: NDA 219407 Donidalorsen Injection

FROM: Craig M. Bertha, CMC Reviewer
OPQ/OPQA II/DPQA VIII

SUBJECT: Integrated Quality Assessment (IQA) addendum memorandum regarding CMC labeling recommendations

BACKGROUND/EVALUATION:
Below are the CMC team's labeling recommendations for NDA 219407, and the outcomes.

1. **§201.57(a)(3) requires the actual four-digit year of initial U.S. approval. "YYYY" is a placeholder, not a year. The applicant must replace "YYYY" with the correct four-digit year of the drug's initial U.S. approval.**

Evaluation: Adequate. Since the Agency has not approved the application, the year that should appear in the package insert (PI) is not known yet.

2. **The dosage forms and strengths section does not include the following equivalency statement: "80 mg of donidalorsen (equivalent to 84 mg donidalorsen sodium)".**

Evaluation: Adequate. As per the labeling review tool: "It is not necessary to include an equivalency statement in [the Dosage Forms and Strengths] section because an equivalency statement is recommended for inclusion in the DESCRIPTION section." Note that the equivalency statement is in the DESCRIPTION section of the PI.

3. **The listing of inactive ingredients in the DAWNZERA product description and carton labeling do not follow strict alphabetical order, and it omits the required quantities for each ingredient.**

Evaluation: Adequate. The applicant has reordered the inactive ingredients in alphabetical order. No quantitative information for the inactive ingredients is provided, however, as per the labeling review tool: "Both qualitative (list of ingredients) and quantitative information (e.g., amounts) for all inactive ingredients except those added to adjust pH or tonicity or water for injection." (b) (4)

(b) (4) for the donidalorsen injection product.

4. **Latex: If product does not contain latex and manufacturing of product and container did not include use of natural rubber latex or synthetic derivatives of natural rubber latex, state: "Not made with natural rubber latex. Avoid statements such as "latex-free."**

Evaluation: Adequate. Applicants can include information about latex if they wish to, as per the 2014 guidance entitled "*Recommendations for Labeling Medical Products to Inform Users that the Product or Product Container is not Made with Natural Rubber Latex Guidance for Industry and Food and Drug Administration Staff.*" Apparently the applicant does not choose to include latex-related statements in the labeling.

5. **In the patient information labeling, the established name is missing the route of administration. The dosage form is also not included.**

Evaluation: Adequate. The Information for Use (IFU) labeling from the 12-Sep-2024, amendment complies with the 2022 guidance entitled *Instructions for Use — Patient Labeling for Human Prescription Drug and Biological Products — Content and Format*.

6. **The 'Rx only' designation is missing from the principal display panel of the carton labeling; it is only present on the side panel.**

Evaluation: Adequate. The main panel of the carton has been revised to include 'Rx only.'

7. **For improved clarity and accessibility, the NDC number should be moved from the side panel to the Principal Display Panel (PDP) and placed above the proprietary name.**

Evaluation: Adequate. The human readable NDC number has been added to the PDP and has been removed from the side panel. Also, the NDC number was added to the container label.

8. **Neither the lot number nor the expiration date placeholder is present on the carton label.**

Evaluation: Adequate. The following is to be placed on the end panel of the carton:

Start Applicant Material

GTIN 00371860103010
SN
EXP YYYY/MM
LOT

(01) GTIN
(21) SN
(17) EXP YYMMDD
(10) LOT

End Applicant Material

9. **We recommend revising this sentence to read, "Store refrigerated at 2°C to 8°C (36°F to 46°F) in the original carton and protect from direct light" on the container label for consistency with the carton labeling.**

Evaluation: Adequate. The applicant has revised the storage conditions on the carton label as requested.

10. The package type term 'single dose' is not included in the container labeling.

Evaluation: Adequate. The term “single-dose” now appears on the container label (use of the hyphen is consistent with the labeling review tool):

Start Applicant Material

(b) (4)

End Applicant Material

11. The carton labeling does not list the inactive ingredients in alphabetical order and lacks the quantities of inactive ingredients.

Evaluation: Adequate. The carton label now includes the inactive ingredients in alphabetical order. See the response to comment 3 above with respect to the quantitative information for the inactive ingredients.

RECOMMENDATION TO DPACC FROM CMC: The labeling is considered to be adequate from a CMC perspective. The application is recommended to be **approved.**

_____
Craig M. Bertha, CMC Reviewer/ATL

cc:
Orig. NDA 219407
OPQ/OPQAII/DPQAVIII/CBertha
OPQ/OPQAII/DPQAVII/GHamad
OPQ/OPQAII/DPQAVIII/JPinto
OPQ/OPRO/DPRBPMIII/EGimose
OND/ORO/DROII/CChee
OND/OII/DPACC/SKlauer
OND/OII/DPTII/ESalicru

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/s/

CRAIG M BERTHA
06/10/2025 10:07:59 AM

Office of Pharmaceutical Quality

New Drug Application (NDA) 219407
Integrated Quality Assessment

RECOMMENDATION

☒ Approval
☐ Approval with Post-Marketing Commitment
☐ Complete Response

NDA 219407
Assessment #1

Drug Product Name	Donidalorsen Injection
Dosage Form	Injection
Strength	80 mg/0.8 mL
Route of Administration	Subcutaneous injection
Rx/OTC Dispensed	Rx
Applicant	Ionis Pharmaceuticals, Inc.
US agent, if applicable	N/A

Submission(s) Assessed	Document Date	Discipline(s) Affected
Original (SD-1)	21-Aug-2024	All
Amendment (SD-2)	12-Sep-2024	Drug product (labeling)
Amendment (SD-4)	23-Sep-2024	Manufacturing/facilities, CDRH
Amendment (SD-7)	11-Oct-2024	Drug product
Amendment (SD-9)	30-Oct-2024	Microbiology
Amendment (SD-16)	26-Dec-2024	Manufacturing/facilities
Amendment (SD-23)	28-Feb-2025	CDRH
Amendment (SD-24)	14-Mar-2025	Drug product
Amendment (SD-25)	17-Mar-2025	Drug product
Amendment (SD-26)	11-Apr-2025	Drug product (labeling)
Amendment (SD-27)	16-Apr-2025	Manufacturing/facilities
Amendment (SD-30)	24-Apr-2025	Microbiology

QUALITY ASSESSMENT TEAM

Discipline	Primary Assessor	Secondary Assessor
Drug Substance	Brian Cawrse	Lawrence Perez (Donna Christner)
Drug Product	Ghaled Hamad	Craig M. Bertha

Manufacturing	Chaoying Ma	Shujun Chen
Microbiology	Catherine Gilbert	Yan Zheng
Biopharmaceutics	N/A	
Regulatory Business Process Manager	Emma Gimose	
Application Technical Lead	Craig M. Bertha	
Laboratory (OTR)	N/A	
Environmental	Ghaled Hamad	Craig M. Bertha

Table of Content Links

QUALITY ASSESSMENT DATA SHEET

1. RELATED/SUPPORTING DOCUMENTS

A. DMFs:

DMF #	Type	Holder	Item Referenced	Status	Date Assessment Completed	Comments
(b) (4)	III		(b) (4)	Adequate	N/A	Sufficient information provided in the NDA
	III			Adequate	N/A	Sufficient information provided in the NDA
	III			Adequate	N/A	Sufficient information provided in the NDA
	III			Adequate	N/A	Sufficient information provided in the NDA
	III			Adequate	N/A	Sufficient information provided in the NDA
	III			Adequate	N/A	Sufficient information provided in the NDA

B. OTHER DOCUMENTS: *IND, RLD, RS, Approved NDA*

Document	Application Number	Description

2. CONSULTS

Discipline	Status	Recommendation	Date	Assessor
Biostatistics				
Pharmacology/ Toxicology				

CDRH	Complete	**Approvable**	06-Nov-2024 &11-Apr-2025	Tiffani C. Chance & Shruti N. Mistry
Clinical				
Other				

Title:	NDA IQA Template Title Page- EXEC SUMMARY
Document ID:	OPQ-ALL-TEM-0040
Effective Date:	26 Sep 2023 Revision: 00
Total Pages:	8

Template Revision: 03

Office of Pharmaceutical Quality

New Drug Application (NDA) 219407
Integrated Quality Assessment (IQA)

NDA Executive Summary

1. Application/Product Information

NDA Number	219407		
Applicant Name	Ionis Pharmaceuticals, Inc.		
Drug Product Name	Donidalorsen Injection		
Dosage Form	Injection		
Proposed Strength(s)	80 mg/0.8 mL		
NDA Classification	Type 1 - NME		
Route of Administration	Subcutaneous		
Maximum Daily Dose	(b) (4)		
Rx/OTC Dispensed	Rx		
Proposed Indication	Indicated for prophylaxis to prevent attacks of hereditary angioedema (HAE) in adult and pediatric patients 12 years of age and older		
Drug Product Description	Donidalorsen is an *N*-acetyl galactosamine (GalNAc)-conjugated antisense oligonucleotide that is formulated as a sterile solution for subcutaneous injection via an autoinjector (AI) device (i.e., a drug/device combination product).		
Co-packaged product information	N/A		
Device information	The applicant states that the device is a platform AI called (b) (4). This device is said to be FDA approved as part of other combination products from various applicants.		
Storage Temperature/ Conditions	Store refrigerated 2ºC - 8ºC (36ºF - 46ºF); product can be stored at room temperature up to 30°C (86°F) for up to six weeks		
Review Team	**Discipline**	**Primary**	**Secondary**

	Drug Substance	Brian Cawrse	Lawrence Perez (Donna Christner)
	Drug Product/ Labeling	Ghaled Hamad	Craig M. Bertha
	Manufacturing	Chaoying Ma	Shujun Chen
	Biopharmaceutics	N/A	
	Microbiology	Catherine Gilbert	Yan Zheng
	Other (specify)	N/A	
	RBPM	Emma Gimose	
	ATL	Craig M. Bertha	
Consults	CDRH for technical engineering/device design		

2. Final Overall Recommendation - Approval

3. Action Letter Information

a. Expiration Dating: 30 months

b. Additional Comments for Action: N/A

4. Basis for Recommendation:

a. Summary of Rationale for Recommendation:

All deficiencies identified during the review have been addressed satisfactorily by the applicant.

b. Is the overall recommendation in agreement with the individual discipline recommendations? Yes

Recommendation by Subdiscipline:

Drug Substance - Adequate
Drug Product - Adequate
Quality Labeling - Pending[1]
Manufacturing - Adequate
Biopharmaceutics - N/A

[1]The labeling review decision is pending for this IQA due to ongoing negotiations with the applicant. There are only minor labeling deficiencies from the CMC perspective and we expect the applicant will accept our recommendations. Refer to the CMC sections of the final approved labeling.

Microbiology - Adequate

Environmental Assessment: Categorical Exclusion - Adequate
QPA for EA(s): No

5. Life-Cycle Considerations
Established Conditions per ICH Q12: No
Comments: N/A

Comparability Protocols (PACMP): No
Comments: N/A

Additional Lifecycle Comments:
N/A

Integrated Assessment of Marketing Applications – CMC Summary

Drug Substance

Donidalorsen sodium drug substance is a chimeric 2′-O-methoxyethyl-modified antisense oligonucleotide (ASO) that is covalently bonded to a *N*-acetylgalactosamine (GalNAc) moiety. GalNAc is a ligand for the hepatocyte-specific asialoglycoprotein receptor. The donidalorsen sequence is:

5′-THA-AH$_o$^{Me}U$_s$G$_s$^{Me}C$_o$A$_o$A$_s$G$_s$T$_s$^{Me}C$_s$T$_s$^{Me}C$_s$T$_s$T$_s$G$_s$G$_s$^{Me}C$_s$A$_o$A$_o$A$_s$^{Me}C$_s$A-3′

Where:

- Underlined residues are 2′-O-(2-methoxyethyl) nucleosides (MOE)
- All other residues are 2′-deoxynucleosides
- The locations of phosphorothioate and phosphate diester linkages are designated by subscripted S and O, respectively
- AH designates the position of the aminohexyl linker
- THA is 5-[(tris{3-[6-(2-acetamido-2-deoxy-β-D-galactopyranosyloxy)hexylamino]-3-oxopropoxymethyl})methyl]-amino-5-oxopentanoyl

The drug substance is synthesized through (b) (4) [redacted]

The starting materials for the manufacture of donidalorsen are (b) (4) [redacted] and these materials are adequately justified and are acceptable based on the principles in ICH Q11. Proven acceptable ranges have been established for the critical process parameters (CPPs) which ensure the quality of the drug substance.

The drug substance structure has been characterized by proton, carbon, and phosphorous nuclear magnetic resonance spectroscopy, mass spectrometry, and failure sequence analysis.

The drug substance is an (b) (4) [redacted] solid and is freely soluble in water at physiological pH.

The application included sufficient information about the structures, origins, fates, and control strategies for the oligonucleotide-related impurities and these have been quantified and qualified in groups based on their structures and mechanisms of

formation, which is acceptable considering the complexities of characterizing oligonucleotide impurities and with the expectation that impurities with similar structural changes will have similar toxicity profiles. The specified impurities of the drug substance were qualified through toxicology studies. No ICH Q3C Class 1 solvents are used in the manufacture and there are no genotoxic or (b) (4) impurities in the drug substance.

The drug substance specification includes tests and acceptance criteria to ensure the identity, purity, strength, and quality of the drug substance. The non-compendial analytical methods are sufficiently described and validated and are appropriate for their intended uses for quality control. Analyses data provided were compliant with the specification.

The drug substance is stored (b) (4) The retest period for the drug substance granted is (b) (4) months (long-term storage conditions of (b) (4) °C) which is supported by long-term stability results from both primary stability batches (12-month data available) and supporting stability batches (60-month data available).

Product

Donidalorsen injection product is a sterile, single-dose, ready-to-use parenteral solution containing an antisense oligonucleotide (ASO) in pre-filled syringe within an autoinjector device. The drug/device combination product is intended for subcutaneous injection by the patient or caregiver at home and is indicated for the prophylaxis of hereditary angioedema (HAE) attacks in adult and pediatric patients aged 12 years and older. Donidalorsen, an ASO, reduces the production of prekallikrein (PKK) protein. Each product unit contains 80 mg/0.8 mL of donidalorsen drug. The labeling recommends a starting dose for patients aged 12 years and older of 80 mg donidalorsen (b) (4) (equivalent to 84 mg of donidalorsen sodium), although a dosing interval of 80 mg (b) (4) (b) (4) may also be appropriate for some patients.

All excipients in the product are of USP/NF grade and in quantities that do not exceed the maximum daily amounts approved for other injection drug products or products, according to the Inactive Ingredient Report. None of the excipients are novel and none are derived from animal sources.

The product is manufactured through a process involving several key steps: (b) (4) The manufacturing process is based on prior knowledge for similar approved products from the same applicant with similar oligonucleotide-based drugs.

The specification for the product is aligned with the relevant guidances (ICH Q6A and Q3B) and the acceptance criteria are adequate with respect to the batch release and stability data in the application. The non-compendial analytical methods and associated

validation reports have been evaluated and the methods are deemed suitable for regulatory purposes.

The primary container closure system (CCS) for the product consists of a 1 mL staked needle syringe barrel and a plunger stopper. The filled primary container is assembled into an autoinjector and packaged in an opaque carton (donidalorsen is photolabile). The autoinjector is based on the (b) (4) autoinjector. This autoinjector platform has been used as part of other approved combination products. Refer to the CDRH consult review for a review of the (b) (4) autoinjector/device from an engineering/device perspective.

The applicant submitted product analysis data for three batches (CP721744-004-AI-A, CP721744-005-AI-B, and CP721744-006-AI-A) and these batches were used for clinical, registration stability, and bioequivalence studies. All batches were manufactured using the proposed commercial manufacturing process (Section 3.2.P.3.3) and they all met the specification acceptance criteria.

Stability studies were conducted to evaluate the product at long-term (2-8°C) and accelerated (25°C/60%RH) storage conditions. Registration stability studies are ongoing for product batches CP721744-004-AI-A, CP721744-005-AI-B, and CP721744-006-AI-A. Based on the long-term and accelerated stability data available, an **expiration dating period of 30 months is granted when stored in the proposed container closure system (CCS) and carton at 2-8°C (36°F to 46°F).** Data have also shown that the product may also be stored at room temperature (up to 86°F or 30°C) in the original carton for up to 6 weeks.

Manufacturing/Facilities

The product manufacturing process consists of (b) (4) The next unit operation includes the autoinjector assembly process, and final QC testing and release of the autoinjector packaged in a secondary packaging. The proposed critical process parameters, in-process controls, as well as overall control strategy for the commercial manufacturing of the product are supported by the registration batch data.

The production of the bulk PFS and assembly of the autoinjector occur at a (b) (4) Bulk PFS batches for registration stability were manufactured using the (b) (4) the commercial batch size ((b) (4) L for registration stability batches vs. (b) (4) L for commercial batches).

Fifteen facilities are used to produce the product and all are found to be adequate with the exception of the two (b) (4) facilities responsible for secondary packaging and labeling, as these did not require evaluation.

Microbiology

Donidalorsen injection is sterilized by (b) (4) The syringes and the rubber stoppers are purchased ready to use.

Conclusion

Based on the recommendations of the CMC review team, the application is recommended for approval.[1]

Application Technical Lead Name and Date:

Craig M. Bertha, CMC Reviewer, 30-Apr-2025

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Template Revision: 03

CHAPTER VII: MICROBIOLOGY

For more details about the items in this template, please see Chapter VII (Microbiology) of the NDA IQA Guide (OPQ-ALL-WI-0006)

Product Information	
NDA Number	219407
Assessment Cycle Number	01
Drug Product Name/ Strength	Donidalorsen (Dawnzera)
Route of Administration	Subcutaneous Injection
Applicant Name	Ionis Pharmaceticals, Inc.
Therapeutic Classification/ OND Division	DROII
Manufacturing Site	DP PFS Manufacturing: (b) (4)
Method of Sterilization	

Assessment Recommendation: **Adequate**

Assessment Summary: The drug product is (b) (4) (b) (4) (b) (4) (b) (4). The glass syringes and rubber stoppers are purchased RTU.

List Submissions Being Assessed (table):

Document(s) Assessed	Date Received
Original (0001)	08/21/2024
Labeling IR Response (0002)	09/12/2024
Facilities IR Response (0004)	09/23/2024
IR Response (0009)	10/30/2024
DP IR Response (0016)	12/26/2024
DP IR Response (0025)	03/17/2025
IR Response (00030)	04/24/2025

Highlight Key Issues from Last Cycle and Their Resolution: No previous quality microbiology IND or meeting package reviews could be located for this product. Validation and method suitability data were requested in the Microbiology Filing Review for this NDA.

Remarks: This is an eCTD submission.

Concise Description of Outstanding Issues *(list bullet points with key information and update as needed)*: N/A

Supporting Documents:

- N NON-RESPONSIVE MR01.doc dated 05/04/2023 for the EM program and actions taken upon (b) (4)
- N (b) (4) MR01.pdf dated 09/03/2024 for (b) (4) validation
- DMF (b) (4)
  - D (b) (4) M11R01.docx, dated 04/13/2022 for validation data
  - D (b) (4) M12R01 dated 07/05/2024 for recent dose audit data
- DMF (b) (4)
  - D (b) (4) M30R01.doc dated 07/25/2024 for recent RQ data
  - D (b) (4) M32R01.doc dated 02/07/2025 for recent RQ data
- D (b) (4) M107R01.doc dated 06/04/2024 for recent RQ data
- D (b) (4) M42R01.doc dated 03/24/2023 for recent RQ data
- DMF (b) (4)
  - D (b) (4) M14R01.doc dated 03/08/2024 for recent RQ data
  - D (b) (4) M16R01.doc dated 03/25/2025 for recent RQ data
- N (b) (4) MR01.pdf dated 09/03/2024 for media fill data

S DRUG SUBSTANCE – N/A, the drug product is (b) (4).

P.1 DESCRIPTION OF THE COMPOSITION OF THE DRUG PRODUCT

- **Description of drug product –** Donidalorsen, 100 mg/mL, is a sterile, pyrogen-free, clear solution indicated for prophylaxis to prevent attacks of hereditary angioedema (HAE). It is administered via subcutaneous injection.
- **Drug product composition –**

Ingredient	Content (%w/w)	Function
Donidalorsen	9.55%	API
Sodium dihydrogen phosphate (b) (4)	(b) (4)	
Disodium hydrogen phosphate (b) (4)		
NaCl		
HCl	q.s.	pH adjustment
NaOH	q.s.	pH adjustment
WFI	q.s. to 100%	Solvent

- **Description of container closure system –**

Component	Packaging	Description (Gland material code)	Manufacturer
PFS	Primary	(b) (4) 1 mL long PFS with 0.5 inch 27G (b) (4) staked needle syringe and RNS	(b) (4)
Stopper	Primary	(b) (4) plunger stopper	
Autoinjector	Secondary	(b) (4) Autoinjector	

Figure 1: Donidalorsen Autoinjector

(b) (4)

(Section 3.2.R: Regional Information pg. 3, 7)

Assessment: *Adequate*

The applicant has adequately described the drug product composition and the container closure system designed to maintain product sterility.

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Yan Zheng

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Catherine Gilbert

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Date: 4/30/2025 09:58:22AM
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CHAPTER IV: LABELING

For more details about the items in this template, please see Chapter IV (Labeling) of the NDA IQA Guide (OPQ-ALL-WI-0006)

NDA Number	NDA 219407
Assessment Cycle Number	1
Drug Product Name	Dawnzera (donidalorsen) injection, 80 mg/0.8 mL

Assessment Recommendation: Inadequate

Item	Assessment Conclusion	SDN # where labeling is adequate ("N/A" otherwise)
Prescribing Information Labeling	Inadequate	
Patient Information	Inadequate	
Instruction for Use (IFU)	Adequate	
Container Labels	Inadequate	
Carton Labeling	Inadequate	

Brief Description of Outstanding Issues:

Submissions being reviewed:

Document Reviewed (eCTD #, SDN #)	Date Received	Information Provided
0001	08/21/2024	IFU, Carton, and Container labeling
0002	09/12/2024	Prescribing and patient information

1.0 PRESCRIBING INFORMATION[1]

Assessment of Product Quality Related Aspects of the Prescribing Information:

[1] Labeling Review Tool (LRT) (March 2022), including use of consistent terminology for dosage form and unit of measure for strength in the product title and DOSAGE FORMS AND STRENGTHS heading in Highlights, in the DOSAGE AND ADMINISTRATION, DOSAGE FORMS AND STRENGTHS, DESCRIPTION, and HOW SUPPLIED/STORAGE AND HANDLING sections (see page 2 of LRT)

(b) (4)

1.1 HIGHLIGHTS OF PRESCRIBING INFORMATION

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
Product Title in Highlights[2] [21 CFR 201.57(a)(2)]		
Established name(s)[3]	Adequate	
Route(s) of administration	Adequate	
Controlled drug substance symbol (if applicable)	N/A	
Initial U.S. Approval [§201.57(a)(3)]	Inadequate	§201.57(a)(3) requires the actual four-digit year of initial U.S. approval. "YYYY" is a placeholder, not a year. The applicant must replace "YYYY" with the correct four-digit year of the drug's initial U.S. approval.
Dosage Forms and Strengths Heading in Highlights [§ 201.57(a)(8)]		
Dosage form(s)[4] and strength(s) in metric system[5]	Adequate	

[2] Draft guidance: *Product Title and Initial U.S. Approval in the Highlights of Prescribing Information for Human Prescription Drug and Biological Products — Content and Format* (January 2018)
[3] Established name = [Drug] [Route of Administration] [Dosage Form]. Do use not "USP" descriptor in the product title or within the Highlights (see page 3 of LRT).
[4] Draft guidance: *Product Title and Initial U.S. Approval in the Highlights of Prescribing Information for Human Prescription Drug and Biological Products — Content and Format* (January 2018); USP <1151>; USP Nomenclature Guideline
[5] Labeling Review Tool (March 2022, page 13), include limited packaging information; USP <7>

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
If the drug product contains an active ingredient that is a salt, clearly state whether the strength is based on the active moiety (e.g., Tablets: 10 mg of drug-x) or active ingredient (e.g., Tablets: 10 mg of drug-x hydrochloride).[6]	Adequate	
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored."[7]	N/A	
For injectable drug products for parenteral administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package terms include pharmacy bulk package and imaging bulk package.[8]	Adequate	

Assessment: *Inadequate*

[6] Guidance: *Naming of Drug Products Containing Salt Drug Substances* (June 2015); MAPP 5021.1
[7] Guidance: *Tablet Scoring: Nomenclature, Labeling, and Data for Evaluation* (March 2013)
[8] Guidance: *Selection of the Appropriate Package Type Terms and Recommendations for Labeling Injectable Medical Products Packaged in Multiple-Dose, Single-Dose, and Single-Patient-Use Containers for Human Use* (October 2018); USP <659>

1.2 FULL PRESCRIBING INFORMATION

1.2.1 Section 2 (DOSAGE AND ADMINISTRATION)[9]

(b) (4)

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage

(b) (4)

Missed Dose

Administer DAWNZERA as soon as possible (b) (4). Resume (b) (4) dosing frequency from the date of the most recently administered dose.

2.2 Administration Instructions

Prior to treatment initiation, train patients and/or caregivers on proper preparation and administration 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 as a subcutaneous injection 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.

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
DOSAGE AND ADMINISTRATION section		

[9] See § 201.57(c)(3); draft guidance: *Dosage and Administration Section of Labeling for Human Prescription Drug and Biological Products — Content and Format* (January 2023); Labeling Review Tool (March 2022, page 25)

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
Special instructions for product preparation (e.g., reconstitution and resulting concentration, dilution, compatible diluents and/or soft food[10], storage conditions needed to maintain the stability of the reconstituted or diluted product).	N/A	
Important administration instructions supported by product quality information (e.g., do not crush or chew extended-release tablets, instructions for mixing with food).	Adequate	
For parenteral products: include statement: *"Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit."*[11]	Adequate	
If there is a USP monograph for the drug product and it contains a labeling requirement, ensure the labeling requirement is fulfilled.[12] Note the labeling requirement may be applicable to another section of the PI (e.g., Section 11).	N/A	
For radioactive products, include radiation dosimetry for the patient and healthcare practitioner(s) who administer the drug	N/A	
For hazardous products, include the statement *"DRUG X is a hazardous drug. Follow applicable special handling and*	N/A	

[10] Draft Guidance: Use of Liquids and/or Soft Foods as Vehicles for Drug Administration: General Considerations for Selection and In Vitro Methods for Product Quality Assessments
[11] §201.57(c)(3)(iv)
[12] USP General Notices 2.30 Legal Recognition

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
disposal procedures.[x]" with x numerical citation to "OSHA Hazardous Drugs."		

Assessment: *Adequate*

1.2.2 Section 3 (DOSAGE FORMS AND STRENGTHS)[13]

(b) (4)

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.

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
DOSAGE FORMS AND STRENGTHS section		
Available dosage form(s)	Adequate	
Strength(s) in metric system	Adequate	
If the active ingredient is a salt, apply the USP Salt Policy per FDA Guidance. Clearly state whether the strength is based on the active moiety (e.g., Tablets: 10 mg of drug-x) or active ingredient (e.g., Tablets: 10 mg of drug-x hydrochloride). No equivalency statement.	Inadequate	Include an equivalency statemen: 80 mg of donidalorsen (equivalent to 84 mg donidalorsen sodium).
A description of the identifying characteristics of the dosage forms, including shape, color, coating, scoring, imprinting, and color and clarity of the solution, when applicable.	Adequate	

[13] See § 201.57(c)(4); Labeling Review Tool (March 2022, page 29)

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored."	N/A	
For injectable drug products for parenteral administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package type terms include pharmacy bulk package and imaging bulk package (see USP <659>).	Adequate	

Assessment: *Inadequate*

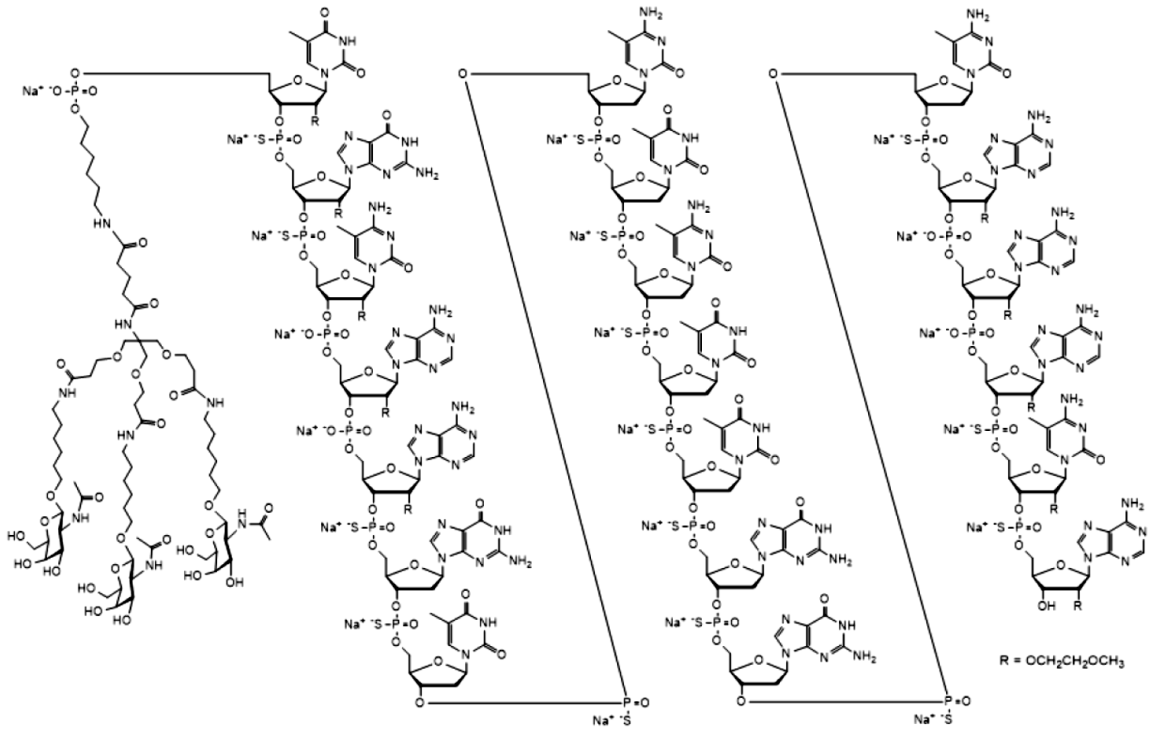
1.2.3 Section 11 (DESCRIPTION)[14]

Donidalorsen is an antisense oligonucleotide (ASO) (b) (4)

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)]m^{5}rU-s^p-[2′-*O*-(2-methoxyethyl)]rG-s^p-[2′-*O*-(2-methoxyethyl)]m^{5}rC-[2′-*O*-(2-methoxyethyl)]rA-[2′-*O*-(2-methoxyethyl)]rA-s^p-G-s^p-T-s^p-m^{5}C-s^p-T-s^p-m^{5}C-s^p-T-s^p-T-s^p-G-s^p-G-s^p-m^{5}C-s^p-[2′-*O*-(2-methoxyethyl)]rA-[2′-*O*-(2-methoxyethyl)]rA-[2′-*O*-(2-methoxyethyl)]rA-s^p-[2′-*O*-(2-methoxyethyl)]m^{5}rC-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:

[14] See § 201.57(c)(12); Labeling Review Tool (March 2022, page 56)



DAWNZERA is a sterile, preservative-free solution for subcutaneous injection. 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 water for injection; sodium dihydrogen phosphate; disodium hydrogen phosphate; and sodium chloride 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.

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
DESCRIPTION section		
Proprietary and established name(s)[15] [§ 201.57(c)(12)(i)(A)].	Adequate	Proprietary name: Deferred to DMEPA.
Dosage form(s) and route(s) of administration [§ 201.57(c)(12)(i)(B)].	Adequate	
If the active ingredient is a salt, apply the USP Salt Policy and	Adequate	

[15] Use of "USP" descriptor is not required to be included next to the established name throughout Prescribing Information (PI) labeling. If an applicant wants to use the "USP" descriptor next to the established name in the PI, recommend limiting its use to the product quality sections of the Full Prescribing Information (FPI) (i.e., DOSAGE FORMS AND STRENGTHS, DESCRIPTION, HOW SUPPLIED/STORAGE AND HANDLING) (see page 3 of LRT).

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
include the equivalency statement per Salt Guidance and MAPP. For example: "TRADENAME contains 100 mg of drug-x (equivalent to 123.7 mg of drug-x hydrochloride)" [§ 201.57(c)(12)(i)(C)].		
List inactive ingredients (not required for oral use, except for colorant) by the USP/NF names in alphabetical order.[16] Avoid brand names. [§ 201.57(c)(12)(i)(C)].	Inadequate	The listing of inactive ingredients in the DAWNZERA product description does not follow strict alphabetical order. To ensure clarity and consistency, revise the labeling to present the inactive ingredients in the following alphabetical sequence: disodium hydrogen phosphate; hydrochloric acid and/or sodium hydroxide (for pH adjustment); sodium chloride; sodium dihydrogen phosphate; water for injection. Note: The phrase "hydrochloric acid and/or sodium hydroxide for pH adjustment" can be placed together in the alphabetized list, as it describes one function.
For parenteral injectable dosage forms, include the name and quantities of all inactive ingredients. For ingredients added to adjust the pH or make isotonic, include the name and statement of effect. [§ 201.100(b)(5)(iii)].	Inadequate	The listing of inactive ingredients in the DAWNZERA product description does not follow strict alphabetical order, and it omits the required quantities for each ingredient. To ensure clarity, consistency, and compliance with 21 CFR 201.100(b)(5)(iii), revise the labeling to present the inactive ingredients in the following alphabetical sequence, including the quantity of each

[16] Per § 201.100(b)(5)(i) and (ii), flavoring and colorants may be designated as such without naming their components except for FD&C Yellow No 5 and FD&C Yellow No 6, which must be listed per § 201.20. Per § 201.100(b)(5)(iii), trace amounts of harmless substances added solely for individual product identification need not be named. If an applicant wants to use the National Formulary (NF) descriptor next to excipients, recommend limiting its use to the product quality sections of the FPI (see page 3 of LRT). Do not list brand names, e.g., Opadry, Eudragit, Polistirex, etc.

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
		ingredient: disodium hydrogen phosphate; hydrochloric acid and/or sodium hydroxide (for pH adjustment); sodium chloride; sodium dihydrogen phosphate; water for injection.
If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol at 60 °F. (15.56 °C) [§ 201.10(d)(2)].	N/A	
Sterility statement (if applicable) [§ 201.57(c)(12)(i)(D)].	Adequate	
Pharmacological/Therapeutic class[17] [§ 201.57(c)(12)(i)(E)].	Adequate	
Chemical name[18], structural formula, molecular weight [§ 201.57(c)(12)(i)(F)].	Adequate	
If radioactive, statement of important nuclear characteristics [§ 201.57(c)(12)(i)(G)].	N/A	
Other important chemical or physical properties (such as pKa or pH) [201.57(c)(12)(ii)].	Adequate	
For oral prescription drug products, include gluten statement[19] (if applicable).	N/A	
Remove statements that may be misleading or promotional (e.g., "synthesized and developed by Drug Company X," "structurally unique molecular entity").	Adequate	
If there is a USP monograph for the drug product and it contains a labeling requirement, ensure the labeling requirement is	N/A	

[17] Listed before "indicated for" in INDICATIONS AND USAGE of Highlights section [§ 201.57(a)(6)]; can also search the term "FDA EPC Text Phrases" in FDA's Labeling Resources for Human Prescription Drugs for the most recent EPC list.

[18] Chemical names do not need to be capitalized unless it appears at the beginning of a sentence (see *Preferred IUPAC Names Provisional Recommendation*, September 2004; Chapter 1, par. 16 Name writing, p.80-90).

[19] Draft guidance: *Gluten in Drug Products and Associated Labeling Recommendations* (December 2017)

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
fulfilled. Note the labeling requirement may be applicable to another section of the PI (e.g., Section 2).		

Assessment: *Inadequate*

1.2.4 Section 16 (HOW SUPPLIED/STORAGE AND HANDLING)[20]

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

DAWNZERA 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.

DAWNZERA is supplied in a carton containing one 80 mg single-dose autoinjector.

The NDC is: 71860-103-01.

16.2 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 light.

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
HOW SUPPLIED/STORAGE AND HANDLING section		
Available dosage form(s) [§ 201.57(c)(17)].	Adequate	

[20] See § 201.57(c)(17); Labeling Review Tool (March 2022, page 70). Consider including proprietary name and established name.

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
Strength(s) in metric system. [§ 201.57(c)(17)(i)] If the active ingredient is a salt, apply the USP Salt Policy per FDA Guidance. Clearly state whether the strength is based on the active moiety. No equivalency statement.	Adequate	
Available units (e.g., bottles of 100 tablets) [§ 201.57(c)(17)(ii)].	Adequate	
Identification of dosage forms (e.g., shape, color, coating, scoring, imprinting, and color and clarity of the solution, when applicable); Include NDC(s) [§ 201.57(c)(17)(iii)].	Adequate	
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored."	N/A	
For injectable drug products for parenteral administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package terms include pharmacy bulk package and imaging bulk package (see USP <659>).	Adequate	
Special handling about the supplied product (e.g., protect from light, refrigerate). If there is a statement to "Dispense in original container," provide reason why (e.g., to protect from light or moisture, to maintain stability, etc.). For hazardous drugs, state "DRUG X is a hazardous drug. Follow applicable special handling and disposal procedures.[x]" with x numerical citation to "OSHA Hazardous Drugs." [§ 201.57(c)(17)(iv)]	Adequate	

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
Storage conditions. Where applicable, use USP storage range rather than storage at a single temperature. (see USP <659>).	Adequate	
Latex: If product does not contain latex and manufacturing of product and container did not include use of natural rubber latex or synthetic derivatives of natural rubber latex, state: *"Not made with natural rubber latex. Avoid statements such as "latex-free."*[21]	Inadequate	Not provided.
Include information about child-resistant packaging[22] (if chosen by manufacturer).	N/A	

Assessment: *Inadequate*

1.2.5 Other Sections of Labeling

-None

[21] Guidance: *Recommendations for Labeling Medical Products to Inform Users that the Product or Product Container is not Made with Natural Rubber Latex* (December 2014)
[22] Guidance: *Child-Resistant Packaging Statements in Drug Product Labeling* (August 2019)

1.2.6 Manufacturing Information After Section 17 (for drug products)[23]

Item	Item in Proposed Labeling (choose "Adequate" or "Inadequate")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
Manufacturing Information After Section 17		
Name and location of business (street address, city, state, and zip code) of the manufacturer, distributor, and/or packer.	Adequate	

Assessment: *Adequate*

2.0 PATIENT LABELING

Assessment of Product Quality Related Aspects of Patient Labeling (e.g., Medication Guides, Instructions for Use, Patient Information):

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments about Labeling (If an item is Inadequate, provide more details on the issues, as appropriate)
Established name[24]	Inadequate	The route of administration is not included. The dosage form is not included.
Special preparation instructions (if applicable).	N/A	
Storage and handling information (if applicable).	Adequate	
If the product contains a desiccant, ensure the desiccant has a warning (e.g., "Do not eat.") and the size and shape of the desiccant differ from the dosage form.	N/A	
Active ingredient(s) (if applicable).	Adequate	
Alphabetical listing of inactive ingredients (if applicable).	Inadequate	The inactive ingredients do not follow strict alphabetical order.
Name and location of business (street address, city, state, and	Adequate	

[23] § 201.1(h)(5) and 201.1(i); Labeling Review Tool (March 2022, page 74)
[24] Established name = [Drug] [Route of Administration] [Dosage Form]

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments about Labeling (If an item is Inadequate, provide more details on the issues, as appropriate)
zip code) of manufacturer, distributor, and/or packer.		

Assessment: *Inadequate*

3.0 CONTAINER AND CARTON LABELING[25]

2 Page(s) of Draft Labeling have been Withheld in Full as B4 (CCI/TS) immediately following this page

[25] Carton and Container Labeling Resources

Item	Item in Proposed Carton Labeling (choose "Adequate", "Inadequate", or "N/A")	Is item in Container Labels same as that of Carton Labeling?	Assessor's Comments about Container Labels and Carton Labeling (If an item is Inadequate or different, provide more details, as appropriate)
Proprietary name and established name[27], (font size and prominence) [§ 201.10(g)(2)].	Adequate	Yes	
Strength(s) in metric system [§ 201.100(b)(4) & 201.100(d)].[28]	Adequate	Yes	
Route(s) of administration, not required for oral use [§ 201.100(b)(3)].	Adequate	Yes	
If the active ingredient is a salt, include the equivalency statement per Salt Guidance and MAPP [§ 201.10(d)(1) & 201.100(b)(4), USP <1121>].	Adequate	Yes	
Net contents (e.g., tablet count, volume of liquid) [§ 201.51(a)].[29]	Adequate	Choose an item.	NO
"Rx only" displayed on the principal display [§ 201.100(b)(1)].	Inadequate	No	The 'Rx only' designation is not present on the principal display panel of the carton labeling. However, it is present on the container labeling.
NDC (requested, but not required for all labels or labeling) [§ 201.2 & 207.35].	Adequate	Yes	For improved clarity and accessibility, the NDC number should be moved from the side panel to the Principal Display Panel (PDP) and placed above the proprietary name.

[27] Established name = [Drug] [Route of Administration] [Dosage Form]

[28] Express as " XX mg per tablet" or "XX mg per capsule" for strength of professional samples of solid oral dosage form with small net quantities per container (e.g., 5 or less) or blister pack/carton. See Guidance: *Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors* (May 2022)

[29] § 201.51(h): A drug shall be exempt from compliance with the net quantity declaration required by this section if it is an ointment labeled "sample", "physician's sample", or a substantially similar statement and the contents of the package do not exceed 8 grams.

Item	Item in Proposed Carton Labeling (choose "Adequate", "Inadequate", or "N/A")	Is item in Container Labels same as that of Carton Labeling?	Assessor's Comments about Container Labels and Carton Labeling (If an item is Inadequate or different, provide more details, as appropriate)
Lot number and expiration date [§ 201.18 & 201.17].	Inadequate	No	Neither the lot number nor the expiration date placeholder is present on the carton label. Per USP General Chapter <7>, include an expiration date placeholder on all packaging. Use the specified date formats (YYYY-MM-DD, YYYY-MM, YYYY-MMM-DD, or YYYY-MMM). Avoid placing other numbers near the expiration date. Clearly define the chosen format.
Storage conditions. If applicable, include a space on the carton labeling for the user to write the beyond-use-date (BUD).	Adequate	No	**Carton:** Store refrigerated at 2°C to 8°C (36°F to 46°F) in the original container and protect from direct light. **Container:** Store refrigerated at 2°C to 8°C (36°F to 46°F) in the original container. We recommend revising this sentence to read, "Store refrigerated at 2°C to 8°C (36°F to 46°F) in the original carton and protect from direct light" on the container label for consistency with the carton labeling.
For injectable drug products for parenteral administration, use appropriate package type term (e.g., single-dose,	Adequate	No	The package type term 'single dose' is not included in the container labeling.

Item	Item in Proposed Carton Labeling (choose "Adequate", "Inadequate", or "N/A")	Is item in Container Labels same as that of Carton Labeling?	Assessor's Comments about Container Labels and Carton Labeling (If an item is Inadequate or different, provide more details, as appropriate)
multiple-dose, single-patient-use). Other package terms include pharmacy bulk package and imaging bulk package, and these products require a "Not for direct infusion" statement. (See USP <659>).			
Name of all inactive ingredients, in alphabetical order [§ 201.10(a)] [except for oral drug per § 201.100(b)(5) or limited space per § 201.10(i)(2)].	Inadequate	No	The carton labeling does not list the inactive ingredients in alphabetical order.
For parenteral injectable dosage forms, include quantities of all inactive ingredients. For ingredients added to adjust the pH or make isotonic, include the name and statement of effect. [§ 201.100(b)(5)(iii)].	Inadequate	No	Carton labeling lacks the quantities of inactive ingredients.
If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol at 60 °F. (15.56 °C) [§ 201.10(d)(2)].	N/A	Yes	
Linear Bar code [§ 201.25(c)(2)].[30]	Adequate	Yes	
Adequate directions for use: "Recommended Dosage: See Prescribing Information" [§ 201.5 & 201.55].	Adequate	No	
Name of manufacturer/distributor /packer [§ 201.1(a), 201.1(h)(5)].	Adequate	Yes	

[30] See § 201.25(b)(1)(i) for a list where bar code is not required, e.g., prescription drug samples, medical gases, radiopharmaceuticals, etc.

Item	Item in Proposed Carton Labeling (choose "Adequate", "Inadequate", or "N/A")	Is item in Container Labels same as that of Carton Labeling?	Assessor's Comments about Container Labels and Carton Labeling (If an item is Inadequate or different, provide more details, as appropriate)
"Keep out of reach of children" statement, optional for Rx, required for OTC [§ 201.66(c)(5)(x)].	Adequate	No	
If there is a Medication Guide, must include a statement about dispensing a Medication Guide to each patient.	Adequate	Yes	
No text on Ferrule and Cap overseal of a vial of injectable products unless a cautionary statement is required. (USP <7>).	N/A	Choose an item.	
If there is a USP monograph for the drug product and it contains a labeling requirement, ensure the labeling requirement is fulfilled.	N/A	Choose an item.	
When a drug product differs from the relevant USP standard of strength, quality, or purity, as determined by the application of the tests, procedures, and acceptance criteria set forth in the relevant compendium, its difference shall be plainly stated on its label.[31]	N/A	Choose an item.	
And others if space is available.	N/A	Choose an item.	

Assessment of Carton Labels and Container Labeling: *Inadequate*

[31] USP General Notices 3.20 Indicating Conformance

4. OUTSTANDING ISSUES AND RECOMMENDATIONS

- §201.57(a)(3) requires the actual four-digit year of initial U.S. approval. "YYYY" is a placeholder, not a year. The applicant must replace "YYYY" with the correct four-digit year of the drug's initial U.S. approval.
- The dosage forms and strengths section does not include the following equivalency statement: “80 mg of donidalorsen (equivalent to 84 mg donidalorsen sodium)”.
- The listing of inactive ingredients in the DAWNZERA product description and carton labeling do not follow strict alphabetical order, and it omits the required quantities for each ingredient.
- Latex: If product does not contain latex and manufacturing of product and container did not include use of natural rubber latex or synthetic derivatives of natural rubber latex, state: “Not made with natural rubber latex. Avoid statements such as “latex-free.”
- In the patient information labeling, the established name is missing the route of administration. The dosage form is also not included.
- The 'Rx only' designation is missing from the principal display panel of the carton labeling; it is only present on the side panel.
- For improved clarity and accessibility, the NDC number should be moved from the side panel to the Principal Display Panel (PDP) and placed above the proprietary name.
- Neither the lot number nor the expiration date placeholder is present on the carton label.
- We recommend revising this sentence to read, “Store refrigerated at 2°C to 8°C (36°F to 46°F) in the original carton and protect from direct light” on the container label for consistency with the carton labeling.
- The package type term 'single dose' is not included in the container labeling.
- The carton labeling does not list the inactive ingredients in alphabetical order and lacks the quantities of inactive ingredients.

Primary Drug Product Assessor Name and Date:
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Drug Product Reviewer
OPQ/OPQA II/ Division VII/Unit 1
Date:03/14/2025

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Julia Pinto - APPROVED 04/21/2025
Ghaled Hamad - APPROVED 04/21/2025

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

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