

Risk Evaluation and Mitigation Strategy (REMS) Document

Part A. Aveed¹ REMS Program

I. Administrative Information

Application Number: NDA 22219

Application Holder: Endo Pharmaceuticals, Inc.

Initial REMS Approval: 03/2014

Most Recent REMS Update: 12/2018

II. REMS Goals

The goals and objectives of the Aveed REMS are to mitigate the negative outcomes associated with Aveed-induced pulmonary oil microembolism (POME) and anaphylaxis by:

1. Ensuring that Aveed is dispensed only in certified healthcare settings that have immediate access on-site to equipment and personnel trained to manage POME and anaphylaxis
2. Informing healthcare providers that Aveed can cause POME and anaphylaxis, which have the potential to lead to serious medical consequences (e.g., respiratory distress and syncope);
3. Informing healthcare providers about the safe use of Aveed, including proper administration technique and patient observation; and
4. Informing patients about the risks of POME and anaphylaxis associated with Aveed and the importance of remaining at the healthcare setting for 30 minutes after each injection.

III. REMS Requirements

Endo Pharmaceuticals, Inc. must ensure that healthcare providers, patients, healthcare settings, and wholesalers-distributors comply with the following requirements:

1. Healthcare Providers who prescribe Aveed must:

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| To become certified to prescribe | <ol style="list-style-type: none">1. Review Aveed's Prescribing Information.2. Review the following: Education Program for Healthcare Providers.3. Successfully complete the Knowledge Assessment and submit it to the REMS Program.4. Enroll in the REMS by completing the Healthcare Provider Enrollment Form and submitting it to the REMS Program. |
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¹ The AVEED-specific requirements contained in this document apply until the date of full approval of the first abbreviated new drug application (ANDA) referencing AVEED.

Before treatment initiation (first dose)	<ol style="list-style-type: none"> 5. Counsel the patient on the risks, including pulmonary oil embolism (POME) and anaphylaxis, and the need to remain at the healthcare setting for 30 minutes following each injection using the Patient Guide. 6. Provide the patient with a copy of Patient Guide.
During treatment, before each injection	<ol style="list-style-type: none"> 7. Counsel the patient on the risks, including pulmonary oil embolism (POME) and anaphylaxis, and the need to remain at the healthcare setting for 30 minutes following each injection using Patient Guide. Provide a copy of the Patient Guide to patient.

2. Patients who are prescribed Aveed:

Before treatment initiation	<ol style="list-style-type: none"> 1. Receive counseling from the prescriber on the risks, including pulmonary oil microembolism (POME) and anaphylaxis, and the need to remain at the healthcare setting for 30 minutes following each injection using Patient Guide.
Before administering	<ol style="list-style-type: none"> 2. Receive counseling on risks, including POME and anaphylaxis, and the need to remain at the healthcare setting for 30 minutes following each injection from the prescriber using Patient Guide.
After administration, for 30 minutes	<ol style="list-style-type: none"> 3. Be monitored for pulmonary oil embolism (POME) or anaphylaxis by remaining at the healthcare setting after the injection.

3. Healthcare settings that dispense Aveed must:

To become certified to dispense	<ol style="list-style-type: none"> 1. Have immediate access to the necessary equipment and personnel to manage POME and anaphylaxis on-site. 2. Designate an authorized representative to carry out the certification process and oversee implementation and compliance with the REMS Program on behalf of the healthcare setting. 3. Have the authorized representative review the Education Program for Healthcare Settings. 4. Have the authorized representative enroll in the REMS Program by completing the Healthcare Settings Enrollment Form and submitting it to the REMS Program. 5. Train all relevant staff involved in dispensing Aveed using the Education Program for Healthcare Settings. 6. Establish processes and procedures to verify that all healthcare providers at the healthcare setting who prescribe Aveed are certified prior to prescribing Aveed, each patient is counseled before administration of the drug, and each patient is observed within the healthcare setting for 30 minutes following each injection.
Before dispensing	<ol style="list-style-type: none"> 7. Verify the prescriber is certified.

Before administering	8.	Counsel the patient on the risk of POME and anaphylaxis. Provide the patient with a copy of the Patient Guide .
After administering, for 30 minutes	9.	Assess the patient for POME and anaphylaxis.
To maintain certification to dispense	10.	Have a new authorized representative enroll in the REMS Program by completing the Healthcare Settings Enrollment Form if the authorized representative changes.
To maintain certification to dispense, every 2 years	11.	Have authorized representative review the Education Program for Healthcare Settings
	12.	Have the authorized representative re-enroll in the REMS Program by completing the Healthcare Settings Enrollment Form
At all times	13.	Not distribute, transfer, loan, or sell Aveed, except to certified dispensers with the same authorized representative.
	14.	Maintain records of staff training and certified prescribers.
	15.	Comply with audits carried out by Endo Pharmaceuticals, Inc. to ensure that all processes and procedures are in place and are being followed.

4. Wholesalers-distributors that distribute Aveed must:

To be able to distribute	1.	Establish processes and procedures to ensure that the drug is distributed only to certified healthcare settings that have one or more certified prescribers associated with that address.
At all times	2.	Distribute only to certified healthcare settings that have one or more certified prescribers associated with that address.
	3.	Maintain records of all shipments of Aveed.

Endo Pharmaceuticals, Inc. must provide training to healthcare providers who prescribe Aveed. The training includes the following educational materials: [Education Program for Healthcare Providers](#) and [Knowledge Assessment](#). The training is available online, or hardcopy through the Aveed REMS call center.

Endo Pharmaceuticals, Inc. must provide training to healthcare settings that dispense Aveed. The training includes the following educational materials: [Education Program for Healthcare Settings](#). The training is available online or hardcopy through the Aveed REMS call center.

To support REMS Program operations, Endo Pharmaceuticals, Inc. must:

1. Establish and maintain a REMS Program website, www.AveedREMS.com. The REMS Program website must include the capability to complete prescriber and healthcare setting certification or enrollment online, and the option to print the PI, Medication Guide, and REMS materials. All product websites for consumers and healthcare providers must include prominent REMS-specific links to the REMS Program website. The REMS Program website must not link back to the promotional product website(s).
2. Make the REMS Program website fully operational and all REMS materials available through www.AveedREMS.com or by calling the Aveed REMS Program Call Center (1-855-755-0494) within 30 calendar days of REMS modification (XX/XX/XXXX).
3. Establish and maintain a REMS Program call center for REMS participants at 1-855-755-0494.

4. Establish and maintain a validated, secure database of all REMS participants who are enrolled and/or certified in the Aveed REMS Program.
5. Ensure healthcare providers are able to certify, and healthcare settings are able to certify and re-certify, by fax and online.
6. Ensure wholesalers-distributors are able to verify the healthcare setting is certified and has one or more certified prescribers associated with that address prior to distributing Aveed by providing access to the database of certified healthcare settings and prescribers.
7. Provide [REMS Program: An Introduction](#), and the Prescribing Information to REMS participants who (1) attempt to dispense or prescribe Aveed and are not yet certified or (2) inquire about how to become certified.
8. Confirm the healthcare setting has one or more certified prescribers associated with that address before certifying the healthcare setting.
9. Notify healthcare providers and healthcare settings within 2 business days after they become certified in the REMS Program.
10. Provide certified prescribers access to the database of certified healthcare settings.
11. Provide certified healthcare settings access to the database of certified prescribers.
12. Provide wholesalers-distributors access to the database of certified healthcare settings and certified prescribers.

To ensure REMS participants' compliance with the REMS Program, Endo Pharmaceuticals, Inc. must:

13. Verify annually that the authorized representative's name and contact information correspond to those of the current designated authorized representative for the healthcare setting. If different, the healthcare setting must be required to re-certify with a new authorized representative.
14. Maintain adequate records to demonstrate that REMS requirements have been met, including, but not limited to records of: Aveed distribution and dispensing; certification of prescribers and healthcare settings to ensure that all healthcare settings have at least one certified prescriber associated with their address to be able to order and receive Aveed; and audits of REMS participants. These records must be readily available for FDA inspections.
15. Establish a plan for addressing noncompliance with REMS Program requirements.
16. Monitor prescribers, healthcare settings, and wholesalers-distributors on an ongoing basis to ensure the requirements of the REMS are being met. Take corrective action if non-compliance is identified, including de-certification.
17. Audit healthcare settings no later than 180 calendar days after they become certified, to ensure that all REMS processes and procedures are in place, functioning, and support the REMS Program requirements. Thereafter, healthcare settings are included in the annual audit plan.
18. Take reasonable steps to improve implementation of and compliance with the requirements in the Aveed REMS Program based on monitoring and evaluation of the Aveed REMS Program.

IV. REMS Assessment Timetable

Endo Pharmaceuticals, Inc. must submit REMS Assessments at 6 months, 12 months, and annually thereafter from the date of the initial approval of the REMS. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 calendar days before the submission date for that assessment. Endo Pharmaceuticals, Inc. must submit each assessment so that it will be received by the FDA on or before the due date.

V. REMS Materials

The following materials are part of the Aveed REMS:

Enrollment Forms:

Prescriber:

1. [Healthcare Provider Enrollment Form](#)

Healthcare Setting:

2. [Healthcare Setting Enrollment Form](#)

Training and Educational Materials:

Prescriber:

3. [Education Program for Healthcare Providers](#)
4. [Knowledge Assessment](#)
5. [REMS Program: An Introduction](#)

Patient:

6. [What You Need To Know About Aveed Treatment: A Patient Guide](#)

Healthcare Setting:

7. [Education Program for Healthcare Settings](#)
8. [REMS Program: An Introduction](#)

Other Materials:

9. [REMS Program website](#)