I. Administrative Information

Application Number: NDA 215014
Application Holder: Apellis Pharmaceuticals, Inc.
Initial REMS Approval: 05/2021

II. REMS Goal

The goal of the REMS is to mitigate the occurrence and morbidity associated with encapsulated bacteria infections (*Streptococcus pneumoniae*, *Neisseria meningitidis* types A, C, W, Y and B and *Haemophilus influenzae* Type B) by educating healthcare providers and patients about:

1. the potential risk of infections caused by encapsulated bacteria with Empaveli
2. the need for vaccination and antibiotic prophylaxis, if required,
3. the early signs of invasive encapsulated bacteria infections, and
4. the need for immediate medical evaluation of signs and symptoms consistent with possible encapsulated bacteria infections

III. REMS Requirements

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

1. Healthcare providers who prescribe EMPAVELI must:

   To become certified to prescribe

   1. Review the drug’s Prescribing Information.


   3. Enroll in the REMS by completing the Prescriber Enrollment Form and submitting it to the REMS Program.

   Before treatment initiation at least 2 weeks before first dose

   4. Assess the patient’s vaccination status and immunize if needed according to the current Advisory Committee on Immunization Practices for the following: *Streptococcus pneumoniae*, *Neisseria meningitidis* types A, C, W, Y and B and *Haemophilus influenzae* type B.

   5. Provide the patient with a prescription for a 2-week course of antibiotic prophylaxis if EMPAVELI must be started less than 2 weeks after the patient was immunized.

<table>
<thead>
<tr>
<th>Timeframe</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>During treatment</td>
<td>7. Assess the patient for early signs and symptoms of serious bacterial infection and treat immediately, if infection is suspected.</td>
</tr>
<tr>
<td></td>
<td>8. Consider discontinuing EMPAVELI in patients who are being treated for serious bacterial infection.</td>
</tr>
<tr>
<td></td>
<td>9. Revaccinate patients according to the current Advisory Committee on Immunization Practices recommendations.</td>
</tr>
<tr>
<td>At all times</td>
<td>10. Report cases of serious bacterial infection, including the patient's clinical outcomes, to Apellis Pharmaceuticals, Inc.</td>
</tr>
</tbody>
</table>

### 2. Patients who are prescribed EMPAVELI:

**Before treatment initiation at least 2 weeks before first dose**

1. Get *Streptococcus pneumoniae, Neisseria meningitidis* types A, C, W, Y and B and *Haemophilus influenzae* type B vaccines as directed by your doctor.

2. Take antibiotics as directed by your doctor for 2 weeks after you get your vaccine(s) if you have to start EMPAVELI right away.

3. Receive counseling from the prescriber using the [Patient Safety Guide](#) and [Patient Wallet Card](#).

**During treatment**

4. Get *Streptococcus pneumoniae, Neisseria meningitidis* types A, C, W, Y and B and *Haemophilus influenzae* Type B vaccines as directed by your doctor.

**At all times**

5. Inform the prescriber or get emergency medical care right away if any of the following occur: fever with or without shivers or the chills; fever and a rash; shortness of breath; extreme pain or discomfort; headache with nausea or vomiting; high heart rate; headache and a fever; headache with a stiff neck or stiff back; confusion; muscle aches with flu-like symptoms; clammy skin; eyes sensitive to light.

6. Have the [Patient Wallet Card](#) with you.

### 3. Pharmacies that dispense EMPAVELI must:

**To become certified to dispense**

1. Designate an Authorized Representative to carry out the certification process and oversee implementation and compliance with the REMS Program on behalf of the pharmacy.

2. Have the Authorized Representative review the [Healthcare Provider Brochure](#).

3. Have the Authorized Representative enroll in the REMS by completing the [Pharmacy Enrollment Form](#) and submitting it to the REMS Program.

4. Train all relevant staff involved in dispensing EMPAVELI using the [Healthcare Provider Brochure](#).

5. Establish processes and procedures to contact the prescriber to assess the patient’s vaccination history including antibiotic prophylaxis and document the findings.
<table>
<thead>
<tr>
<th>Before dispensing</th>
<th>6. Obtain authorization to dispense each prescription by contacting the REMS Program to verify the prescriber is certified.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>7. Assess the patient’s vaccination history including antibiotic prophylaxis by contacting the prescriber and document the findings through the processes and procedures established as a requirement of the REMS Program.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>To maintain certification to dispense</th>
<th>8. If the Authorized Representative changes, have the new Authorized Representative enroll in the REMS by completing the Pharmacy Enrollment Form and submitting it to the REMS.</th>
</tr>
</thead>
<tbody>
<tr>
<td>At all times</td>
<td>9. Report adverse events suggestive of serious bacterial infections to Apellis Pharmaceuticals, Inc.</td>
</tr>
<tr>
<td></td>
<td>10. Not distribute, transfer, loan, or sell EMPAVELI, except to certified dispensers.</td>
</tr>
<tr>
<td></td>
<td>11. Maintain records of staff’s completion of REMS training.</td>
</tr>
<tr>
<td></td>
<td>12. Maintain records that all processes and procedures are in place and are being followed.</td>
</tr>
<tr>
<td></td>
<td>13. Comply with audits carried out by Apellis Pharmaceuticals, Inc. or a third party acting on behalf of the applicant, to ensure that all processes and procedures are in place and are being followed.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>4. Wholesalers-distributors that distribute EMPAVELI must:</th>
</tr>
</thead>
<tbody>
<tr>
<td>To be able to distribute</td>
</tr>
<tr>
<td>1. Establish processes and procedures to ensure that the drug is distributed only to certified pharmacies.</td>
</tr>
<tr>
<td>2. Train relevant staff involved in EMPAVELI distribution on the REMS requirements.</td>
</tr>
<tr>
<td>At all times</td>
</tr>
<tr>
<td>3. Distribute only to certified pharmacies.</td>
</tr>
<tr>
<td>4. Maintain records of all drug distributions.</td>
</tr>
<tr>
<td>5. Comply with audits carried out by Apellis Pharmaceuticals, Inc. or a third party acting on behalf of the applicant to ensure that all processes and procedures are in place and are being followed.</td>
</tr>
</tbody>
</table>

**Apellis Pharmaceuticals, Inc. must provide training to healthcare providers who prescribe EMPAVELI.**

The training includes the following educational materials: **Patient Wallet Card, Healthcare Provider Brochure, and Patient Safety Guide.** The training will be available online and by hard copy, fax, and mail.

**Apellis Pharmaceuticals, Inc. must provide training to pharmacies that dispense EMPAVELI.**

The training includes the following educational material: **Healthcare Provider Brochure.** The training must be available online and by hard copy, fax, and mail.

**To support REMS Program operations, Apellis Pharmaceuticals, Inc. must:**

1. Establish and maintain a REMS Program Website, [www.EMPAVELIREMS.com](http://www.EMPAVELIREMS.com). The REMS Program website must include the capability to complete prescriber certification online and the option to print the Prescribing Information, 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 the website or call center by the date EMPAVELI is first commercially distributed.

3. Establish and maintain a REMS Program call center for REMS participants at 1-888-343-7073.

4. Establish and maintain a validated, secure database of all REMS participants who are certified in the EMPAVELI REMS Program.

5. Ensure prescribers are able to enroll in the REMS by fax and online.

6. Ensure pharmacies are able to enroll in the REMS by fax.

7. Ensure prescribers and pharmacies are able to report serious bacterial infection adverse events by contacting Apellis Pharmaceuticals, Inc., by phone.

8. Ensure that once a report suggestive of serious bacterial infection is received, Apellis Pharmaceuticals, Inc. will follow-up with the healthcare provider to obtain all required data. This requirement does not affect Apellis Pharmaceutical’s, Inc. other reporting and follow-up requirements under FDA regulations.

9. Provide the Healthcare Provider Brochure, Prescriber Enrollment Form, Patient Safety Guide, Patient Wallet Card, and the Prescribing Information to prescribers who (1) attempt to prescribe EMPAVELI and are not yet certified or (2) inquire about how to become certified.

10. Provide Healthcare Provider Brochure and Pharmacy Enrollment Form to pharmacies that (1) attempt to order/dispense and are not yet certified or (2) inquire about how to become certified.

11. Notify prescribers and pharmacies within 2 business days after they become certified in the REMS Program.

12. Provide certified pharmacies access to the database of certified prescribers.

13. Provide certified prescribers access to the database of certified pharmacies.

14. Provide authorized wholesalers-distributors access to a database of certified pharmacies.

To ensure REMS participants’ compliance with the REMS Program, Apellis Pharmaceuticals, Inc. must:

15. Maintain adequate records to demonstrate that REMS requirements have been met, including, but not limited to, records of: EMPAVELI distribution and dispensing; certification of prescribers and pharmacies; and audits of REMS participants. These records must be readily available for FDA inspections.

16. Verify annually that the designated Authorized Representative for the pharmacy is the same. If different, the pharmacy must re-certify with a new Authorized Representative.

17. Establish a plan for addressing noncompliance with REMS Program requirements.

18. Monitor prescribers and pharmacies 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.

19. Audit pharmacies and wholesalers-distributors no later than 120 calendar days after they become certified/authorized to dispense and distribute the drug, respectively, and annually thereafter, to
ensure that all REMS processes and procedures are in place, functioning, and support the REMS Program requirements.

20. Take reasonable steps to improve implementation of and compliance with the requirements of the EMPAVELI REMS Program based on monitoring and evaluation of the EMPAVELI REMS Program.

IV. REMS Assessment Timetable

Apellis 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. Apellis 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 EMPAVELI REMS:

**Enrollment Forms**

**Prescriber:**

1. Prescriber Enrollment Form

**Pharmacy:**

2. Pharmacy Enrollment Form

**Training and Educational Materials**

**Prescriber:**

3. Healthcare Provider Brochure

**Patient:**

4. Patient Safety Guide

5. Patient Wallet Card

**Pharmacy:**

6. Healthcare Provider Brochure

**Other Materials**

7. REMS Program website