NDA 215014/S-012

SUPPLEMENT APPROVAL

Apellis Pharmaceuticals, Inc.
a wholly owned subsidiary of Biogen MA, Inc.
Attention: Ginny Collins, MS, MBA
Senior Director, Regulatory Affairs
100 5th Avenue, 3rd Floor
Waltham, MA 02451

Dear Ginny Collins:

Please refer to your supplemental new drug application (sNDA) dated October 20, 2025, received October 20, 2025, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Empaveli (pegcetacoplan) injection.

We acknowledge receipt of your risk evaluation and mitigation strategy (REMS) dated October 20, 2025 and amendment dated November 14, 2025.

This Prior Approval sNDA provides for updates to the indication to describe an additional benefit (to reduce the loss of kidney function), in the indicated population: for the treatment of adult and pediatric patients aged 12 years and older with C3 glomerulopathy (C3G) or primary immune-complex membranoproliferative glomerulonephritis (IC-MPGN), to reduce proteinuria and the loss of kidney function, as well as a proposed modification to the approved Empaveli REMS.

APPROVAL & LABELING

We have completed our review of this application. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at FDA.gov.[1] Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information and Medication Guide), with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm

Information on submitting SPL files using eList may be found in guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*.[2]

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in Microsoft Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission(s), provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

We request that the labeling approved today be available on your website within 10 days of receipt of this letter.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because this drug product for this indication has an orphan drug designation, you are exempt from this requirement.

RISK EVALUATION AND MITIGATION STRATEGY (REMS) REQUIREMENTS

The REMS for Empaveli was originally approved on May 14, 2021, and the most recent REMS modification was approved on July 28, 2025. The REMS consists of elements to assure safe use, an implementation system, and a timetable for submission of assessments of the REMS.

Your proposed modification to the REMS consists of changes to the Healthcare Provider Safety Brochure, Patient Guide, and REMS Website to align with the revised indication for the treatment of adult and pediatric patients aged 12 years and older with C3 glomerulopathy (C3G) or primary immune-complex membranoproliferative glomerulonephritis (IC-MPGN), to reduce proteinuria and the loss of kidney function.

[2] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

Your proposed modified REMS, submitted on October 20, 2025, and appended to this letter, is approved.

The timetable for submission of assessments of the REMS remains the same as that approved on May 14, 2021.

The revised REMS assessment plan must include, but is not limited to, the following:

For each metric, provide the two previous, current, and cumulative reporting periods (where applicable) unless otherwise noted.

Program Implementation and Operations:

1. REMS Program Implementation (6-month and 1-year assessments only)

    a. Date of first commercial distribution of Empaveli.

    b. Date of Empaveli REMS launch.

    c. Date when the REMS Website became live and fully operational.

    d. Date when healthcare providers who can prescribe could become certified in the Empaveli REMS.

    e. Date when pharmacies could become certified in the Empaveli REMS.

    f. Date when wholesalers-distributors were authorized to dispense and distribute the drug (i.e., first order placed).

    g. Date when the REMS Coordinating Center was established and fully operational.

2. REMS Certification and Enrollment Statistics

    a. Healthcare Provider (HCP) Certification

        i. The number of HCPs certified: total, newly certified, and active (prescribed Empaveli at least once during the reporting period) stratified by credentials (e.g., Doctor of Medicine, Doctor of Osteopathic Medicine, Advanced Practice Registered Nurse, Physician Assistant, other), medical specialty (e.g., Hematology/Oncology, Immunology, Internal Medicine, Nephrology, Neurology, Rheumatology, and Other), and geographic region (as defined by United States (US) Census).

        ii. Method of certification (e.g., fax, online).

        iii. The number of HCPs who have prescribed but were unable to become certified, accompanied by a summary of the reasons they were unable to be certified.

    b. Pharmacy Certification

i. The number and identity of each pharmacy certified: total, newly certified and active (dispensed Empaveli at least once during the reporting period) stratified by pharmacy type and stratified by geographic region (as defined by US Census).

ii. The number of pharmacies that were unable to become certified, accompanied by a summary of the reason(s) why they were unable to be certified.

c. Wholesalers-Distributors

i. The number and identity of each wholesaler-distributor authorized to distribute Empaveli: total and newly authorized, and active (distributed Empaveli at least once during the reporting period).

3. Empaveli Utilization Data

a. The number of Empaveli shipments sent to pharmacies, overall, and stratified by quantity per shipment, and by geographic region (as defined by US Census).

b. For certified pharmacies, the number of prescriptions dispensed stratified by:

i. Prescriber specialty, degree/credentials, and geographic region.

ii. Patient demographics (e.g., age, sex), and geographic region (as defined by US Census).

iii. Whether the prescription was new, or a refill reported as a total across all pharmacies.

c. For wholesalers-distributors, number of orders distributed.

d. The number of unique patients who received Empaveli stratified by age, sex, and geographic regions (as defined by US Census).

e. The number and percentage (%) of Empaveli dispenses corresponding to prescriptions written by REMS-certified HCPs.

f. The number of prescriptions not dispensed, accompanied by a listing and summary of all reasons for not dispensing the prescription (e.g., HCPs not certified, REMS-related issue).

4. REMS Compliance

a. A summary report of noncompliance identified, associated corrective and preventive action (CAPA) plans, and the status of CAPA plans including, but not limited to:

i. A copy of the Noncompliance Plan, including the criteria for noncompliance for prescribers and certified pharmacies, actions

taken to address noncompliance for each case, and which events will lead to suspension or decertification from the REMS.

ii. The number of instances of noncompliance accompanied by a description of each instance and the reason for the occurrence (if provided). For each instance of noncompliance, report the following information:

a) The unique ID(s) of the stakeholder(s) associated with the noncompliance event or deviation to enable tracking over time.

b) The source of the noncompliance data.

c) The results of root cause analysis.

d) The action(s) taken in response to the noncompliance.

iii. The number and percentage of prescribers who prescribed Empaveli but were not certified as identified by the certified pharmacy

a) The specific reasons why prescribers were not certified at the time of prescribing (e.g., emergency use), and whether these prescribers subsequently became certified.

iv. The number and percentage of pharmacies that obtained Empaveli that were not certified.

a) The specific reasons for the drug distributions to pharmacies that were not certified.

v. The number of pharmacies who became decertified, accompanied by a summary of reasons for decertification.

b. Audits: Summary of audit activities including but not limited to:

i. A copy of the audit plan used for each audited stakeholder type (pharmacies, REMS Coordinating Center, and wholesalers-distributors).

ii. The number of audits expected, and the number of audits performed for each stakeholder.

iii. The number and category of audit observations noted, stratified by category.

iv. A unique ID for each stakeholder that had observations to track observations by stakeholder over time.

v. Documentation of completion of training for relevant staff (those involved in the distribution or dispensing of Empaveli).

vi. A summary report of documented processes and procedures for complying with the REMS requirements including how certified pharmacies obtain patient vaccination status from HCPs.

a) As part of reviewing the processes and procedures, review the methods utilized to determine whether patients received pneumococcal and meningococcal vaccines in accordance with the most current Advisory Committee on Immunization Practice (ACIP) recommendations for patients receiving a complement inhibitor.

vii. Verification that at each audited stakeholder's site, the designated Authorized Representative is up to date. If the Authorized Representative changes, include the number of new Authorized Representatives and verification of each site's recertification.

viii. Describe any corrective actions taken for any noncompliance identified (audit observation) during the audits as well as preventative measures that were developed from uncovering these noncompliance events.

a) For those with deficiencies noted, report the number that successfully completed a CAPA plan by the due date.

b) For any that did not complete the CAPA by the due date, describe additional actions taken.

5. REMS Infrastructure and Performance

a. REMS Website

i. The number of visits and unique visits to the REMS Website.

ii. The number of REMS materials downloaded or printed for each material.

b. REMS Coordinating Center Report

i. The number of contacts by stakeholder type (i.e., patient/caregiver, healthcare provider, pharmacy, etc.).

ii. A table summarizing the reasons for calls (e.g., enrollment question) by stakeholder type.

iii. Details on any complaint(s) received and whether they indicate potential issues with the Empaveli REMS burden or patient access.

iv. Details of any corrective actions implemented due to identified issues.

Safe Use Behaviors

6. Safe Use Behaviors

Determination of patients' vaccination and antibacterial drug prophylaxis compliance is made using data collected via the certified pharmacies documenting the patient's vaccination status.

a. The information captured by pharmacies regarding the number and percentage of patients who were vaccinated against encapsulated bacteria (Streptococcus pneumoniae and Neisseria meningitidis serogroups A, C, W, Y, and B). This information is to include vaccine serogroup (if applicable), dosing, (i.e., first vaccine dose, second vaccine dose, and booster doses), and timing of the vaccination, when the information is provided.
b. Data on the number and percentage of new patients treated with Empaveli whose prescriber reported the patient receiving pneumococcal and meningococcal vaccines out of the total number of patients who received Empaveli. Of those who reported receiving pneumococcal and meningococcal vaccines provide the number and percentage of patients who:
    i. Received vaccines in accordance with the most current ACIP recommendations for pneumococcal and meningococcal vaccines in patients receiving a complement inhibitor stratified by vaccine administered.
    ii. Did not receive vaccines in accordance with the most current ACIP recommendations for pneumococcal and meningococcal vaccines in patients receiving a complement inhibitor stratified by vaccine administered.
    iii. Did not have all the information necessary for determining compliance with the most current ACIP recommendations for pneumococcal or meningococcal vaccination in patients receiving a complement inhibitor.
c. Data on the number and percentage of new patients treated with Empaveli who did not receive pneumococcal or meningococcal vaccination(s) out of the total number of patients who received Empaveli.
d. Data on whether the patient received antibacterial drug prophylaxis and a summary analysis of the timing of antibacterial drug prophylaxis in relation to the dosing of Empaveli (if available).
e. If any of the above information is missing, the reasons why this information is missing such as:
    i. Healthcare provider records do not include this information
    ii. Healthcare provider declined to provide this information

iii. Pharmacy unable to get healthcare provider to respond to queries

f. The number and percentage (%) of patients dispensed Empaveli who received at least one dose of pneumococcal vaccines according to the most current ACIP recommendations in patients receiving a complement inhibitor and antibacterial drug prophylaxis, if needed, before the first dispense.

g. The number and percentage (%) of patients dispensed Empaveli who received at least one dose of meningococcal vaccines (against all of the following serogroups: A, B, C, W, Y) according to the most current ACIP recommendations in patients receiving a complement inhibitor and antibacterial drug prophylaxis, if needed, before the first dispense.

h. The number and percentage (%) of new patients treated with Empaveli who completed or were up to date with vaccination against encapsulated bacteria (Streptococcus pneumoniae and Neisseria meningitidis serogroups A, C, W, Y, and B) as per the most current ACIP recommendations in patients receiving a complement inhibitor at the time of first dose.

i. For patients who were not initially up to date with vaccines (stratify by pneumococcal and meningococcal) when starting treatment, report the number and percentage who, up to 6 months after the first dose:

i. Completed pneumococcal and meningococcal vaccines.

ii. Did not complete pneumococcal and meningococcal vaccines but were receiving antibacterial drug prophylaxis.

iii. Vaccination status was unknown after completed follow-up attempts.

Health Outcomes and/or Surrogates of Health Outcomes

7. Summary of cases of pneumococcal and meningococcal infections in patients receiving Empaveli.

a. For US cases, cases are summarized as follows:

i. In the most recent Periodic Safety Update Report (PSUR) submitted to the Empaveli New Drug Application (NDA) with a link to that PSUR corresponding with the reporting interval.

ii. Cumulative listing of all cases of pneumococcal and meningococcal infections from approval to include cases identified during the current reporting period.

b. For each US case, provide the following information (if available):

i. MedWatch or other case report number.

ii. Date of event and date of report to FDA.

iii. Patient age, race, and sex.

iv. Indication for Empaveli treatment.

v. Pneumococcal and meningococcal vaccination status:

a) Date of vaccine(s) (i.e., pneumococcal and all the meningococcal (A, C, W, Y, and B) vaccines doses that a patient received including the first vaccine dose, second vaccine dose, and booster doses, as applicable).

b) Name of vaccine(s).

c) Timing in relation to Empaveli (i.e., the dates or duration that a patient received Empaveli in relation to the vaccine(s)).

d) ACIP compliance and antibacterial drug prophylaxis status

1) Antibacterial drug prophylaxis regimen.

2) Timing (i.e., include the dates or duration that a patient received Empaveli in relation to antibacterial drug prophylaxis).

e) Clinical course

1) Outcome and causative bacteria (including serogroup where applicable).

2) Source of the vaccine information when available. For information that is not available (listed as “unk” or “unknown”) the number and type (patient, prescriber, etc.) of outreach attempts made to obtain the information for each case. Also, if the information is not available, provide a narrative explaining why the information is unknown (“unk”) or unavailable for each reported case.

vi. Whether or not the patient was administered any antibacterial drug prophylaxis and if so:

a) The specific antibacterial drug, antibacterial drug regimen (dose/frequency/duration), and route(s) of administration.

b) The timing of the course of the antibacterial drug prophylaxis in relation to Empaveli treatment.

vii. Summary of clinical course and the outcome; specifically report whether the patient:

a) Was admitted to an intensive care unit.

b) Experienced any organ system failure, such as (but not limited to) requiring mechanical ventilation or medication (vasopressors) to support blood pressure.

c) Died.

viii. The length of time between onset of symptoms and when the patient presented for medical evaluation (if available).

ix. Causative encapsulated bacteria organism and serogroup.

x. Whether the Patient Safety Card was presented during the process of the patient seeking treatment.

c. For each non-US case, provide the following information, as available:

i. Case report number

ii. Patient age and sex

iii. Indication for Empaveli treatment

iv. Pneumococcal and meningococcal vaccination status if known

v. Outcome

vi. If associated with any clinical trials

8. Pneumococcal and meningococcal infections rate (per year and cumulatively):

a. Among patients who received Empaveli in the US and worldwide, if appliable:

i. The number of reported cases of pneumococcal and meningococcal infections per 100,000 patient-years of post-marketing exposure to Empaveli; reporting rate, summarized cumulatively since the approval of Empaveli and stratified by year and age subgroup (e.g., ≤18 years, 19-55 years, and >55 years).

Knowledge

9. Knowledge

a. Stakeholder Surveys for prescribing HCPs and patients (beginning with the 1-year REMS Assessment Report and provided for each reporting period annually thereafter).

i. Assess HCP and patient awareness regarding:

a) Patients are vaccinated against infections caused by encapsulated bacteria (Streptococcus pneumoniae and Neisseria meningitidis serogroup A, C, W, Y, and B) prior to starting therapy according to the most current ACIP recommendations for patients receiving a complement inhibitor and receive antibacterial drug prophylaxis if needed.

b) The early signs and symptoms of encapsulated bacterial infections.

c) The need for immediate medical evaluation.

Overall Assessment of REMS Effectiveness

10. The requirements for assessments of an approved REMS under section 505-1(g)(3) include with respect to each goal included in the strategy, an assessment of the extent to which the approved strategy, including each element of the strategy, is meeting the goal or whether one or more such goals or such elements should be modified.

We remind you that in addition to the REMS assessments submitted according to the timetable in the approved REMS, you must include an adequate rationale to support a proposed REMS modification for the addition, modification, or removal of any goal or element of the REMS, as described in section 505-1(g)(4) of the FDCA.

We also remind you that you must submit a REMS assessment when you submit a supplemental application for a new indication for use, as described in section 505-1(g)(2)(A) of the FDCA. This assessment should include:

a) An evaluation of how the benefit-risk profile will or will not change with the new indication;

b) A determination of the implications of a change in the benefit-risk profile for the current REMS;

c) *If the new indication for use introduces unexpected risks*: A description of those risks and an evaluation of whether those risks can be appropriately managed with the currently approved REMS.

d) *If a REMS assessment was submitted in the 18 months prior to submission of the supplemental application for a new indication for use*: A statement about whether the REMS was meeting its goals at the time of that last assessment and if any modifications of the REMS have been proposed since that assessment.

e) *If a REMS assessment has not been submitted in the 18 months prior to submission of the supplemental application for a new indication for use:* Provision of as many of the currently listed assessment plan items as is feasible.

f) *If you propose a REMS modification based on a change in the benefit-risk profile or because of the new indication of use, submit an adequate rationale to support the modification, including*: Provision of the reason(s) why the proposed REMS modification is necessary, the potential effect on the serious risk(s) for which the REMS was required, on patient access to the drug, and/or on the burden on the

health care delivery system; and other appropriate evidence or data to support the proposed change. Additionally, include any changes to the assessment plan necessary to assess the proposed modified REMS. *If you are not proposing REMS modifications*, provide a rationale for why the REMS does not need to be modified.

If the methodology for your REMS assessments are not included in the REMS supporting document, or if you propose changes to the submitted methodology, you should update the REMS supporting document to include specific methodology information at least 90 days before the assessments will be conducted. Updates to the REMS supporting document may be included in a new document that references previous REMS supporting document submission(s) for unchanged portions. Alternatively, updates may be made by modifying the complete previous REMS supporting document, with all changes marked and highlighted.

Prominently identify the submission containing the methodology with the following wording in bold capital letters at the top of the first page of the submission:

NDA 215014 REMS ASSESSMENT METHODOLOGY PROTOCOL REVIEW (insert concise description of content in bold capital letters, e.g., **SURVEY METHODOLOGIES, AUDIT PLAN, NONCOMPLIANCE PLAN, DRUG USE STUDY)**

An authorized generic drug under this NDA must have an approved REMS prior to marketing. Should you decide to market, sell, or distribute an authorized generic drug under this NDA, contact us to discuss what will be required in the authorized generic drug REMS submission.

We remind you that section 505-1(f)(8) of FDCA prohibits holders of an approved covered application with elements to assure safe use from using any element to block or delay approval of an application under section 505(b)(2) or (j). A violation of this provision in 505-1(f) could result in enforcement action.

Prominently identify any submission containing the REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission as appropriate:

NDA 215014 REMS ASSESSMENT

or

NEW SUPPLEMENT FOR NDA 215014/S-000
CHANGES BEING EFFECTED IN 30 DAYS
PROPOSED MINOR REMS MODIFICATION

or

NEW SUPPLEMENT FOR NDA 215014/S-000
PRIOR APPROVAL SUPPLEMENT
PROPOSED MAJOR REMS MODIFICATION

or

NEW SUPPLEMENT FOR NDA 215014/S-000
PRIOR APPROVAL SUPPLEMENT
PROPOSED REMS MODIFICATIONS DUE TO SAFETY LABELING CHANGES SUBMITTED IN SUPPLEMENT XXX

or

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA 215014/S-000
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

Should you choose to submit a REMS revision, prominently identify the submission containing the REMS revisions with the following wording in bold capital letters at the top of the first page of the submission:

REMS REVISIONS FOR NDA 215014

To facilitate review of your submission, we request that you submit your proposed modified REMS and other REMS-related materials in Microsoft Word and PDF format. If certain documents, such as enrollment forms, or website screenshots are only in PDF format, they may be submitted as such, but Word format and PDF format are preferred.

SUBMISSION OF REMS DOCUMENT IN SPL FORMAT

As soon as possible, but no later than 14 days from the date of this letter, submit the REMS document in Structured Product Labeling (SPL) format using the FDA automated drug registration and listing system (eLIST). Content of the REMS document must be identical to the approved REMS document. The SPL will be publicly available.

Information on submitting REMS in SPL format may be found in the guidance for industry *Providing Regulatory Submission in Electronic Format – Content of the Risk Evaluation and Mitigation Strategies Document Using Structured Product Labeling.*

For more information on submitting REMS in SPL format, please email FDAREMSwebsite@fda.hhs.gov.

PATENT LISTING REQUIREMENTS

Pursuant to 21 CFR 314.53(d)(2) and 314.70(f), certain changes to an approved NDA submitted in a supplement require you to submit patent information for listing in the Orange Book upon approval of the supplement. You must submit the patent information required by 21 CFR 314.53(d)(2)(i)(A) through (C) and 314.53(d)(2)(ii)(A) and (C), as applicable, to FDA on Form FDA 3542 within 30 days after the date of approval of the supplement for the patent information to be timely filed (see 21 CFR 314.53(c)(2)(ii)). You also must ensure that any changes to your approved NDA that require the submission of a request to remove patent information from the Orange Book are submitted to FDA at the time of approval of the supplement pursuant to 21 CFR 314.53(d)(2)(ii)(B) and 314.53(f)(2)(iv).

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, please contact Anna Park, Regulatory Project Manager, at (301) 796-1129 or anna.park@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Aliza Thompson, MD, MS
Director
Division of Cardiology and Nephrology
Office of Cardiology, Hematology, Endocrinology & Nephrology
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Medication Guide
- REMS

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/

ALIZA M THOMPSON
08/20/2026 10:53:25 AM