

NDA 218037/S-004

SUPPLEMENT APPROVAL

Alexion Pharmaceuticals, Inc.
Attention: Vinayak Rajana
Associate Director, Regulatory Science & Execution
121 Seaport Blvd., Boston, MA 02210

Dear Vinayak Rajana:

Please refer to your supplemental new drug application (sNDA) dated and received April 29, 2025, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Voydeya (danicipan) tablets.

This Changes Being Effected supplemental new drug application proposed modifications to the approved Voydeya risk evaluation and mitigation strategy (REMS).

We have completed our review of this supplemental application. It is approved effective on the date of this letter.

RISK EVALUATION AND MITIGATION STRATEGY (REMS) REQUIREMENTS

The REMS for Voydeya was originally approved on March 29, 2024. 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 removal of the Alexion REMS landing webpage from the REMS Document and REMS Website screenshots.

Your proposed modified REMS, submitted on April 29, 2025, and appended to this letter, is approved.

The timetable for submission of assessments of the REMS remains the same as that approved on March 29, 2024.

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

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

Program Implementation and Operations

1. REMS Implementation (for the first REMS assessment only):
 - a. Date of first commercial distribution of VOYDEYA
 - b. Date of VOYDEYA REMS launch

- c. Date when the VOYDEYA REMS Website became live and fully operational
 - d. Date when healthcare providers (HCPs) who can prescribe could become certified in the VOYDEYA REMS
 - e. Date when pharmacies were able to complete the VOYDEYA REMS certification process
 - f. Date of first prescriber certification
 - g. Date of first pharmacy certification
 - h. Date when the REMS Call Center was established and fully operational
2. REMS Certification and Enrollment Statistics
 - a. Healthcare Provider Certification
 - i. The number of HCPs certified: total, newly certified, and active (prescribed VOYDEYA 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, Doctor of Pharmacy), medical specialty (e.g., Hematology/Oncology, Immunology, Internal medicine, Nephrology, Neurology, Rheumatology, and Other), and geographic region (as defined by US Census)
 - ii. Method of HCP certification (e.g., fax, online, email)
 - iii. The number of HCPs who were unable to become certified, accompanied by a summary of the reason(s) why they were unable to be certified
 - b. Pharmacy Certification (stratify by inpatient and outpatient)
 - i. The number and identity of certified dispensing pharmacies: total, and newly certified and active (dispensed VOYDEYA at least once during the reporting period) and by geographic region (as defined by US Census)
 - ii. Method of pharmacy certification (e.g., fax, email)
 - iii. The number of pharmacies that were unable to become certified, accompanied by a summary of the reason(s) why they were unable to become certified
3. Patient Statistics
 - a. The number and percent of new patients treated with VOYDEYA
 - b. The number of patients treated with VOYDEYA stratified by sex, age, diagnosis, and geographic region (as defined by US Census)
4. VOYDEYA Utilization Data (stratify by inpatient and outpatient)
 - a. The number of VOYDEYA 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
- c. Percentage (%) of VOYDEYA dispenses corresponding to prescriptions written by REMS certified HCPs
- d. The number of prescriptions not dispensed, accompanied by a listing and summary of all reasons for not dispensing the prescription (e.g., HCP not certified, REMS related issue)

5. REMS Compliance

- a. A summary report of non-compliance identified, associated corrective and preventive action (CAPA) plans, and the status of CAPA plans. Provide a summary of non-compliance identified, including, but not limited to:
 - i. A copy of the non-compliance plan, including the criteria for determination of non-compliance for prescribers, outpatient pharmacies and inpatient pharmacies, actions taken to address non-compliance for each case, and what events led to suspension or decertification from the REMS
 - ii. The number of instances of non-compliance accompanied by a description of each instance and the reason for the occurrence (if provided). For each instance of non-compliance, the following information will be reported:
 - a) The unique identification (ID) of the stakeholder(s) associated with the non-compliance event or deviation to enable tracking over time
 - b) The source of the non-compliance data
 - c) The results of root cause analysis
 - d) The action(s) taken in response to non-compliance
 - iii. The number and percentage of prescribers who prescribed VOYDEYA but were not certified as identified by the certified pharmacy
 - iv. The specific reasons why prescribers were not certified at the time of prescribing and whether these prescribers subsequently became certified
 - v. The number and percentage of outpatient and inpatient pharmacies who obtained VOYDEYA that were not certified
 - vi. The specific reasons for the drug distributions to outpatient and inpatient pharmacies that were not certified
 - vii. The number of outpatient and inpatient pharmacies who became decertified, accompanied by a summary of reasons for decertification

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

- a. A copy of the audit plan used for each audited stakeholder (i.e., outpatient and inpatient pharmacies)

- b. The number of audits expected, and the number of audits performed for each stakeholder
 - c. The number and category of observations noted, stratified by category
 - d. A unique ID for each stakeholder that had observations to track observations by stakeholder over time
 - e. Documentation of completion of training for relevant staff
 - f. A summary report of documented processes and procedures for complying with the REMS requirements including how certified pharmacies obtain patient vaccination status from HCPs
 - g. Verification that at each audited pharmacy location, the designated Authorized Representative is up to date and the pharmacy is certified. If the Authorized Representative has changed, include the number of newly Authorized Representatives and verification of each site's recertification.
 - h. Describe any corrective actions taken for any non-compliance (audit observation) identified during the audits, as well as preventative measures that were developed from uncovering these non-compliance events
 - i. For those with deficiencies noted, report the number that successfully completed a CAPA plan by the due date
 - ii. For any that did not complete the CAPA plan by the due date, describe additional actions taken
7. REMS Infrastructure and Performance
- a. REMS Website (www.VoydeyaREMS.com)
 - i. The number of visits and unique visits to the REMS Website (www.VoydeyaREMS.com)
 - ii. The number of REMS materials downloaded or printed for each material
 - b. REMS Call Center Report
 - i. The number of contacts by stakeholder type (patient/caregiver, healthcare provider, etc.)
 - ii. A table summarizing the reasons for calls (e.g., enrollment question) by stakeholder type
 - iii. If the reason for the call(s) indicates a complaint, provide details on the nature of the complaint(s) and whether they indicate potential REMS burden or patient access issues
 - iv. A summary report of corrective actions resulting from issues identified

Safe Use Behaviors

8. Safe Use Behaviors

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

- a. Methods utilized to determine whether or not patients received meningococcal and pneumococcal vaccines in accordance with the most current Advisory Committee on Immunization Practices (ACIP)

recommendations for patients receiving a complement inhibitor. Include vaccine serogroup (if applicable), dosing (i.e., first vaccine dose, second vaccine dose and booster doses), and timing of the vaccinations, when the information is provided.

- b. Data on the number and percentage of new patients treated with VOYDEYA who report receiving meningococcal and pneumococcal vaccines out of the total number of patients who received VOYDEYA. Of those who reported receiving meningococcal and pneumococcal vaccines provide the number and percentage of patients who:
 - i. Received vaccines in accordance with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for meningococcal and pneumococcal vaccinations in patients receiving a complement inhibitor
 - ii. Did not receive vaccines in accordance with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for meningococcal and pneumococcal vaccinations in patients receiving a complement inhibitor
- c. Data on the number and percentage of new patients treated with VOYDEYA who reported not receiving meningococcal and pneumococcal vaccines out of the total number of patients who received VOYDEYA
- d. Whether the patient received antibacterial drug prophylaxis, and timing of antibacterial drug prophylaxis in relation to the dosing of VOYDEYA (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 information
 - iii. Healthcare provider did not respond to pharmacy queries
- f. The number and percentage of patients dispensed VOYDEYA who received at least one dose of meningococcal vaccines (against all of the following serogroups: A, C, W, Y and B) according to the most current Advisory Committee on Immunization Practices (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 VOYDEYA who received at least one dose of pneumococcal vaccines according to the most current Advisory Committee on Immunization Practices (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 VOYDEYA who completed or were up to date with meningococcal vaccinations (against all of the following serogroups: A, C, W, Y and B) and pneumococcal vaccinations as per the most current Advisory Committee on Immunization Practices (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 meningococcal and pneumococcal vaccines when starting treatment, report the number and percentage who, for up to 6 months after the first dose:

- i. Completed meningococcal and pneumococcal vaccines
- ii. Did not complete meningococcal and pneumococcal 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

9. Summary of cases of meningococcal and pneumococcal infections in patients receiving VOYDEYA:
 - a. For US, cases are summarized as follows:
 - i. In the most recent Periodic Safety Update Report (PSUR) submitted to the VOYDEYA New Drug Application (NDA) with reference to the PSUR corresponding with the reporting interval
 - ii. Cumulative listing of all cases of meningococcal and pneumococcal infections from approval to include cases identified during the current reporting period
 - b. For each US case, the following information is provided:
 - 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 VOYDEYA treatment
 - v. Meningococcal and pneumococcal vaccination status
 - a) Date of vaccine(s) [i.e., all of the meningococcal vaccines (serogroups: A, C, W, Y, and B) and pneumococcal vaccine(s) doses that a patient receives including the first vaccine dose, second vaccine dose, and booster doses, as applicable]
 - b) Name of vaccine(s)
 - c) Timing in relation to VOYDEYA (i.e., the dates or duration that a patient receives VOYDEYA 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 receives VOYDEYA in relation to antibacterial drug prophylaxis)
 - e) Clinical course
 - 1) Outcome and causative encapsulated bacteria (include serogroup where applicable)
 - 2) Include the 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, a narrative is presented 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 VOYDEYA 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, if applicable, the following information is provided:
 - i. Case report number
 - ii. Patient age and sex
 - iii. Indication for VOYDEYA treatment
 - iv. Meningococcal and pneumococcal vaccination status if known
 - v. Outcome
 - vi. If associated with any clinical trials

10. Meningococcal and Pneumococcal Infections Rate (per year and cumulatively)

- a. Among patients who received VOYDEYA in the US and worldwide, if applicable:
 - i. The number of reported cases of meningococcal and pneumococcal infections per 100,000 patient-years of post-marketing exposure to VOYDEYA; reporting rate, summarized cumulatively since the approval of VOYDEYA and also by year and relevant age subgroup (≤ 18 years, 19-55 years, and >55 years)

Knowledge

11. Knowledge

- a. Stakeholder Surveys for prescribing certified healthcare providers and patients (beginning with the 1-year assessment report and provided for each reporting period thereafter)
 - i. Assess certified HCP and patient awareness regarding:
 - a) Patients are vaccinated against infections caused by encapsulated bacteria (*Neisseria meningitidis* serogroups A, C, W, Y, and B; and *Streptococcus pneumoniae*) prior to starting therapy according to the most current Advisory Committee on Immunization Practices (ACIP) recommendations for patients receiving a complement inhibitor and receive antibacterial drug prophylaxis if needed

- b) The early signs and symptoms of serious encapsulated bacterial infections
- c) The need for immediate medical evaluation

Overall Assessment of REMS Effectiveness

1. 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 assessment instruments and methodology for your REMS assessments are not included in the REMS supporting document, or if you propose changes to the submitted assessment instruments or methodology, you should update the REMS supporting document to include specific assessment instrument and 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 assessment instruments and methodology with the following wording in bold capital letters at the top of the first page of the submission:

NDA 218037 REMS ASSESSMENT METHODOLOGY

(insert concise description of content in bold capital letters, e.g.,

ASSESSMENT METHODOLOGY, PROTOCOL, SURVEY METHODOLOGIES, AUDIT 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 218037 REMS ASSESSMENT

or

**NEW SUPPLEMENT FOR NDA 218037/S-000
CHANGES BEING EFFECTED IN 30 DAYS
PROPOSED MINOR REMS MODIFICATION**

or

**NEW SUPPLEMENT FOR NDA 218037/S-000
PRIOR APPROVAL SUPPLEMENT
PROPOSED MAJOR REMS MODIFICATION**

or

**NEW SUPPLEMENT FOR NDA 218037/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 218037/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 218037

To facilitate review of your submission, we request that you submit your proposed modified REMS and other REMS-related materials in Microsoft Word 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 is 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.

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, contact Caden Brennen, Safety Regulatory Project Manager at 301-796-6591 or at Caden.Brennen@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Rosanna Setse, MD, MPH, PhD.
Deputy Director for Safety
Division of Nonmalignant Hematology
Office of Cardiology, Hematology,
Endocrinology, and Nephrology
Center for Drug Evaluation and Research

ENCLOSURE:

- 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/

ROSANNA W SETSE
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