NDA 219627

NDA APPROVAL

Bayer HealthCare Pharmaceuticals, Inc.
Attention: Megan Socaciu
Director, Regulatory Affairs
100 Bayer Blvd.
P.O. Box 915
Whippany, NJ 07981-0915

Dear Megan Socaciu:

Please refer to your new drug application (NDA) received June 12, 2025, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Ambelvist (gadoquatrane) injection.

This NDA provides for the use of Ambelvist (gadoquatrane) injection in adult and pediatric patients, including term neonates, for use with magnetic resonance imaging (MRI) to detect and visualize lesions with abnormal vascularity in:

- the central nervous system (brain, spine, and associated tissues)
- the body (head and neck, thorax, abdomen, pelvis, and musculoskeletal system)

APPROVAL & LABELING

We have completed our review of this application, as amended. 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 (Prescribing Information, Medication Guide) as well as annual reportable changes not included in the enclosed labeling. 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]

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

The SPL will be accessible via publicly available labeling repositories.

CARTON AND CONTAINER LABELING

We acknowledge your May 7, 2026, submission containing final printed carton and container labeling.

DATING PERIOD

Based on the stability data submitted to date, the expiry dating period for Ambelvist (gadoquatrane) injection shall be 36 months from the date of manufacture when stored at 25°C (77°F) with excursions permitted to 15-30°C (59-86°F).

ADVISORY COMMITTEE

Your application for AMBELVIST was not referred to an FDA advisory committee because outside expertise was not necessary; there were no controversial issues that would benefit from advisory committee discussion.

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.

We note that you have fulfilled the pediatric studies requirement for all relevant pediatric age groups for this application.

POSTMARKETING REQUIREMENTS UNDER 505(o)

Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (FDCA) authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to assess signals of serious risks of behavioral and neurological changes that may result from gadolinium retention in the brain and other organs.

Furthermore, the active postmarket risk identification and analysis system as available under section 505(k)(3) of the FDCA will not be sufficient to assess these serious risks.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following study:

5002 Conduct a prospective longitudinal cohort study with one or more matched control group(s) to evaluate the effects of repetitive gadoquatrane administration on a comprehensive battery of neurobehavioral testing over the course of at least five administrations. The study should be sufficiently powered to exclude a prespecified magnitude of decline. As a secondary objective, study patients should also have the option of providing blood and urine samples at the time of reimaging, so that normative estimates of gadolinium concentration across an extended range of post-administration timepoints may be documented.

We acknowledge that you will participate in the existing ODYSSEY study with the other GBCA sponsors.

The Interim Report should contain a summary of patient enrollment listed by:

- Study initiation (first patient enrolled at each site)
- Number of patients at each site listed by condition under yearly contrast MRI surveillance
- Number of patients receiving gadoquatrane
- Number of patients providing blood and urine samples for gadolinium levels
- Number of dropouts

The timetable you submitted on May 18, 2026, states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	10/2026
Final Protocol Submission:	02/2027
Interim Report Submission:	04/2027
Study/Trial Completion:	04/2028
Final Report Submission:	04/2029

FDA considers the term *final* to mean that the applicant has submitted a protocol, the FDA review team has sent comments to the applicant, and the protocol has been revised as needed to meet the goal of the study or clinical trial.[3]

[3] See the guidance for industry *Postmarketing Studies and Clinical Trials—Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act* (October 2019). https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format—Promotional Labeling and Advertising Materials for Human Prescription Drugs.*

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the Prescribing Information, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at FDA.gov.[4] Information and Instructions for completing the form can be found at FDA.gov.[5]

REPORTING REQUIREMENTS

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

POST APPROVAL FEEDBACK MEETING

New molecular entities qualify for a post approval feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, call the Regulatory Project Manager for this application.

COMPENDIAL STANDARDS

A drug with a name recognized in the official United States Pharmacopeia or official National Formulary (USP-NF) generally must comply with the compendial standards for strength, quality, and purity, unless the difference in strength, quality, or purity is plainly stated on its label (see FD&C Act § 501(b), 21 USC 351(b)). FDA typically cannot share application-specific information contained in submitted regulatory filings with third parties, which includes USP-NF. To help ensure that a drug continues to comply with compendial standards, application holders may work directly with USP-NF to revise official USP monographs. More information on the USP-NF is available on USP's website.[6]

[4] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf
[6] https://www.uspnf.com/

If you have any questions, contact Ms.Sharon Thomas, Regulatory Project Manager, at sharon.thomas@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

A. Alex Hofling, M.D., Ph.D.
Director
Office of Specialty Medicine
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Medication Guide
- Carton and Container Labeling

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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