

MEMORANDUM

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FDA / CBER / OTAT / DCEPT

BLA 125613/0

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Product/Trade Name Rabies Immune Globulin (Human)/ KEDRAB

Applicant Kamada Ltd.

Proposed Indication Passive, transient post-exposure prophylaxis of rabies infection, when given immediately after contact with a rabid or possibly rabid animal and in combination concurrently with a full course of rabies vaccine

Product Reviewers Ewa Marszal, PhD; Lu Deng, PhD; Malgorzata Norton, MS; Olga Simakova, PhD; Lilin Zhong

Pankaj Amin

Pharm / Tox Reviewer Evi Struble, PhD

Clinical Reviewers Winson Tang, MD (OTAT)
(clinical studies, David Manschik, MD, MPH (OBE)
Pharmacovigilance, Alvandi Firoozeh, MD (OBE)
BiMO) Erin McDowell (BiMO)

Clinical Pharmacology Reviewer Xiaofei Wang, PhD

Statistical Reviewer Shuya Lu, PhD

Regulatory Project Manager Jiahua Quian

Recommendation Approval

Executive Summary

Kamada Ltd. submitted this Biologics License Application (BLA) to seek U.S. licensure for a plasma-derived concentrate of Rabies Immune Globulin (Human) (KEDRAB) for the passive, transient post-exposure prophylaxis of rabies infection, when given immediately after contact with a rabid or possibly rabid animal and in combination concurrently with a full course of rabies vaccine.

Please see primary reviews from Dr. Winson Tang (clinical), Dr. Shuya Lu (statistical), Dr. Eva Struble (pharmacology/toxicology), Dr. Xiaofei Wang (clinical pharmacology) and Dr. David Manschik (pharmacovigilance) for detailed reviews of this original BLA. The review team recommends approval of this BLA for the above indication.

I concur with the review team's recommendation on approval of the BLA for the proposed indication.

Notable Review Highlights

The BLA was comprised of three clinical studies enrolling 91 subjects: two Phase 1 studies and a single Phase 2/3 study. The primary evidence supporting the approval of KEDRAB for the proposed indication comes from the Phase 2/3 study, which was a single-center, prospective, randomized, double-blind, noninferiority study comparing the safety and efficacy of KEDRAB with another US human licensed rabies immune globulin (HyperRAB) in healthy volunteers. Of note, both rabies immune globulins were co-administered with an approved rabies vaccine, which is standard medical practice for post-exposure prophylaxis of suspected rabies infection worldwide. The study results demonstrated that KEDRAB is not inferior to HyperRAB when co-administered with a rabies vaccine.

Additionally, "real world evidence" procured from the Israeli Ministry of Health by the Applicant was utilized to support the efficacy of KEDRAB for rabies post-exposure prophylaxis. The Israeli Ministry of Health documented that none of the (b) (4) individuals who received post-exposure prophylaxis with Kamada's human rabies immune globulin in combination with an approved rabies vaccine between 2010 – 2015, developed clinical signs and symptoms of rabies. Of note, 1,863 individuals were documented to have had laboratory confirmed exposure to a rabid animal.

The clinical studies provided evidence that the safety profile of KEDRAB is acceptable, and the most common adverse events associated with KEDRAB were local site injection reactions. Routine post-marketing pharmacovigilance is recommended for surveillance.

The overall benefit-risk profile of KEDRAB is favorable.

Recommendations

Infection with rabies is universally fatal following onset of clinical symptoms. Post-exposure prophylaxis consisting of a rabies immune globulin in combination with a rabies vaccine is standard medical practice. KEDRAB offers an additional alternative for rabies immune globulin for post-exposure prophylaxis. Approval for KEDRAB is recommended for the passive, transient post-exposure prophylaxis of rabies infection, when given immediately after contact with a rabid or possibly rabid animal and in combination concurrently with a full course of rabies vaccine, as the clinical evidence provided in this BLA supports the safety/effectiveness of KEDRAB for this indication.