



Food and Drug Administration
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Kaneka Pharma America, LLC
% Miriam C. Provost, Ph.D.
Senior Consultant, Medical Devices
Biologics Consulting Group, Inc.
400 N. Washington Street, Suite 100
Alexandria, VA 22314

Re: H130001
HUD Number: 08-0208
Kaneka Lixelle[®] β 2-microglobulin Apheresis Column
Filed: February 1, 2013
Amended: June 5, 2013, February 4, 2014 (2), June 20, 2014, August 29, 2014, and November 3, 2014
Procodel: PDI

Dear Miriam C. Provost,

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your humanitarian device exemption (HDE) application for the Lixelle[®] β 2-microglobulin Apheresis Column (also called the Beta2-microglobulin Apheresis Column or β 2m). This device is indicated for the treatment of patients with clinically diagnosed dialysis-related amyloidosis (DRA). We are pleased to inform you that your HDE is approved. You may begin commercial distribution of the device in accordance with the conditions of approval described below.

The sale, distribution, and use of this device are limited to prescription use in accordance with 21 CFR 801.109 within the meaning of section 520(e) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) under the authority of section 515(d)(1)(B)(ii) of the FD&C Act. In addition, in order to ensure the safe use of the device, FDA has further restricted the device within the meaning of section 520(e) of the FD&C Act under the authority of section 515(d)(1)(B)(ii) of the FD&C Act insofar as the sale, distribution, and use must not violate sections 502(q) and (r) of the FD&C Act.

Expiration dating for this device has been established and approved at two (2) years.

Continued approval of this HDE is contingent upon the submission of periodic reports, required under 21 CFR 814.126, at intervals of one year (unless otherwise specified) from the date of approval of the original HDE. Two (2) copies of this report, identified as "Annual Report" and bearing the applicable HDE reference number, should be submitted to the address below. The Annual Report should indicate the beginning and ending date of the period covered by the report and should include the information required by 21 CFR 814.126.

In addition to the above, an HDE holder is required to maintain records of the names and addresses of the facilities to which the HUD has been shipped, correspondence with reviewing institutional review boards (IRBs), as well as any other information requested by a reviewing IRB or FDA.

This is a reminder that as of September 24, 2014, class III devices are subject to certain provisions of the final UDI rule. These provisions include the requirement to provide a UDI on the device label and packages (21 CFR 801.20), format dates on the device label in accordance with 21 CFR 801.18, and submit data to the Global Unique Device Identification Database (GUDID) (21 CFR 830 Subpart E). For more information on these requirements, please see the UDI website, <http://www.fda.gov/udi>.

In addition to the Annual Report requirements, you must provide the following data in post-approval study reports (PAS) for the PAS described below. Two (2) copies of the report, identified as an “OSB Lead HDE Post-Approval Study Report” in accordance with how the study is identified below and bearing the applicable HDE reference number, should be submitted to the address below.

OSB Lead HDE Post-Approval Study Report – H130001: Treatment of Dialysis-Related Amyloidosis Using Lixelle® β 2-microglobulin Apheresis Column: The Office of Surveillance and Biometrics (OSB) will have the lead for studies initiated after device approval. The “Treatment of Dialysis-Related Amyloidosis Using Lixelle® β 2-microglobulin Apheresis Column” study is described below:

New Enrollment PAS for the Lixelle β 2m Apheresis Column: You have agreed to conduct a study as follows: The purpose of the study is to evaluate the long-term safety and probable benefit of the Lixelle β 2m Apheresis Column for the treatment of patients with clinically-diagnosed dialysis related amyloidosis (DRA). This will be a prospective, multicenter, double arm study with a total of 40 newly enrolled patients treated at 3 to 15 clinical centers in the United States. The study participants will be followed for 24 months. The study population will consist of 30 DRA patients who will be treated with the device (treatment arm) and 10 patients who will be treated with conventional hemodialysis (HD) (natural history arm). All patients must agree to follow-up requirements, including questionnaires.

The primary study endpoint is the rate of every serious adverse event through two years of Lixelle treatment, compared by descriptive statistics to the rate in the natural history arm. Data on all adverse events will be collected. There are two secondary endpoints to assess the probable benefit of Lixelle in serum β 2m reduction rate following a single Lixelle-treatment: (1) β 2m reduction rates obtained in any week from the 2nd to 7th week of follow-up, statistically compared with what was obtained the week of treatment with conventional HD; (2) β 2m reduction rates obtained in any week from the 46th to 53rd week of follow-up, statistically compared with what was obtained the week of treatment with conventional HD. Paired t-test will be used to compare the reduction rates at baseline with the observed rates at follow-up assessments.

There are four exploratory endpoints to assess the change in quality of life (QoL) evaluated by Dialysis-Related Amyloidosis Questionnaire (DRAQ) and Kidney Disease Quality of Life-Short Form (KDQoL-SF), pre-treatment serum β 2m, and bone cyst through two years of

Lixelle-treatment.

Be advised that the failure to conduct any such study in compliance with the good clinical laboratory practices in 21 CFR part 58 (if a non-clinical study subject to part 58) or the institutional review board regulations in 21 CFR part 56 and the informed consent regulations in 21 CFR part 50 (if a clinical study involving human subjects) may be grounds for FDA withdrawal of approval of the HDE. In addition, the results from any post approval study should be included in the labeling as these data become available. Any updated labeling must be submitted to FDA in the form of a HDE Supplement. For more information on post-approval studies, see the FDA guidance document entitled, "Procedures for Handling Post-Approval Studies Imposed by PMA Order" (<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070974.htm>).

Within 30 days of your receipt of this letter, you must submit an HDE supplement that includes a complete protocol of your post-approval study described above. Your HDE supplement should be clearly labeled as an "OSB Lead HDE Post-Approval Study Protocol" as noted above and submitted in triplicate to the address below. Please reference the HDE number above to facilitate processing. If there are multiple protocols being finalized after HDE approval, please submit each protocol as a separate HDE supplement.

Before making any change affecting the safety or effectiveness of the device, you must submit an HDE supplement or an alternate submission (30-day notice) in accordance with 21 CFR 814.39 except a request for a new indication for use for a humanitarian use device (HUD). A request for a new indication for use for an HUD shall comply with the requirements set forth in 21 CFR 814.110 which includes obtaining a new designation of HUD status for the new indication for use and submission of an original HDE application in accordance with §814.104. The application for the new indication for use may incorporate by reference any information or data previously submitted to the agency.

You are reminded that many FDA requirements govern the manufacture, distribution, and marketing of devices. For example, in accordance with the Medical Device Reporting (MDR) regulation, 21 CFR 803.50 and 21 CFR 803.52, you are required to report adverse events for this device. Manufacturers of medical devices, including in vitro diagnostic devices, are required to report to FDA no later than 30 calendar days after the day they receive or otherwise becomes aware of information, from any source, that reasonably suggests that one of their marketed devices:

1. May have caused or contributed to a death or serious injury; or
2. Has malfunctioned and such device or similar device marketed by the manufacturer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

Additional information on MDR, including how, when, and where to report, is available at www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm.

In accordance with the recall requirements specified in 21 CFR 806.10, you are required to submit a written report to FDA of any correction or removal of this device initiated by you to: (1) reduce a risk to health posed by the device; or (2) remedy a violation of the act caused by the device which

may present a risk to health, with certain exceptions specified in 21 CFR 806.10(a)(2). Additional information on recalls is available at www.fda.gov/Safety/Recalls/IndustryGuidance/default.htm.

FDA has determined that this device meets the conditions of either (I) or (II) under section 520(m)(6)(A)(i) of the Federal Food, Drug, and Cosmetic Act (FD&C Act). This device may be sold for an amount that exceeds the costs of research and development, fabrication, and distribution of the device (i.e., for profit) as long as the number of devices distributed in any calendar year does not exceed the annual distribution number (ADN). The ADN for this device is determined to be 624,000 (4,000 patients * 52 weeks * 3 devices per week). You must immediately notify the agency by submitting an HDE report (21 CFR 814.126) whenever the number of devices shipped or sold in a year exceeds the ADN. FDA may also inspect the records relating to the number of your devices distributed during any calendar year. See section 520(m)(6)(B) of the FD&C Act. If you notify the FDA that the ADN has been exceeded, or if FDA discovers through an inspection that the ADN has been exceeded, then you are prohibited to sell your device for profit for the remainder of the year. See section 520(m)(6)(D) of the FD&C Act. If additional information arises regarding the ADN for your device, you may submit an HDE supplement (21 CFR 814.108) requesting that FDA modify the ADN based upon this additional information. See section 520(m)(6)(C) of the FD&C Act.

If this device is indicated and labeled for use in pediatric patients or in a pediatric subpopulation and is permitted by FDA to be sold for profit in accordance with section 520(m)(6)(A)(i)(1) of the FD&C Act, and therefore will be subject to annual review by the agency's Pediatric Advisory Committee (PAC). As stated in section 520(m)(8) of the FD&C Act, the PAC annually reviews all HUDs described in section 520(m)(6)(A)(i)(1) of the FD&C Act, which are HUDs approved under an HDE that are intended for the treatment or diagnosis of a disease or condition that occurs in pediatric patients or in a pediatric subpopulation, and such device is labeled for use in pediatric patients or in a pediatric subpopulation in which the disease or condition occurs, and that are exempt from the profit prohibition, in accordance with section 520(m)(6) of the FD&C Act. See section 520(m)(8) of the FD&C Act, as amended by FDASIA. The PAC reviews these devices to ensure that the HDE remains appropriate for the pediatric populations for which it is approved, in accordance with 520(m)(2) of the FD&C Act. The requirements under section 520(m)(2) of the FD&C Act include that (1) the target population of the device is fewer than 4,000 individuals in the United States; (2) the device would not be available to a person with the disease or condition without the HDE and there is no comparable device to available to treat or diagnose such disease or condition; and (3) the device does not expose patients to an unreasonable risk or significant risk of illness or injury and the probable benefit to health from the use of the device outweighs risk of injury or illness from its use, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment. The PAC will also conduct periodic review of adverse events for this device.

Failure to comply with any post-approval requirement constitutes a ground for withdrawal of approval of an HDE. The introduction or delivery for introduction into interstate commerce of a device that is not in compliance with its conditions of approval is a violation of law.

CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading. CDRH will notify the public of its decision to approve your HDE by making available a summary of the safety and probable benefit of

the device upon which the approval was based. The information can be found on the FDA CDRH Internet HomePage located at <http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/HDEApprovals/ucm161827.htm>. Written requests for this information can also be made to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. The written request should include the HDE number or docket number. Within 30 days from the date that this information is placed on the Internet, any interested person may seek review of this decision by requesting an opportunity for administrative review, either through a hearing or review by an independent advisory committee, under section 515(g) of the FD&C Act.

You are reminded that, as soon as possible and before commercial distribution of your device, you must submit an amendment to this HDE submission with copies of all approved labeling in final printed form. The labeling will not routinely be reviewed by FDA staff when HDE applicants include with their submission of the final printed labeling a cover letter stating that the final printed labeling is identical to the labeling approved in draft form. If the final printed labeling is not identical, any changes from the final draft labeling should be highlighted and explained in the amendment.

Any information to be submitted to FDA regarding this HDE should be submitted in triplicate, unless otherwise specified, to the address below and should reference the above HDE number to facilitate processing:

U.S. Food and Drug Administration
Center for Devices and Radiological Health
HDE Document Control Center – WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

If you have any questions concerning this approval order, please contact Frank Hurst, M.D. at (301) 796-5968.

Sincerely yours,

William H. Maisel -S

William Maisel, M.D.
Acting Director
Office of Device Evaluation
Center for Devices and Radiological Health
Food and Drug Administration