DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 020937 S-026
NDA 020975 S-027
NDA 020976 S-028

SUPPLEMENT APPROVAL

Liebel-Flarsheim Company LLC
Attention: Alice Lorenzo, MJ, MBe, RAC
Compliance Officer, North America Head Regulatory and Quality
821 Alexander Road, Suite 204
Princeton, NJ 08540

Dear Ms. Lorenzo:

Please refer to your Supplemental New Drug Applications (sNDAs) dated June 10, 2014, received June 10, 2014, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

Application	Submission Date	Received Date	Product Name
NDA 020937 S-026	July 21, 2016	July 21, 2016	Optimark (gadoversetamide) injection
NDA 020975 S-027	July 21, 2016	July 21, 2016	Optimark (gadoversetamide) injection Pharmacy Bulk Package
NDA 020976 S-028	July 21, 2016	July 21, 2016	Optimark (gadoversetamide) injection, solution

These "Prior Approval" supplements provide for revisions to the Prescribing Information that include:

In the Clinical Pharmacology (12.3 Pharmacokinetics section):

Deposition with Repeated Dosing

Increased signal intensity on non-contrast T1-weighted images within the brain, mainly the globus pallidus and the dentate nucleus, has been observed after multiple administrations of linear (ionic and nonionic) gadolinium-based contrast agents due to gadolinium deposition.

Following repeated GBCA administration, gadolinium deposits may be present for months or years in bone, liver, skin, brain, and other organs. Deposition depends on multiple factors and may be greater following administration of gadoversetamide and other linear GBCAs than following administration of macrocyclic GBCAs. GBCAs have been associated with the development of NSF in patients with renal impairment [see Boxed Warning]. The clinical significance of gadolinium retention in the body and brain is otherwise unknown.

We referred to our August 10, 2016, teleconference.

We acknowledge your amendments dated August10, 2016, and August 23, 2016.

APPROVAL & LABELING

We have completed our review of these supplemental applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

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 http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (text for the package insert), 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.

Information on submitting SPL files using eList may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/U CM072392.pdf

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 MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, 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).

Marketing the product(s) with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

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, call Su-Lin Sun, PharmD, Regulatory Project Manager, at (301) 796-0036 or email su-lin.sun@fda.hhs.gov .

Sincerely,

{See appended electronic signature page}

Alexander Gorovets, M.D.
Deputy Director
Division of Medical Imaging Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

ENCLOSURE:
Content of Labeling

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

ALEXANDER GOROVETS
08/29/2016