NDA 009190/S-029 and S-031

SUPPLEMENT APPROVAL

Guerbet LLC
Attention: Alice Lorenzo, MJ, MBe, RAC
Compliance Officer, NA Director of RA and Quality
821 Alexander Road, Suite 204
Princeton, NJ 08540

Dear Ms. Lorenzo:

Please refer to your supplemental new drug application (sNDA) dated June 28, 2019 and April 27, 2020, received June 28, 2019 and April 27, 2020, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for LIPIODOL® (ethiodized oil) Injection.

The June 28, 2019, Prior Approval supplemental new drug application provides for the labeling complying with the PLLR (Pregnancy and Lactation Labeling Rule) requirements as requested by the FDA letter dated June 17, 2019. The April 27, 2020, Change Being Effected (CBE-0) supplemental new drug application provides for the labeling changes to reflect the new safety information recommended in the FDAAA Safety Labeling Change Notification Letter issued on April 6, 2020.

We also refer to our letter dated April 6, 2020, notifying you, under Section 505(o)(4) of the FDCA, of new safety information that we believe should be included in the labeling for LIPIODOL® (ethiodized oil) Injection. This information pertains to the risk of a thyroid dysfunction risk in all patients (including euthyroid patients) undergoing hysterosalpingography (HSG) with Lipiodol and to the fetus or neonate of a subsequent pregnancy. The risk is characterized in the medical literature and FAERS reports.[1] Reference is also made to our Labeling Discussion Comments Letter dated May 13, 2020, that included proposed labeling changes to the Prior Approval Labeling Supplement to comply with the Pregnancy and Lactation Labeling (PLLR) requirements.

[1]Representative publications:
Mekaru et al. Thyroid function after hysterosalpingography using oil-soluble iodinated contrast medium. Gynecol Endocrinol. 2008;24: 498-501.

Kaneshige T et al. Changes in serum iodine concentration, urinary iodine excretion and thyroid function after hysterosalpingography using an oil-soluble iodinated contrast medium (lipiodol). J Clin Endocrinol Metab. 2015;100: 469-72.

These supplemental new drug applications provide for revisions to the labeling for LIPIODOL® (ethiodized oil) Injection, consistent with our April 6, 2020 and May 13, 2020 letters.

APPROVAL & LABELING

We have completed our review of these applications, as amended. They are 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 [21CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at FDA.gov.[2] Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information, 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 *SPL Standard for Content of Labeling Technical Qs and As*.[3]

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 Microsoft Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission(s), 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).

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety information that appears in the revised labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4).

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[2] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm
[3] 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.

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 Rene' Tyson, Safety Regulatory Project Manager, at (301) 796-1476.

Sincerely,

{See appended electronic signature page}

Ira Krefting, M.D.
Deputy Director for Safety
Division of Imaging and Radiation Medicine
Office of Specialty Medicine
Center for Drug Evaluation and Research

ENCLOSURE(S):

- Content of Labeling
- Prescribing Information

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/

IRA P KREFTING
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