DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 204781/S-005

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 September 1, 2017, received September 1, 2017, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Dotarem® (Gadoterate Meglumine) Injection.

This Prior Approval supplemental new drug application proposes the following changes to the Prescribing Information for the Pharmacy Bulk Package:

Page 1: Highlights: Dosage and Administration: after pediatric patients, missing "(including term neonates)."
Adverse Events: "burning sensation" updated to "rash" to match Table 2
Page 5: Section 6.1 Clinical Studies Experience:
Table 2: last line reads Burning Sensation but should state "Rash".
Remove comma before parenthesis "injection site reactions, (inflammation…"
Correct spelling of "paraestheisa" to paresthesia.
Under Adverse Reactions in Pediatric Patients: the word "years" is missing "…43 aged 12 – 17 years")
Last sentence: last word "severity" should be "intensity"
Page 6: Section 8.1 Pregnancy
Remove "Pregnancy Category C"
Correct spelling of "fertal" to "fetal" exposure
Under Animal Data:
Correct "intravenously in doses" to "intravenous doses"
Correct "[or 3, 6, and 16" to "[3, 7, 16…"
Add parenthesis to BSA: "(BSA)"
Remove the word or from "(or 3, 10 and 23 times)"
Remove in rats or rabbits, "No effects on embryo-fetal development were observed in rats or rabbits …"
Page 7: replace "or" with "and": "…in rats and 3 mmol/kg/day in rabbits"
Under 8.2 Lactation, missing "Risk Summary"

Make italic "(see Data)."
Section 8.4 Pediatric Use: add the "s" after week: "…37 weeks gestational age)"
Make Italic "[see Adverse Reactions (6.1)]
Correct "dosage" to "dose"
Lower case "s" and add comma to "[See Dosage and Administration (2.1), Pharmacokinetics"
Make italic the brackets for "[see Warnings and Precautions (5.1)]."
8.5 Geriatric Use: Correct number of patients from 312 to 306.
Page 8: Section 10: Overdosage: add adult to read "and to adult patients at cumulative doses"
Page 11: Section 14: Clinical Studies: underline the subsection "CNS Imaging"
Finally, additional spacing corrections were made to improve readability.

APPROVAL & LABELING

We have completed our review of this supplemental application, as amended. It is 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/UCM072392.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).

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, please contact Su-Lin Sun, PharmD, Senior Regulatory Project Manager by email su-lin.sun@fda.hhs.gov , or by phone (301)796-0036.

Sincerely,

{See appended electronic signature page}

Libero Marzella, M.D., Ph.D.
Director
Division of Medical Imaging Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

ENCLOSURE:
Content of Labeling for Pharmacy Bulk Pack

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

/s/

LIBERO L MARZELLA
09/14/2017