DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202342

NDA APPROVAL

Hanmi USA Inc.
c/o Parexel International, LLC
Attention: Young-Sil (Anna) Yim
Consultant, Parexel Consulting
4600 East-West Hwy, Suite 350
Bethesda, MD 20814

Dear Ms. Yim:

Please refer to your New Drug Application (NDA) dated and received October 15, 2010, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for esomeprazole strontium delayed-release capsules, 24.65 mg and 49.3 mg.

We acknowledge receipt of your amendments dated October 19, 2010, November 23, 2010, December 10, 2010, December 13, 2010, January 14, 2011, February 1, 2011, February 15, 2011, March 31, 2011, May 13, 2011, May 26, 2011, May 27, 2011, May 31, 2011, June 3, 2011, June 10, 2011, June 16, 2011, June 27, 2011, August 17, 2011, September 8, 2011, September 19, 2011, September 26, 2011, October 4, 2011, October 13, 2011, October 26, 2011, November 1, 2011, November 30, 2011, December 5, 2011, December 12, 2011, December 21, 2011, March 27, 2012, May 31, 2012, June 13, 2012, June 20, 2012, October 29, 2012, November 20, 2012, November 21, 2012, February 5, 2013, February 7, 2013, February 14, 2013, February 27, 2013, March 19, 2013, April 2, 2013, April 9, 2013, April 18, 2013, April 24, 2013, April 29, 2013, June 6, 2013, June 18, 2013, and July 16, 2013.

The June 6, 2013, submission constituted a complete response to our April 29, 2013, action letter.

This new drug application provides for the use of esomeprazole strontium delayed-release capsules in adults for the treatment of gastroesophageal reflux disease (GERD), including healing of erosive esophagitis, maintenance of healing of erosive esophagitis and symptomatic gastroesophageal reflux disease; risk reduction of NSAID-associated gastric ulcer; *Helicobacter pylori (H. pylori*) eradication to reduce the risk of duodenal ulcer recurrence (in combination with amoxicillin and clarithromycin as triple therapy); and pathological hypersecretory conditions, including Zollinger-Ellison syndrome.

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

WAIVER OF HIGHLIGHTS SECTION

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

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 and Medication Guide). 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*, available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

CARTON AND IMMEDIATE-CONTAINER LABELS

Submit final printed carton and immediate-container labels that are identical to the enclosed immediate-container labels submitted on June 6, 2013, as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (June 2008)*. Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "**Final Printed Carton and Container Labels for approved NDA 202342**." Approval of this submission by FDA is not required before the labeling is used.

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

PROPRIETARY NAME

If you intend to have a proprietary name for this product, the name and its use in the labels must conform to the specifications under 21 CFR 201.10 and 201.15. We recommend that you submit a request for a proposed proprietary name review. (See the guidance for industry *Contents of a Complete Submission for the Evaluation of Proprietary Names*, available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/u

cm075068.pdf and "PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2008 through 2012".)

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirements for the following ages based on specific indications for this application because necessary studies are impossible or highly impractical:

- *Healing of erosive esophagitis:* Waive birth to less than 1 month
- *Maintenance of healing of erosive esophagitis:* Waive birth to less than 1 month
- *Symptomatic gastroesophageal reflux disease*: Waive birth to less than 1 month
- *Risk reduction of NSAID-associated gastric ulcer:* Waive birth to 23 months of age inclusive
- *H. pylori eradication to reduce the risk of duodenal ulcer recurrence:* Waive birth to 23 months of age inclusive
- *Pathological hypersecretory conditions including Zollinger-Ellison Syndrome:* Waive birth to 17 years of age inclusive

We are waiving the pediatric study requirements for *Symptomatic gastroesophageal reflux disease* in patients one month to less than 12 months of age because there is evidence that the product would be ineffective in that age group.

We are deferring submission of your pediatric studies for the following ages based on specific indications for this application because this product is ready for approval for use in adults and the pediatric studies have not been completed:

- *Healing of erosive esophagitis:* study deferred in patients 1 month to 17 years of age inclusive
- *Maintenance of healing of erosive* esophagitis: study deferred in patients 1 month to 17 years of age inclusive
- *Symptomatic gastroesophageal reflux disease:* study deferred in patients 1 year to 17 years of age inclusive.
- *Risk reduction of NSAID-associated gastric ulcer:* study deferred in patients 2 years to 17 years of age inclusive
- *H. pylori eradication to reduce the risk of duodenal ulcer recurrence:* study deferred in patients 2 years to 17 years of age inclusive

Your deferred pediatric studies required by section 505B(a) of the FDCA are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(B) of the FDCA. The required studies are listed below.

2054-1 Deferred pediatric study under PREA to evaluate the pharmacokinetics, pharmacodynamics, and safety of esomeprazole strontium for healing and maintenance of healing of erosive esophagitis (EE) in patients 1 month to 17 years, inclusive. The study must also assess the efficacy of esomeprazole strontium in maintenance of healing of EE, including determination of the dose and treatment duration required to maintain healing of EE in this pediatric population. The study must include an adequate number of patients in different age groups to inform dosing, and to evaluate the effect of esomeprazole strontium on bone, given that pediatric patients undergo different rates of growth depending on age. Baseline and post-treatment bone-related safety assessments must be included.

Final Report Submission: April 2018

2054-2 Deferred pediatric study under PREA to evaluate the safety of esomeprazole strontium for treating symptomatic gastroesophageal reflux disease (GERD) in patients 1 year to 17 years, inclusive. The study must include an adequate number of patients in different pediatric age groups to evaluate the effect of esomeprazole strontium on bone, given that pediatric patients undergo different rates of growth depending on age. Baseline and post-treatment bone-related safety assessments must be included. This study may not be needed if the data from PMR 2054-1 are adequate to fulfill the requirement.

Final Report Submission: April 2021

2054-3 Deferred pediatric study under PREA to evaluate the pharmacokinetics, pharmacodynamics, and safety of esomeprazole strontium for reducing the risk of NSAID-associated gastric ulcer in patients 2 years to 17 years, inclusive. The study must include an adequate number of patients in different age groups to inform dosing, and to evaluate the effect of esomeprazole strontium on bone, given that pediatric patients undergo different rates of growth depending on age. Baseline and post-treatment bone-related safety assessments must be included.

Final Report Submission: October 2018

2054-4 Deferred pediatric study under PREA to evaluate the safety and efficacy of esomeprazole strontium in combination with clarithromycin and amoxicillin for the eradication of *Helicobacter pylori* in symptomatic pediatric patients 2 to 17 years, inclusive, with or without duodenal ulcer disease.

Final Report Submission: April 2021

Submit the protocols to your IND 078801, with a cross-reference letter to this NDA.

Reports of these required pediatric postmarketing studies must be submitted as a new drug application (NDA) or as a supplement to your approved NDA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.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 CDR Stacy Barley, Senior Regulatory Project Manager, at (301) 796-2137.

Sincerely,

{See appended electronic signature page}

Donna Griebel, M.D.
Director
Division of Gastroenterology and Inborn Errors Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

ENCLOSURE(S): Content of Labeling & Container Labeling

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

/s/

DONNA J GRIEBEL
08/06/2013