DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 200153

NDA APPROVAL

Merck Sharp & Dohme Corp.
US Agent for MSD International GmbH
Attention: Catherine Kohler, Pharm. D.
Director Worldwide Regulatory Affairs
P.O. Box 1000
North Wales, PA 19454

Dear Dr. Kohler:

Please refer to your New Drug Application (NDA) dated and received September 2, 2009, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Liptruzet (ezetimibe and atorvastatin) Tablets, 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, and 10 mg/80 mg.

We acknowledge receipt of your amendments dated September 2 (2), 11, October 27, November 12 and 13, 2009, and April 13, 28 and 29, June 23, July 7, 18, 22, 28, and 29, August 10, 22, and 26, September 12, 14, and 22 (2), October 11, 17, and 31, November 11 and 14, 2011, and March 20, April 16, May 3, October 31, November 5, and December 14, 2012, February 6, 7, and 25, March 6, and April 2, 2013. We also acknowledge receipt of your email dated May 1, 2013, stating your agreement to the labeling revisions (Patient Information) that we communicated to you by email on May 1, 2013. Lastly, we acknowledge receipt of your email dated May 2, 2013, stating your agreement to the labeling revisions (Package Insert) that we communicated to you on May 2, 2013.

The November 5, 2012, submission constituted a complete response to our February 29, 2012, action letter.

This new drug application provides for the use of Liptruzet tablets as adjunctive therapy to diet to:

- reduce elevated total-C, LDL-C, Apo B, TG, and non-HDL-C, and to increase HDL-C in patients with primary (heterozygous familial and non-familial) hyperlipidemia or mixed hyperlipidemia.
- reduce elevated total-C and LDL-C in patients with homozygous familial hypercholesterolemia (HoFH), as an adjunct to other lipid-lowering treatments.

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, text for the patient package insert). 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 carton and immediate-container labels (submitted on April 2, 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 200153**." Approval of this submission by FDA is not required before the labeling is used.

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.

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 requirement for this application because for ages 0 through 9 years necessary studies are impossible or highly impracticable; for pediatric patients aged 10 through 17 this product does not represent a meaningful therapeutic benefit over existing

therapies for pediatric patients **and** is not likely to be used in a substantial number of pediatric patients.

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.

METHODS VALIDATION

We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified.

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 Kati Johnson, Regulatory Project Manager, at (301) 796-1234.

Sincerely,

{See appended electronic signature page}

Eric Colman, MD
Deputy Director
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosures: Content of Labeling (Package Insert and Patient Information)

Carton and Container Labeling

Sample Labeling:

Liptruzet 10/10 foil pouch (7 tablets)
Liptruzet 10/10 blister (7 tablets)
Liptruzet 10/10 carton (28 tablets)

Liptruzet 10/20 foil pouch (7 tablets)
Liptruzet 10/20 blister (7 tablets)
Liptruzet 10/20 carton (28 tablets)

Liptruzet 10/40 foil pouch (7 tablets)
Liptruzet 10/40 blister (7 tablets)
Liptruzet 10/40 carton (28 tablets)

Liptruzet 10/80 foil pouch (7 tablets)
Liptruzet 10/80 blister (7 tablets)
Liptruzet 10/80 carton (28 count)

Trade Labeling:

Liptruzet 10/10 foil pouch (10 tablets)
Liptruzet 10/10 plastic case front
Liptruzet 10/10 plastic case back
Liptruzet 10/10 foil lidding
Liptruzet 10/10 carton (30 tablets)
Liptruzet 10/10 carton (90 tablets)

Liptruzet 10/20 foil pouch (10 tablets)
Liptruzet 10/20 plastic case front
Liptruzet 10/20 plastic case back
Liptruzet 10/20 foil lidding
Liptruzet 10/20 carton (30 tablets)
Liptruzet 10/20 carton (90 tablets)

Liptruzet 10/40 foil pouch (10 tablets)
Liptruzet 10/40 plastic case front
Liptruzet 10/40 plastic case back
Liptruzet 10/40 foil lidding
Liptruzet 10/40 carton (30 tablets)
Liptruzet 10/40 carton (90 tablets)

Liptruzet 10/80 foil pouch (10 tablets)
Liptruzet 10/80 plastic case front
Liptruzet 10/80 plastic case back
Liptruzet 10/80 foil lidding
Liptruzet 10/80 carton (30 tablets)
Liptruzet 10/80 carton (90 tablets)

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

/s/

ERIC C COLMAN
05/03/2013