DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022519

NDA APPROVAL

Horizon Pharma, Inc.
Attention: Timothy P. Walbert
President and Chief Executive Officer
1033 Skokie Boulevard, Suite 355
Northbrook, IL 60062

Dear Mr. Walbert:

Please refer to your New Drug Application (NDA) dated March 22, 2010, received March 23, 2010, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for DUEXIS (ibuprofen and famotidine) Tablets, 800 mg/26.6 mg.

We acknowledge receipt of your amendments dated April 16, 2010; June 25, 2010; July 9, 2010; July 22, 2010; July 27, 2010; August 12, 2010; August 13, 2010; September 7, 2010; September 21, 2010; September 24, 2010; October 13, 2010; October 18, 2010; October 21, 2010; November 10, 2010; November 18, 2010; November 22, 2010; December 16, 2010; December 21, 2010; February 8, 2011; February 15, 2011; March 16, 2011; March 22, 2011; March 29, 2011; April 4, 2011; April 14, 2011; April 18, 2011; April 21, 2011; and April 22, 2011.

This new drug application provides for the use of DUEXIS (ibuprofen/famotidine) tablets for the relief of signs and symptoms of rheumatoid arthritis and osteoarthritis and to decrease the risk of developing upper gastrointestinal ulcers, which in the clinical trials was defined as a gastric and/or duodenal ulcer, in patients who are taking ibuprofen for those indications. The clinical trials primarily enrolled patients less than 65 years of age without a prior history of gastrointestinal ulcer. Controlled trials do not extend beyond 6 months.

After consultations between the Office of New Drugs and the Office of Surveillance and Epidemiology, we have reconsidered the need for a REMS for this product. We believe that a Medication Guide is necessary to inform patients of the serious risks of cardiovascular and gastrointestinal adverse events. However, since other drugs currently approved in the nonsteroidal anti-inflammatory drug (NSAID) class have Medication Guides with identical safety information regarding these risks that are not included in a REMS, we will not require a REMS.

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.

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, Medication Guide). 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/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

IMMEDIATE CONTAINER LABELS

Submit final printed container labels that are identical to the immediate container labels submitted on March 29, 2011, 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 titled "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 Container Labels for approved NDA 022519**." 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.

MARKET PACKAGE

Please submit one market package of the drug product when it is available.

If sending via USPS, please send to:

Jagjit Grewal
Food and Drug Administration
Center for Drug Evaluation and Research
White Oak Building 22, Room: 5109
10903 New Hampshire Avenue
Silver Spring, Maryland 20993

If sending via any carrier other than USPS (e.g., UPS, DHL), please send to:

Jagjit Grewal
Food and Drug Administration
Center for Drug Evaluation and Research
White Oak Building 22, Room: 5109
10903 New Hampshire Avenue
Silver Spring, Maryland 20903

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 in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for ages 0 to 1 year, 11 months because necessary studies are impossible or highly impracticable. This is because of the low incidence of juvenile idiopathic arthritis in children less than 2 years of age.

We are deferring submission of your pediatric studies for ages 2 years to 16 years, 11 months for this application because this product is ready for approval for use in adults and the pediatric studies have not been completed.

Your deferred pediatric studies required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act 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 Federal Food, Drug, and Cosmetic Act. These required studies are listed below.

1758-1 Development of an age appropriate formulation of ibuprofen/famotidine to be used in pediatric patients.

Final Protocol Submission:	July 2013
Study/Trial Completion:	July 2015
Final Report Submission:	March 2016

1758-2 A study to characterize ibuprofen and famotidine pharmacokinetic (PK) parameters following administration of a single dose of a new formulation (suspension) of ibuprofen/famotidine combination in healthy human subjects. PK endpoints must include PK parameters for both ibuprofen and famotidine such as CT, C_{max}, T_{max}, AUC, $T_{1/2}$, clearance, and Vd_{ss}, as applicable.

Final Protocol Submission:	July 2016
Study/Trial Completion:	December 2016
Final Report Submission:	March 2017

1758-3 A study to evaluate the pharmacokinetics (PK) and safety of HZT-501 in children and adolescents ages 10 years through 16 years, 11 months of age who require chronic treatment with NSAIDs. The pediatric study will be a 6-month (24-week), multicenter, open-label study to evaluate the safety of DUEXIS in children and adolescents ages 10 years to 16 years, 11 months.

Final Protocol Submission:	October 2011
Study/Trial Completion:	October 2013

Final Report Submission: May 2014

1758-4 A study to evaluate the pharmacokinetics (PK) and safety of an age-appropriate formulation of ibuprofen/famotidine to be used in children and adolescents ages 2 years through 9 years, 11 months of age who require chronic treatment with NSAIDs. The pediatric study will be a 6-month (24-week), multicenter, open-label study to evaluate the safety of DUEXIS in children and adolescents ages 2 years to 9 years, 11 months.

Final Protocol Submission: January 2016
Study/Trial Completion: January 2018
Final Report Submission: July 2018

Submit final reports to this NDA. For administrative purposes, all submissions related to these required pediatric postmarketing studies must be clearly designated "**Required Pediatric Assessments**".

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

We acknowledge receipt of your submission dated March 22, 2010, of a proposed risk evaluation and mitigation strategy (REMS). We have determined that, at this time, a REMS is not necessary for DUEXIS to ensure that its benefits outweigh its risks. We will notify you if we become aware of new safety information and make a determination that a REMS is necessary.

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
Division of Drug Marketing, Advertising, and Communications
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 Division of Drug Marketing, Advertising, and Communications (DDMAC), 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 Jagjit Grewal, Regulatory Project Manager, at (301) 796-0846.

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

Enclosures: Package Insert Label and Medication Guide
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
04/23/2011