DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-332

Amylin Pharmaceuticals, Inc.
Attention: Joann L. Data, M.D., Ph.D.
Senior Vice President, Regulatory Affairs and Quality Assurance
9360 Towne Centre Drive, Suite 110
San Diego, CA 92121-3030

Dear Dr. Data:

Please refer to your new drug application (NDA) dated December 7, 2000, received December 8, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for SYMLIN® (pramlintide acetate) Injection, 5 mL vials.

We acknowledge receipt of your submissions dated December 18, 2003, January 7, February 13, May 27, June 21, July 2 and 16, August 9, September 8, 9, and 17, and December 3 and 17, 2004, and January 31, February 2, 3, 7, 9, 11, 16, 17 (2), 18, 24 (3), 25 (2), and 28 (2), and March 1, 3, 7, 8, 9, 10, 14, and 16, 2005.

The September 17, 2004, submission constituted a complete response to our December 17, 2003, action letter.

This new drug application provides for the use of SYMLIN (pramlintide acetate) Injection for the following indications:

- Type 1 diabetes, as an adjunct treatment in patients who use mealtime insulin therapy and who have failed to achieve desired glucose control despite optimal insulin therapy.

- Type 2 diabetes, as an adjunct treatment in patients who use mealtime insulin therapy and who have failed to achieve desired glucose control despite optimal insulin therapy, with or without a concurrent sulfonylurea agent and/or metformin.

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 agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed labeling submitted on March 14, 2005, (text for the package insert, text for the Medication Guide, immediate container and carton labels for 5 mL vials). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format – NDAs*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission as "**FPL for approved NDA 21-332**." Approval of this submission by FDA is not required before the labeling is used.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. For this application, we are waiving the pediatric study requirement for ages less than or equal to 11 years and deferring pediatric studies for ages 12 to less than or equal to 17 years.

Your deferred pediatric study required under section 2 of the Pediatric Research Equity Act (PREA) is considered a required postmarketing study commitment. The status of this postmarketing study shall be reported annually according to 21 CFR 314.81. This commitment, as outlined in your submission dated March 7 and 16, 2005, is listed below.

1. A study of SYMLIN in adolescents ages 12 to less than or equal to 17 years with type 1 and type 2 diabetes to evaluate the pharmacokinetics and relevant pharmacodynamic effects of different subcutaneous doses of the drug**.**

   Final Report Submission: September 30, 2007

   For administrative purposes, all submissions related to this pediatric postmarketing study commitment should be clearly designated "**Required Pediatric Study Commitment**."

We also remind you of your postmarketing study commitment to conduct an observational study as described in your submissions dated March 1 and 9, 2005, and listed below.

2. A multicenter, open-label, observational study to prospectively collect data that characterize the use of SYMLIN following introduction into the marketplace. This study will include non-targeted prescribers in the same approximate proportion as targeted prescribers.

Protocol Submission:	April 30, 2005
Study Start:	September 30, 2005
Final Report Submission:	September 30, 2008

Submit clinical protocols for these postmarketing commitment studies to your IND for this product. Submit study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and number of patients entered to date into each study. All submissions, including supplements, relating to these

postmarketing study commitments should be prominently labeled "**Postmarketing Study Protocol**", "**Postmarketing Study Final Report**", or "**Postmarketing Study Correspondence**."

Additionally, we remind of your agreements, in your submissions dated February 24 and March 8, 2005, to risk management procedures designed to encourage the safe and effective use of SYMLIN. These agreements include the following:

- No direct-to-consumer advertisement.
- No journal advertisement for one year after SYMLIN is launched.
- Promotion limited primarily to physicians who specialize in diabetes management and are supported by certified diabetes educators.
- Gradual introduction of SYMLIN into the marketplace, with concomitant evaluation of patterns of SYMLIN use by "targeted" and "non-targeted" health care providers. To this end, you will assess available databases for information regarding SYMLIN prescription practices and submit the results of these assessments on a semiannual basis.
- Education and outreach programs for health care providers and patients.
- Conduct of a postmarketing observational study to assess the potential hypoglycemic risk for SYMLIN in the actual use setting (an effort will be made to also enroll "non-targeted" health care providers").
- Surveillance Plan: reporting of severe hypoglycemic events in an expedited manner for two years or as long as the postmarketing observational study remains ongoing, whichever is longer.
- A 24/7 nationwide call center to assist patients and physicians with the use of SYMLIN.

Submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to the Division of Metabolic and Endocrine Drug Products and two copies of both the promotional materials and the package inserts directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

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

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

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is eligible to receive

copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at www.fda.gov/medwatch/report/mmp.htm.

If you have any questions, call Julie Rhee, Regulatory Project Manager, at (301) 827-6424.

Sincerely,

{See appended electronic signature page}

Robert J. Meyer, M.D.
Director
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosures:
1. Physician insert
2. Medication Guide
3. Carton label for 5 mL vial
4. Immediate container label for 5 mL vial

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

/s/

Robert Meyer

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