

REMS Document

Initial REMS Approval: 06/2014

Most Recent Modification: 09/2015

NDA 021-332

SYMLIN[®] (pramlintide acetate) injection

Drug Class: Synthetic analog of human amylin

AstraZeneca Pharmaceuticals LP

1800 Concord Pike

P.O Box 8355

Wilmington, DE, 19803-8355

1-800-236-9933

RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOAL(S):

The goal of the SYMLIN REMS is to mitigate the risk of severe hypoglycemia associated with SYMLIN by:

- informing health care providers about the risk of severe hypoglycemia as SYMLIN is used with insulin and the importance of insulin dose reduction
- informing health care providers of the importance of proper patient selection for treatment with SYMLIN

II. REMS ELEMENTS:

A. Communication Plan

AstraZeneca will implement a communication plan to health care providers to support implementation of this REMS.

1. REMS Communications
 - a. REMS Letters

REMS Letters will be sent to a selected group of health care providers and professional societies. The REMS Letter will address the risk of severe hypoglycemia, the importance of insulin dose reduction and proper patient selection. The letter will be distributed within 60 days of approval of the SYMLIN REMS and again one year from the date of initial approval for the SYMLIN REMS. SYMLIN REMS Letter will be distributed via electronic means (email and/or fax) or by mail within one week if no email or fax contact information is available. If the electronic communication is returned due to an invalid email address or

undeliverable for any other reason, the health care providers will receive the letter through mail within 30 days.

A copy or a link to the Prescribing Information and REMS Factsheet will accompany each REMS Letter.

In addition, the REMS Letter, Prescribing Information and REMS Factsheet will also be available on the SYMLIN REMS website [www.symlinrems.com].

i. REMS Letter for Health Care Providers

The intended audience for this *REMS Letter for Health Care Providers* will be providers who have prescribed SYMLIN and/or have frequently prescribed mealtime insulin within the past 12 months, including physicians, nurse practitioners, and physician assistants.

ii. REMS Letter for Professional Organizations

A *REMS Letter for Professional Societies* will be distributed by direct mail or electronic delivery within 60 days of the REMS approval date. This communication to professional organizations will include the same information as that contained in the *REMS Letter for Health Care Providers*. AstraZeneca will request that these organizations disseminate this information to their members. AstraZeneca will communicate the letter to the leadership of the following professional organizations:

- American Association of Clinical Endocrinologists (AACE)
- American College of Endocrinology (ACE)
- American Diabetes Association (ADA)
- The Endocrine Society (Endo)
- National Diabetes Education Program (NDEP)
- National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)
- American Academy of Family Physicians (AAFP)
- American College of Physicians (ACP)
- National Medical Association (NMA)
- Society of General Internal Medicine (SGIM)
- American Academy of Nurse Practitioners (AANP)
- American Academy of Physician Assistants (AAPA)
- American Association of Diabetes Educators (AADE)
- Endocrine Nurses Society (ENS)
- American Nurses Association (ANA)
- Family Medicine Residency Nurses Association (FMRNA)
- American Pharmacists Association (APhA)
- American Society of Health-System Pharmacists (ASHP)
- National Association of Chain Drug Stores (NACDS)
- National Community Pharmacy Association (NCPA).

The REMS Factsheet and Prescribing Information will be provided in conjunction with the Letter.

The following REMS Correspondences are part of the REMS and are appended.

- REMS Letter for Health Care Providers (print version)
- REMS Letter for Health Care Providers (email version)
- REMS Letter for Professional Societies (print version)
- REMS Letter for Professional Societies (email version)

2. REMS Factsheet

A REMS Factsheet for health care providers will be distributed via non-personal (as an enclosure in the Letters) and personal methods (by field personnel during the first discussion of SYMLIN with health care providers during the 12-months following REMS approval).

The REMS Factsheet for health care providers is part of the REMS and is appended.

3. Scientific Meetings

The SYMLIN Factsheet and the Prescribing Information will be prominently displayed at scientific meetings where AstraZeneca has a presence (e.g., booth) 18 months after approval of the initial REMS.

4. REMS Website

The Symlin REMS Program Website [www.symmlinrems.com] will include the option to print the PI, Medication Guide, REMS Letters, and REMS Factsheet. The SYMLIN product website will include a prominent REMS-specific link to SYMLIN REMS Program Website. All website information will be updated within 60 days post approval of the most recent modification. The SYMLIN REMS website is part of the REMS and is appended.

B. Timetable for Submission of Assessments

AstraZeneca will submit REMS Assessments to the FDA at 18 months, 3 years, and 7 years from the date of the REMS approval. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 days before the submission date for that assessment. AstraZeneca will submit each assessment so that it will be received by the FDA on or before the due date.

FDA Required REMS Safety Information

- Risk of severe hypoglycemia with use of SYMLIN added to mealtime insulin
- Importance of insulin dose reduction
- Proper patient selection

Important Safety Update

The FDA has required this safety update as part of the SYMLIN REMS (Risk Evaluation and Mitigation Strategy) program to inform health care providers about the following **serious risks of SYMLIN (pramlintide acetate)**:

- **Increased risk of severe hypoglycemia, particularly in patients with type 1 diabetes.**
- **Importance of insulin dose reduction**
Counsel and instruct your patients on insulin dose reduction to minimize the risk of hypoglycemia.
- **Proper patient selection.** SYMLIN is **contraindicated** in patients with any of the following:
 - Hypoglycemia unawareness
 - Confirmed gastroparesis
 - Serious hypersensitivity to SYMLIN or any of its product components

A non-promotional factsheet, reviewed by the FDA, with more detailed safety information is enclosed.

Indication: SYMLIN is an amylin analog indicated for patients with type 1 or type 2 diabetes who use mealtime insulin and have failed to achieve desired glycemic control despite optimal insulin therapy.

Please visit www.SYMLINREMS.com for more information.

This letter does not contain the complete safety profile for SYMLIN. Please see the Prescribing Information and Medication Guide, enclosed.

Reporting Adverse Events

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Sincerely,



James Blasetto MD, MPH
VP US Medical Affairs, Evidence Generation

Enclosure: REMS Factsheet, SYMLIN Prescribing Information with Medication Guide



SYMLIN and SymlinPen are registered trademarks of the AstraZeneca group of companies.

Subject: Risk of severe hypoglycemia and the importance of proper patient selection with SYMLIN

To: < First Name Last Name >

From: AstraZeneca [AstraZeneca@message.pdr-mail.com]

Date: MM/DD/YYYY

Can't see the images? [View the Web version](#). Add AstraZeneca@message.pdr-mail.com to your safe senders list.

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(pramlintide acetate)
pen-injector

FDA Required REMS Safety Information



Risk of severe hypoglycemia with use of SYMLIN added to mealtime insulin



Importance of insulin dose reduction



Proper Patient Selection

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[Prescribing Information](#) | [Medication Guide](#)

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FDA Required REMS Safety Information

- Risk of severe hypoglycemia with use of SYMLIN added to mealtime insulin
- Importance of insulin dose reduction
- Proper patient selection

Important Safety Update

Dear [Professional Organization]

The FDA has required AstraZeneca to distribute this safety update to your organization as part of their SYMLIN REMS (Risk Evaluation and Mitigation Strategy) program. We request that you inform your members about the following **serious risks of SYMLIN (pramlintide acetate)**:

- **Increased risk of severe hypoglycemia, particularly in patients with type 1 diabetes.**
- **Importance of insulin dose reduction**
It is important to counsel and instruct patients on insulin dose reduction to minimize the risk of hypoglycemia.
- **Proper patient selection.** SYMLIN is **contraindicated** in patients with any of the following:
 - Hypoglycemia unawareness
 - Confirmed gastroparesis
 - Serious hypersensitivity to SYMLIN or any of its product components

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James Blasetto MD, MPH
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Enclosure: REMS Factsheet, SYMLIN Prescribing Information with Medication Guide



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To: < First Name Last Name >

From: AstraZeneca [AstraZeneca@message.pdr-mail.com]

Date: MM/DD/YYYY

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FDA Required REMS Safety Information

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FDA Required SYMLIN REMS Safety Information

WARNING: SEVERE HYPOGLYCEMIA

SYMLIN use with insulin increases the risk of severe hypoglycemia, particularly in patients with type 1 diabetes. When severe hypoglycemia occurs, it is seen within 3 hours following a SYMLIN injection. Serious injuries may occur if severe hypoglycemia occurs while operating a motor vehicle, heavy machinery, or while engaging in other high-risk activities. Appropriate patient selection, careful patient instruction, and insulin dose reduction are critical elements for reducing this risk.



Proper Patient Selection

SYMLIN is contraindicated in patients with any of the following:

- serious hypersensitivity reaction to SYMLIN or to any of its ingredients;
- hypoglycemia unawareness;
- confirmed gastroparesis

Proper patient selection is critical to the safe and effective use of SYMLIN.

Before initiating SYMLIN, the patient's HbA1c, recent blood glucose monitoring data, history of insulin-induced hypoglycemia, current insulin regimen, and body weight should be reviewed. SYMLIN therapy should only be considered in patients with type 1 diabetes or patients with type 2 diabetes using mealtime insulin who fulfill the following criteria:

- have failed to achieve adequate glycemic control despite individualized insulin management;
- are receiving ongoing care under the guidance of a healthcare professional skilled in the use of insulin and supported by the services of diabetes educator(s)

Patients meeting any of the following criteria should **NOT** be considered for SYMLIN therapy:

- poor compliance with current insulin regimen;
- poor compliance with prescribed self blood glucose monitoring;
- have a HbA1c >9%;
- recurrent severe hypoglycemia requiring assistance during the past 6 months;
- presence of hypoglycemia unawareness;
- confirmed diagnosis of gastroparesis;
- require the use of drugs that stimulate gastrointestinal motility;
- pediatric patients;
- SYMLIN should be prescribed with caution to persons with visual or dexterity impairment



Insulin Dose Adjustment

When initiating SYMLIN, **reduce mealtime insulin doses, including premixed insulins, by 50% to reduce the risk of hypoglycemia (see DOSAGE and ADMINISTRATION of the SYMLIN prescribing information).**

Monitor blood glucose frequently, including pre- and post-meals and at bedtime, particularly when initiating SYMLIN or increasing the SYMLIN dose.

After the initial 50% reduction in mealtime insulin dose, individualize insulin dose adjustments based on glycemic control and tolerability (e.g., if nausea occurs it may affect the dose of insulin required).

An increased frequency of mild to moderate hypoglycemia should be viewed as a warning sign of increased risk for severe hypoglycemia.

SYMLIN alone does not cause hypoglycemia. However, SYMLIN is indicated to be co-administered with mealtime insulin therapy and in this setting there is an increased risk of severe hypoglycemia, particularly in patients with type 1 diabetes.

The addition of any anti-diabetic medication such as SYMLIN to an existing regimen of one or more anti-diabetic medications (e.g., sulfonylurea), or other medications that can increase the risk of hypoglycemia may necessitate further insulin dose adjustments and particularly close monitoring of blood glucose.

SYMLIN dosage differs depending on whether the patient has type 1 or type 2 diabetes. Please read the recommendations in the SYMLIN Prescribing Information on proper DOSAGE and ADMINISTRATION.

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pen-injector



FDA Required SYMLIN REMS Safety Information

A Risk Evaluation and Mitigation Strategy (REMS) is a strategy to manage known or potential serious risks associated with a drug product and is required by the Food and Drug Administration (FDA) to ensure that the benefits of a drug outweigh its risks. The FDA has required a REMS for SYMLIN.

The purpose of this non-promotional Factsheet is to mitigate the risk of severe hypoglycemia associated with SYMLIN by:

- informing health care providers about the risk of severe hypoglycemia as SYMLIN is used with insulin and the importance of insulin dose reduction
- informing health care providers of the importance of proper patient selection for treatment with SYMLIN

Reporting Adverse Events

To report all suspected adverse events associated with the use of SYMLIN, please contact:



1-800-236-9933



FDA Medwatch Program at 1-800-FDA-1088 or www.fda.gov/medwatch

For more information regarding SYMLIN, please contact the Medical Information department at 1-800-236-9933 or visit the website at www.SYMLIN.com.



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The screenshot shows a web browser window with the URL <http://www.symlinrems.com>. The page title is "SYMLIN REMS". The main content area features the SymlinPen logo (pramlintide acetate pen-injector) and a navigation menu with "Prescribing Information" and "Medication Guide". A disclaimer states "This site is for U.S. Health Care Providers only." and there is a "Bookmark This Page" button. The main heading is "FDA Required SYMLIN REMS Safety Information".

SYMLIN REMS Purpose

The purpose of the SYMLIN REMS program is to inform health care providers about the following serious risks of SYMLIN:

- Increased risk of severe hypoglycemia, particularly in patients with type 1 diabetes.
- Importance of insulin dose reduction

Counsel and instruct your patients on insulin dose reduction to minimize the risk of hypoglycemia.

- Proper patient selection.** SYMLIN is **contraindicated** in patients with any of the following:
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Please see the non-promotional [SYMLIN Factsheet](#), reviewed by the FDA for more detailed safety information.

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Navigation: [Prescribing Information](#) | [Medication Guide](#) | [REMS](#)

AstraZeneca logo

BROWSER PAGE TITLE:
SYMLIN REMS page

PROGRAMMING NOTES:
1) AstraZeneca will include a prominent link on the SYMLIN HCP homepage for REMS materials. The link will direct HCPs to this separate webpage (<http://www.SYMLINREMS.com>).

2) This REMS website is independent of link to the promotional and/or commercial website and non-REMS materials about the product.

3) The REMS website will be accessible directly through a search engine.