



PRIOR AUTHORIZATION POLICY

POLICY: Diabetes – Symlin® (pramlintide injection – Amylin)

TAC APPROVAL DATE: 08/22/2018

OVERVIEW

Symlin, an antihyperglycemic agent for subcutaneous (SC) injection, is indicated in adjunct to mealtime insulin in patients with type 1 or type 2 diabetes who have failed to achieve desired glucose control despite optimal insulin therapy.¹ Symlin is contraindicated in patients with a confirmed diagnosis of gastroparesis and in patients with hypoglycemia unawareness. At the initiation of Symlin, preprandial rapid/short-acting insulin should be decreased by 50%.¹

Pramlintide is a synthetic analog of the naturally occurring neuroendocrine hormone amylin which is synthesized by pancreatic β -cells and complements the actions of insulin in controlling postprandial glucose homeostasis by suppressing postprandial glucagon secretion (leading to a decrease in hepatic glucose production) and by slowing gastric emptying.¹ Pramlintide has also been shown to reduce food intake via a proposed satiety mechanism.

Efficacy

In clinical trials with Symlin, glycosylated hemoglobin (HbA_{1C}) has been reduced by 0.5% to 0.7% and body weight has been reduced by approximately 0.5 kg to 1.4 kg over a 6-month course in patients with type 1 or type 2 diabetes.²⁻⁷

The efficacy of a range of Symlin doses (in adjunct to insulin) was evaluated in several placebo-controlled and open-label clinical trials in patients with type 2 diabetes.¹ In two, long-term (26 weeks to 52 weeks), randomized double-blind, placebo-controlled trials in patients with type 2 diabetes the addition of Symlin (120 μ g) to insulin (with or without a sulfonylurea and/or metformin) resulted in a greater mean (\pm standard error [SE]) change from baseline HbA_{1C} ($-0.57 \pm 0.06\%$) at Month 6 (baseline HbA_{1C} $9.1 \pm 0.06\%$) than addition of placebo to insulin therapy (mean reduction: $-0.17 \pm 0.07\%$; baseline HbA_{1C} $9.3\% \pm 0.08$) [$P < 0.05$ for the difference].¹ In an open-label study Symlin was added to insulin therapy in patients with type 2 diabetes who were unable to achieve glycemic targets using insulin alone ($n = 166$). Mean baseline HbA_{1C} was 8.3% and mean body mass index (BMI) was 38.6 kg/m². After 6 months of treatment, the baseline subtracted mean (\pm SE) HbA_{1C} was $-0.56 \pm 0.15\%$ and baseline-subtracted mean weight reduction was -2.76 ± 0.34 kg.

In three long-term (26 to 52 week), randomized, double-blind, placebo-controlled studies of Symlin in patients with type 1 diabetes ($n = 1,717$; baseline HbA_{1C} values 8.7% to 9.0%) the addition of Symlin (30 or 60 μ g) to existing insulin therapy for 6 months resulted in a mean (\pm SE) change in HbA_{1C} from baseline of $-0.43 \pm 0.04\%$; the mean reduction in HbA_{1C} from baseline at Month 6 was $-0.10 \pm 0.05\%$ in the placebo arm ($P < 0.05$ vs. placebo). In a dose-titration study in patients with type 1 diabetes (mean baseline HbA_{1C} was 8.1%) the addition of Symlin to insulin therapy resulted in a similar mean (\pm SE) reduction in HbA_{1C} from baseline ($-0.47 \pm 0.07\%$) compared with placebo ($-0.49 \pm 0.07\%$) at Month 6. In an open-label study in patients with type 1 diabetes unable to achieve glycemic control on insulin therapy, the addition of Symlin (30 or 60 μ g) for 6 months reduced mean HbA_{1C} from baseline by -0.18% (baseline HbA_{1C} 8.0%).

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Guidelines/Consensus Statements

The American Diabetes Association (ADA) Standards of Medical Care in Diabetes (2018) do not address the use of Symlin for glycemic management.⁸

The comprehensive management algorithm from the AACE (2018) only addresses the availability of Symlin and its weight loss benefits but does not address its place in therapy for patients with type 2 diabetes.⁹ A position statement from ADA and the European Association for the Study of Diabetes (EASD) for the management of hyperglycemia in type 2 diabetes (2012) notes that, Symlin is typically reserved for patients treated with intensive insulin therapy, usually in type 1 diabetes mellitus.¹⁰ A supplemental update to this position statement does not provide any additional recommendations for Symlin.¹²

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Symlin. The goal of this Express Scripts prior authorization program is to appropriately limit the coverage of Symlin to use in type 1 and 2 diabetes mellitus and to prevent the use in unapproved conditions (e.g., weight loss). All approvals are provided for 3 years unless otherwise noted below.

Automation: If criteria for previous use of insulin (automated) within the past 130 days are not met at the point of service, coverage will be determined by prior authorization criteria.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Symlin is recommended in those who meet the following criteria:

Food and Drug Administration (FDA)-Approved Indications

- 1. Diabetes Mellitus, Type 1 or Type 2.** Approve Symlin for 3 years if Symlin is prescribed in adjunct to insulin therapy.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Symlin has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

- 1. Weight Loss Treatment.** Exception is not recommended. Symlin is not indicated for this condition.

Symlin was studied in non-diabetic men and women with abdominal obesity (n = 411).¹¹ In this multicenter, randomized, double-blind, placebo-controlled, dose-ranging study, patients received placebo three times daily (TID) or Symlin (120, 240, and 360 µg twice daily [BID] and TID) in conjunction with lifestyle intervention (a program emphasizing diet, activity, and behavioral modification) for 4 months. Symlin was initiated at 120 µg and increased in 120 µg increments until the assigned maintenance dose was reached. At the end of the double-blind study (Month 4), placebo-corrected weight loss was statistically significant in patients randomized to 120 µg TID and 360 µg BID (-3.2 ± 1.2 kg and -3.3 ± 1.1 kg respectively [P < 0.01]) vs. placebo. Subjects who completed the main study were eligible to continue the same treatment for 8 months during a single-

blind extension. Placebo-corrected weight loss remained significant at the end of the single-blind study (Month 12) in both the Symlin 120 µg TID and 360 µg BID groups (6.1 ± 2.1 kg and 7.2 ± 2.3 kg, respectively [$P < 0.01$]).

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria.

REFERENCES

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HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date
Integrated Policy	--	08/01/2012
Annual Revision	--	08/31/2013
Annual Revision	--	08/20/2014
Selected Revision	3 year duration	08/06/2014
Annual Revision	No criteria changes	08/26/2015
Selected Revision	Automation updated to add 130-day time frame in reference to insulin use.	03/16/2016
Annual Revision	No criteria changes	08/31/2016
Annual Revision	No criteria changes	08/30/2017
Annual Revision	No criteria changes	08/22/2018

TAC – Therapeutic Assessment Committee; * For a further summary of criteria changes, refer to respective TAC minutes available at: <http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx>.