

Pramlintide (Symlin®)

Pramlintide acetate (Symlin) is a new antihyperglycemic drug that was approved by the Food and Drug Administration (FDA) for use in adult diabetic patients currently treated with insulin.

The primary therapeutic effect of pramlintide is to improve postprandial glucose control in diabetics using insulin. The drug also induces patient satiety, leading to potential weight loss by reducing caloric intake.

■ **Indications**

Pramlintide was evaluated in clinical studies with both type 1 (N = 2,375) and type 2 (N = 1,688) diabetics. The drug is indicated for type 1 and type 2 diabetes in patients that are unable to achieve desired glucose control with optimal insulin therapy.

Pramlintide may be used in type 2 diabetic patients that are using insulin with or without concurrent metformin or sulfonylureas. Pramlintide is **not currently indicated** for non-insulin using diabetics or in patients that are able to achieve and maintain adequate glucose control.

■ **Mechanism of Action**

Pramlintide mimics the effects of endogenous amylin. Amylin is secreted, along with insulin, by normal functioning pancreatic beta cells in response to food intake. The physiological effects of endogenous amylin and the administered pramlintide are similar. These include: 1) Slowed gastric emptying, resulting in reduced rate of glucose absorption. 2) Suppressed glucagon secretion, which reduces postprandial hepatic glucose output and 3) Modulated appetite

■ **Drug Metabolism**

Pramlintide is absorbed systemically after a subcutaneous injection in the thigh or abdomen. The body mass index or amount of adipose tissue in the patient does not appear to affect absorption or bioavailability. Pramlintide is not extensively bound to blood cells or albumin, and the drug's distribution is minimally affected by the availability of binding sites. The drug is metabolized predominantly in the kidneys with a half-life of approximately 48 minutes. Although metabolized in the kidney, renal function does not appear to have a significant affect on drug clearance.

■ **Contraindications**

Specific contraindications are limited to those patients with confirmed gastroparesis. The drug is also contraindicated for patients unable to self-monitor for hypoglycemic events.

- poor compliance with current insulin regimens;
- poor compliance with prescribed self-blood glucose monitoring;
- hemoglobin A1c > 9%
- recurrent severe hypoglycemia requiring assistance during the past 6 months;

■ **Adverse Reactions**

Nausea is the most common adverse event reported by patients using pramlintide, and dosing is initially adjusted by monitoring the level of nausea. Pramlintide-induced nausea

generally decreases with time and when the dose is titrated gradually. Other reported adverse events in both type 1 and type 2 diabetic patients include anorexia, vomiting, fatigue, and dizziness.

The drug insert for pramlintide contains a black box warning related to its potential for severe hypoglycemic events; particularly in type 1 diabetics. In the first 3 months, hypoglycemic events (as ascertained by the patient) occurred in 16.8% and required medical assistance in 7.3% of type 1 diabetic patients enrolled in the clinical studies. Patients unable to monitor for hypoglycemic episodes are unsuitable for pramlintide therapy.

■ **Dosage and Administration**

When initiating pramlintide therapy, the preprandial, rapid-acting, or short-acting insulin dosages should be reduced by one-half. With a reduction of the insulin dose, a corresponding increase in blood sugar may occur and therefore, patients must be monitored carefully at regular intervals.

Pramlintide should be initiated at 15 mcg sub-Q and titrated at 15 mcg increments to a maintenance dose of 30 mcg to 60 mcg as tolerated. This drug is given just before the meal.

For insulin-using type 2 diabetics, pramlintide should be started at a dose of 60 mcg sub-Q just prior to each meal and increased to a dose of 120 mcg when the patient has no nausea for 3 to 7 days.

Pramlintide may delay the absorption of other medications taken at the same time.

Pramlintide Doses

Prescribed Dosage (mcg)	U-100 Syringe Increments (units)
15	2.5 units
30	5 units
45	7.5 units
60	10 units
120	20 units

Pramlintide and insulin should always be administered as separate injections.(???)

Pramlintide is supplied in 5 mL vials that contain 0.6 mg/mL.

Unopened vials should be kept refrigerated and protected from light.

Cost of non-insulin injectable diabetes medications

Drug	Indication	Usual Maintenance Dose	AWP per month (\$)	WAC per month (\$)
Pramlintide Symlin®	Type 1 diabetes	30 to 60 mcg prior to meals*	99.38 – 178.88	79.50 - 143.10
	Type 2 diabetes	60 to 120 mcg prior to meals*	178.88 – 357.77	143.10 -286.20