# Criteria for Non formulary Use of
# Pramlintide (Symlin®)

**VHA Pharmacy Benefits Management Strategic Healthcare Group and Medical Advisory Panel**

*The following recommendations are based on current medical evidence and expert opinion from clinicians. The content of the document is dynamic and will be revised as new clinical data becomes available. The purpose of this document is to assist practitioners in clinical decision making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. The clinician should utilize this guidance and interpret it in the clinical context of the individual patient situation.*

## Inclusion criteria (all inclusion criteria must be met)

- The prescriber specializes in diabetes management
- Patient is on insulin therapy
- Documentation that patient has not achieved desired HbA1c despite multiple titration and adjustments with various basal/bolus insulin dosing regimens (including the use of insulin analogs)
- Patient is willing to accept 2-3 injections/day of pramlintide in addition to that of insulin
- Patient has demonstrated proficiency and compliance of SMBG and is willing to perform self-monitoring of blood glucose pre- and postprandially and at bedtime (until stabilized on dose)

## Exclusion criteria

- Patient has a HbA1c > 9%
- Patient experiences frequent or severe hypoglycemia*
- Patient has hypoglycemia unawareness
- Patient has a confirmed diagnosis of gastroparesis
- Patient is taking drugs known to alter GI motility (e.g. GI anticholinergics, metoclopramide, tegaserod)
- Patient is using an α-glucosidase inhibitor (acarbose, miglitol)

* Pramlintide carries a black box warning for insulin-induced severe hypoglycemia. Hypoglycemic risk in higher in patients with type 1 diabetes, and usually occurs within 3 hours of injection.

## Patient and/or caregiver must be educated on the following

- **Patient and/or caregiver must be taught not to confuse insulin and pramlintide**
- Do not mix pramlintide and insulin in the same syringe. Use a separate syringe and needle for pramlintide
- Pramlintide must be injected into a site that is different from where insulin is injected. Injection sites should be rotated
- Patient and/or caregiver must be able to demonstrate how do draw up a dose of pramlintide using an insulin syringe (see caution box on page 2)
- Pramlintide is injected into abdomen or thigh immediately prior to each major meal containing $\geq$250kcal or $\geq$ 30gm of carbohydrate
- If a dose of pramlintide is missed, an additional injection should not be given
- Patient should be warned for the potential for hypoglycemia and signs and symptoms of hypoglycemia be reiterated

## Cautions

Presently, the manufacturer recommends using a U-100 insulin syringe for administering pramlintide. As a result, there is significant concern regarding the potential for errors in dosing pramlintide.

- There is a risk that users may confuse micrograms with units. For example, 30 mcg (5 units on an insulin syringe) could be mistaken for 30 units, leading to a 6-fold overdose of pramlintide.
- For prescriptions, the dose of pramlintide must be written in micrograms. Do not express the dose in insulin syringe equivalents. For example, the dose of pramlintide should be written as 120mcg not as 20 units.
- If a tuberculin syringe was to be substituted for the U-100 syringe, there may be confusion because the conversion table in the patient information leaflet does not contain the volumetric measure (3rd column on conversion table below)

**Conversion of pramlintide dose to insulin unit equivalents**

| Pramlintide dose (mcg) | Increment using a U-100 syringe (units) | Volume (mL) |
|---|---|---|
| 15 | 2.5 | 0.025 |
| 30 | 5.0 | 0.05 |
| 45 | 7.5 | 0.075 |
| 60 | 10 | 0.1 |
| 120 | 20 | 0.2 |

From pramlintide product package insert

- Thiazolidinediones (rosiglitazone, pioglitazone) have not been studied in combination with pramlintide; concurrent use should be avoided.

## Dosing

**Dosing for type 2 diabetes**

- Initial dose is 60mcg given subcutaneously immediately prior to major meals (≥ 250kcal or containing ≥ 30 g of carbohydrate).
- Reduce the dose of preprandial rapid-acting or short-acting insulin (including premixed 70/30 or 75/25 preparations) by 50%
- If no clinically significant nausea has occurred for 3-7 days, increase the dose to 120mcg prior to major meals. If the 120mcg dose is not tolerated due to nausea, reduce the dose to 60mcg
- Once a stable dose of pramlintide has been reached (nausea subsided), the dose of insulin may be adjusted to optimize glycemic control, as directed by a healthcare practitioner

**Dosing for type 1 diabetes**

- Initial dose 15mcg subcutaneously immediately prior to major meals (≥250kcal or containing ≥ 30 g of carbohydrate).
- Reduce the dose of preprandial rapid-acting or short-acting insulin (including premixed 70/30 or 75/25 preparations) by 50%
- The dose is titrated in 15mcg increments to 30, 45, or 60mcg. If no clinically significant nausea has occurred for at least 3 days, increase the dose to the next increment. If the 30mcg dose is not tolerated, consider discontinuing pramlintide
- Once a stable dose of pramlintide has been reached (nausea subsided), the dose of insulin may be adjusted to optimize glycemic control, as directed by a healthcare practitioner

*Concomitantly administered oral agents that require rapid onset (e.g. analgesics) should be taken at least 1 hour prior to or 2 hours after pramlintide injection

| **Follow-up** |
| --- |
| Initially, patient should have at least monthly follow ups to ensure safety and efficacy<br><br>Discontinue if patient has:<br>• Less than a 10% decrease in HbA1c (unless glycemic target has been met)<br>• Significant or frequent episodes of hypoglycemia<br>• Has persistent or clinically significant nausea<br>• Is noncompliant with SMBG, dosing adjustments, clinic appointments<br>• Now has any of the exclusion criteria since starting pramlintide |

The drug monograph for pramlintide can be found www.pbm.va.gov