Information on indications for use or diagnosis is assumed to be unavailable. All criteria may be applied retrospectively; prospective application is indicated with [*].

1.* Dosage/Administration

A. Adults

Pramlintide, a synthetic analog of human amylin, is FDA-approved for use as adjunct therapy in type 1 diabetics using mealtime insulin who are not adequately controlled with optimal insulin therapy, as well as type 2 diabetics not adequately controlled with optimal insulin therapy, including mealtime insulin, with or without concomitant sulfonylurea and/or metformin therapy. Amylin is a neuroendocrine hormone secreted concurrently with insulin in response to food intake to decrease hepatic glucose output and slow gastric emptying, which results in reduced carbohydrate absorption and lower postprandial glucose levels. Similarly, pramlintide works by delaying gastric emptying, decreasing postprandial increases in glucagon levels, and causing satiety which promotes decreased caloric intake and potential weight loss. Pramlintide is available as a 1.5 ml disposable, multidose 60-pen injector or a 2.7 ml disposable, multidose 120-pen injector containing pramlintide 1000 mcg/ml. The 60-pen injector provides doses of 15 mcg, 30 mcg, 45 mcg, or 60 mcg while the 120-pen injector provides pramlintide doses of 60 mcg or 120 mcg. Recommended pramlintide dosages are summarized in Table 1.

<table>
<thead>
<tr>
<th>Type 1 Diabetes Mellitus</th>
<th>Initial Dose</th>
<th>Dosage Titration</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>15 mcg subcutaneously immediately prior to each major meal</td>
<td>15 mcg increments</td>
<td>60 mcg subcutaneously immediately prior to each major meal</td>
</tr>
<tr>
<td>Type 2 Diabetes Mellitus (insulin-using)</td>
<td>60 mcg subcutaneously immediately prior to each major meal</td>
<td>60 mcg increments</td>
<td>120 mcg subcutaneously immediately prior to each major meal</td>
</tr>
</tbody>
</table>

In type 1 diabetics, dosage titrations should be initiated when clinically significant nausea has been absent for at least 3 days. If nausea persists with the 45 mcg or 60 mcg dose, the dosage may be reduced to 30 mcg. If patients do not tolerate the 30 mcg dose, discontinuing therapy may be necessary. In insulin-using type 2 diabetics, dosage titrations may be initiated when significant nausea is absent for 3 to 7 days. If the 120 mcg dose is not tolerated, the dosage may be decreased to 60 mcg. In both type 1 and type 2 diabetics, pre-prandial rapid or short-acting insulin dosages, including fixed-mixed insulin, should be decreased by 50% when adjunctive pramlintide therapy is instigated to minimize hypoglycemic episodes. Insulin doses may be titrated upward as needed when a maintenance pramlintide dose is established.

Patient profiles containing pramlintide prescription quantities of greater than 2 x 60-pen injectors or 1 x 120-pen injector per 30 days for type 1 diabetics will be reviewed. Likewise, patient profiles containing pramlintide prescription quantities of greater than 2 x 120-pen injectors per 30 days for type 2 diabetics will be reviewed.
Pramlintide should not be administered to patients who:
- have been diagnosed with gastroparesis within the last 2 years
- have recurrent episodes of hypoglycemia requiring intervention in the last 6 months and/or hypoglycemia unawareness
- have an HbA1c > 9%
- require therapy with medications that stimulate gastrointestinal motility
- are poorly compliant with insulin regimens and/or self-monitoring of blood glucose serum concentrations

B. Pediatrics
Safety and efficacy of pramlintide injections in pediatric patients have not been established. However, a few small, short-term crossover studies have evaluated pramlintide use in adolescents with type 1 diabetes and demonstrated significant reductions in postprandial hyperglycemia. Further long-term studies are necessary to solidify results.

2. Duration of Therapy

Pramlintide is indicated for the management of diabetes mellitus and may be continued indefinitely based on patient need to achieve desired glucose control.

3. Drug-Drug Interactions

Patient profiles will be assessed to identify those drug regimens which may result in clinically significant drug-drug interactions.
Drug-drug interactions considered clinically relevant for pramlintide are summarized in Table 2. Only those drug-drug interactions identified as clinical significance level 1 or those considered life-threatening which have not yet been classified will be reviewed:
<table>
<thead>
<tr>
<th>TARGET DRUG</th>
<th>INTERACTING DRUG</th>
<th>INTERACTION</th>
<th>RECOMMENDATIONS</th>
<th>CLINICAL SIGNIFICANCE*</th>
</tr>
</thead>
<tbody>
<tr>
<td>pramlintide</td>
<td>medications that slow gastrointestinal motility (e.g., antimuscarinics, diphenoxylate, opiate agonists, tricyclic antidepressants)</td>
<td>adjunctive administration may potentiate pramlintide pharmacologic effects, increasing potential for additional blood glucose reductions and risk of hypoglycemia</td>
<td>concurrent administration not recommended by manufacturer</td>
<td>2-major (CP)</td>
</tr>
<tr>
<td>pramlintide</td>
<td>gastric stimulants (e.g., metoclopramide, tegaserod)</td>
<td>concurrent administration may attenuate pharmacologic effects of both agents</td>
<td>manufacturer states that pramlintide/gastric stimulant combination should be avoided</td>
<td>2-major (CP)</td>
</tr>
<tr>
<td>pramlintide</td>
<td>alpha glucosidase inhibitors (e.g., acarbose, miglitol)</td>
<td>alpha glucosidase inhibitors slow nutritive absorption; adjunctive administration may potentiate pramlintide pharmacologic effects, increasing potential for additional blood glucose reductions and risk of hypoglycemia</td>
<td>concurrent administration not recommended by manufacturer</td>
<td>3-moderate (CP)</td>
</tr>
<tr>
<td>pramlintide</td>
<td>oral medications with hypoglycemic effects (e.g., oral antidiabetic agents, angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, disopyramide, fibric acid derivatives, salicylates, sulfonamide antibiotics)</td>
<td>concomitant administration may result in enhanced hypoglycemic pharmacologic and adverse effects</td>
<td>monitor blood glucose levels closely and adjust dosages as necessary if drug combination required to minimize excessive hypoglycemia and associated adverse events</td>
<td>moderate (DrugReax) 3-moderate (CP)</td>
</tr>
<tr>
<td>pramlintide</td>
<td>oral medications requiring rapid gastrointestinal absorption, or have narrow therapeutic index</td>
<td>concurrent administration may reduce serum levels of drugs with a narrow therapeutic index, or those requiring rapid GI absorption as pramlintide delays gastric emptying</td>
<td>use cautiously together</td>
<td>undetermined</td>
</tr>
<tr>
<td>pramlintide</td>
<td>oral medications requiring threshold concentrations for effect (e.g., acetaminophen, oral contraceptives)</td>
<td>concurrent administration may reduce serum levels of drugs with threshold concentrations as pramlintide delays gastric emptying</td>
<td>use cautiously together; administer medications having threshold concentrations for effect at least 1 hour before or 2 hours after pramlintide</td>
<td>4-minor (CP)</td>
</tr>
</tbody>
</table>
REFERENCES


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