

## Focus on Symlin®



Symlin® also known as pramlintide is an amylin agonist. Pramlintide is not a well known medication, but may be a reasonable choice for the right patient.

**Background:** Amylin is a hormone produced in the beta cells of the pancreas and is involved in glucose regulation. Amylin is co packaged and excreted with insulin, plasma concentrations of the two hormones are similar. Since amylin is produced in the beta cells of the pancreas one would expect and it is true that patients with type 1 diabetes have an absolute deficiency of amylin and insulin. Patients with type 2 diabetes have a relative deficiency of both amylin and insulin. Having an amylin agonist on the market, pramlintide, gives us an additional tool for the treatment of diabetes.

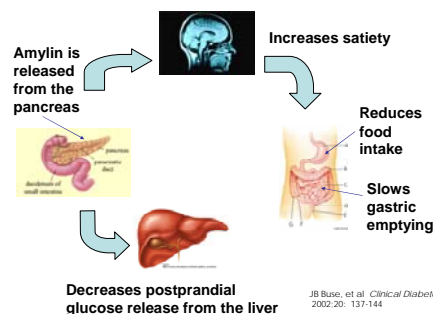
**Mechanism of Action:** Pramlintide is a synthetic analog of amylin and acts as a neuroendocrine hormone that complements the actions of insulin particularly in postprandial blood

**Goal.**

- *The goal of the Diabetes Dispatch is to increase the reader's knowledge of diabetes treatments and technologies and to provide the most current information on new drugs, therapies, and devices.*
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glucose control. Pramlintide acts like amylin. It is responsible for the modulation of gastric emptying, prevention of the postprandial glucagon secretion, and satiety which leads to decreased caloric intake and potential weight loss. Figure 1 shows amylin's role in glucose

Figure 1. Amylin's Role in Glucose Regulation



control.

**Therapeutics Summary:** FDA labeled indications are for patients with type 1 or type 2 diabetes who have failed to achieve desired glucose control despite optimal insulin therapy.

**Efficacy:** Decreases A1c 0.4-0.6%. You could think of pramlintide as a tool to fine tune glucose control.

**Dosing:** Type 1 diabetes, initial dose, 15 mcg subcutaneously (SC) immediately prior to major meals titrate at 15 mcg increments to 30 to 60 mcg SC as tolerated.

Type 2 diabetes, initial dose, 60 mcg SC immediately prior to major meals increase as tolerated to 120 mcg maintenance subcutaneously.

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**Objectives.**

1. Become familiar with the dosing and indications for Symlin®
2. Explore treatment options for children and adolescents with type 2 diabetes
3. Recognize the diagnostic criteria and self monitoring blood glucose goals for women with gestational diabetes

# Treatment of Type 2 Diabetes in Children and Adolescents

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For years, non-insulin-dependent diabetes was known to clinicians as an “adult-onset” disease. Since it was first documented in children in 1979, however, the incidence of type-2 diabetes (T2DM) in pediatric patients has risen alarmingly.<sup>1</sup> Data from several small studies suggest that somewhere between 8 - 45% of all childhood diabetes is now T2DM.<sup>1,3</sup> However, there is very little published research regarding T2DM in this population.<sup>1</sup> Healthcare providers must be vigilant and resourceful to create treatment regimens for these new pediatric type 2 diabetes patients.

Since the pathology of diabetes in children is parallel to that of adults, the two major treatment goals are also the same. The most easily measured blood glucose indicator is hemoglobin A1c (HbA1c). The optimal goal is 7.0%.<sup>5</sup> The primary goal of therapy is to prevent micro- and macrovascular complications.<sup>5</sup> Some research indicates that patients diagnosed at a younger age are more likely to experience microvascular complications, so clinicians should pay special attention to microalbumin, retinopathy, and nephropathy.<sup>4,5</sup>

Pharmacists should always reinforce the importance of self blood glucose monitoring and lifestyle modifications such as diet, exercise, and weight loss. However, due to the progressive nature of the disease, many patients will need drug therapy.<sup>2,3</sup> Until 2000, insulin was the only medication indicated for treatment of pediatric T2DM. In that year, the Food and Drug Administration (FDA) approved metformin as oral therapy for type 2 diabetes in children and adolescents over ten years of age.<sup>2</sup> The American Diabetes Association recommends metformin as the first oral agent to be used in asymptomatic pediatric patients if treatment with nutrition and exercise fail to meet therapy goals.<sup>1,2</sup> It is contraindicated in renal or hepatic disease, severe infection, or unstable asthma.<sup>1</sup> Other oral therapies have been used in practice both alone and in combination, but are not FDA-approved. Most pediatric endocrinologists will use sulfonylureas alone or with other agents when the patient has not reached goal. One recent study did show that glimeperide decreased HbA<sub>1c</sub> similarly to metformin, but with greater weight gain.<sup>6</sup>

In patients who have severe hyperglycemia, severe insulin deficiency/ketoacidosis, or who are overtly symptomatic, insulin is the initial therapy of choice (see table 1).<sup>1,5</sup> Short-term therapy with insulin has been shown to reverse pancreatic damage in adults, and has been used to rapidly achieve metabolic control in children with diabetes.<sup>1,7</sup> The recommended starting dose of insulin in children with T2DM is 0.5 – 1.0 U/kg/day, but this may need to be raised over time.<sup>5</sup> Insulin therapy should always be individualized to the patient.<sup>5</sup>

**Table 1: Criteria for use of insulin as initial therapy in children with type 2 diabetes<sup>1</sup>**

Criteria	Definition
Severe hyperglycemia	fasting blood glucose $\geq$ 200
Severe long-term hyperglycemia	HbA <sub>1c</sub> $\geq$ 8.5%
Severe insulin deficiency	diabetic ketoacidosis
Overt diabetic symptoms	polydipsia, polyuria, dysuria, vaginitis, sleep apnea

Diabetes is a disease that requires life-long attention on the part of all patients and their healthcare providers. Patients diagnosed with T2DM at such an early age are faced with the prospect of managing the disease for upwards of fifty years, with more complications than their adult-diagnosed counterparts.<sup>1,4</sup> Preventing the disease for as long as possible is the best way to protect these patients’ health. Pharmacists should especially consider prevention measures in patients at increased risk; including the obese, those with family history of diabetes, and those of African American or Native American ethnicity.<sup>1</sup> Patients should always be informed that exercise, a healthy diet, and weight loss (when needed) are crucial to DM prevention and also to overall health. Regardless of their risk and time of diagnosis, diabetes patients will require the help of their entire healthcare team to achieve the best possible outcomes. It is the responsibility of the pharmacist to provide medication education, emphasize the importance of lifestyle changes and a lifelong commitment to better health.

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# Gestational Diabetes– Screening and Diagnosis

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Gestational diabetes occurs when a woman is diagnosed with diabetes while pregnant<sup>1-5</sup>. Each year 3-8% of pregnant women are diagnosed with gestational diabetes. Roughly 135,000 cases of gestational diabetes occur each year in the United States. As a woman’s body changes, it can be difficult for her body to regulate the balance of blood sugars<sup>1</sup>. Each person has hormones that regulate the sugars in their blood. Insulin is released in response to sugars in the blood. With all the changes in a pregnant woman’s body, it is common for her body to be less sensitive to insulin, rendering her less able to control her blood sugars<sup>1</sup>.

Gestational diabetes can occur as result of these imbalances in some women. The resulting high blood glucose levels can cause complications throughout the pregnancy for the mother and the baby; therefore monitoring and treating blood sugars is imperative<sup>1,4</sup>. Women with gestational diabetes do not produce enough insulin to lower the blood sugars to a normal level. The elevated sugar levels the baby is exposed to cause an increase in the fetus’ insulin production as well as changes in other hormones which may cause the baby to grow abnormally large (called macrosomia). Some of the issues the baby may face include: shoulder damage during the birthing process, low blood sugars in response to overproducing insulin, and possible breathing problems. Babies of mothers with gestational diabetes are also at a higher risk of developing diabetes at a younger age than babies of a pregnancy without diabetes. For these reasons, it is optimal for the mother to try to maintain near normal blood sugars during the pregnancy<sup>1,4</sup>.



Some women are at higher risk for gestational diabetes (GDM) than others. Risk factors for gestational diabetes will be assessed at the first prenatal visit. Risk factors for gestational diabetes include: age greater than 25 years, being overweight, having a family history of diabetes, prior GDM, certain ethnic backgrounds such as American Indian/Alaska Native heritage, and having protein in the urine determined from a urine sample. If a woman has risk factors for gestational diabetes, she will be tested for glucose intolerance early in the pregnancy. If a woman does not have any risk factors she may need to have a glucose tolerance test between 24-28 weeks of pregnancy but glucose testing is not universal at the current time<sup>1,3-5,7</sup>.

Women who have risk factors maybe given a screening test for gestational diabetes. One screening test for gestational diabetes is a 50-gram glucose tolerance test where a sample of blood is drawn 1 hour after ingesting the glucose. References differ in determining what blood glucose value mandates further testing. Most healthcare providers agree that a serum level above 140 mg/dL warrants further testing. In the event the result of the screening test is over 200 mg/dL many providers will diagnosis gestational diabetes without additional testing. The two diagnostic tests for gestational diabetes involves drinking a 75-gram or a 100-gram bottle of a glucose substance and having the blood glucose tested each hour for 2 hours with the 75-gram test or for 3-hours with 100-gram glucose tolerance test. **Table 1** shows the diagnostic criteria for the oral glucose tolerance tests. From the diagnostic tests, if two of the results from the blood draw fall into any of the above categories, a diagnosis of gestational diabetes can be made<sup>1-5,7</sup>. *Continued on page 4.*

Table 1. Gestational Diabetes Diagnostic Criteria following a 75-gram & a 100-gram oral glucose tolerance test.*		
Time	Blood glucose level (mg/dL)	
	75-gram	100-gram
Fasting	≥ 95	≥ 95
1 hours	≥ 180	≥ 180
2 hours	≥ 155	≥ 155
3 hours		≥ 140



# Focus on Symlin®, continued



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**Dosing:** Special attention to dosing of pramlintide is recommended to avoid potential errors of measuring pramlintide in an insulin syringe. The Symlin® dose conversion chart to the right can help simplify patient education.

**Noteworthy:** Pramlintide is used with insulin and has been associated with an increased risk of insulin-induced severe hypoglycemia, particularly in patients with type 1 diabetes. When severe hypoglycemia associated with pramlintide use occurs, it is seen within 3 hours following the injection. For these reasons it is recommended to decrease the dose of any short acting insulin by 50% when pramlintide is started. After titration of pramlintide is complete, the short acting insulin should be readjusted to enable patient to meet blood glucose goals.

SYMLIN DOSE CONVERSION	
If your dose is	Draw up
15 micrograms	2.5 units
30 micrograms	5 units
45 micrograms	7.5 units
60 micrograms	10 units
120 micrograms	20 units

References:

1. JB Buse, et al. Clinical Diabetes 2002;20: 137-144.
2. [www.symlin.com](http://www.symlin.com)

## Gestational Diabetes- Treatment and Monitoring, continued

Once diagnosed with gestational diabetes, it is important to monitor blood sugar content through a finger stick testing method and start treatment. The American College of Obstetricians and Gynecologists recommends daily testing<sup>4</sup>. A specific number of times to test are not mentioned, however, the medical provider may recommend a specific number of times to test blood sugars in the patient's individualized treatment plan. Optimal times to test blood sugars may include: before eating a meal, 2 hours after eating a meal, at bedtime, and occasionally in the middle of the night (3:00am)<sup>4</sup>.

Table 2 describes optimal blood glucose levels depending on when the blood sample is taken<sup>6</sup>.

Time	Blood Glucose Goal
Before meals	<95 mg/dl
1-hour after meals	<140 mg/dl
2-hours after meals	<120 mg/dl

Treatment is aimed at keeping blood glucose levels similar to pregnant women who do not have gestational diabetes. Most treatment regimens begin with diet and exercise and include blood glucose monitoring. If tighter control of blood sugars is needed, insulin injections are commonly prescribed. Oral medication use in pregnancy for treatment of gestational diabetes is controversial and may have a place in therapy. Non-pharmacological treatment consists of good nutritional habits and scheduled physical activity. Eating a variety of foods that incorporate fresh fruits and vegetables, watching portion sizes, and limiting calories and fat intake are healthy habits to help control blood sugars as well as to promote a healthy lifestyle<sup>1,4,5</sup>. Exercising will help the pregnant body use extra glucose. Integrating these changes may decrease the need for a cesarean section birth, complications during pregnancy and childbirth, and may help to prevent developing diabetes later in life for the mother<sup>1,4,5</sup>.

Gestational diabetes usually resolves after pregnancy<sup>1-5</sup>. For some women, however, pregnancy unmasks type 1 or type 2 diabetes<sup>5</sup>. For these women, it is unknown whether the woman has true gestational diabetes or if diabetes is being unmasked during the pregnancy. Women who had type 1 or type 2 diabetes uncovered during pregnancy will need to continue diabetes treatment after pregnancy.

Having had gestational diabetes puts a woman at a higher risk of developing gestational diabetes in future pregnancies, as well as type 2 diabetes. For this reason, it is recommended to check for diabetes at 6-12 weeks postpartum<sup>5</sup>. Incorporating healthy habits, such as walking 30 minutes a day five times a week and if overweight losing 5-7% of body weight is known to help prevent diabetes later in life. Seeing a team of healthcare providers such as nurses, doctors, pharmacists, and dieticians, along with employing help from family members will enhance the success of treating gestational diabetes in a pregnant woman, as well as, preventing type 2 diabetes in the future<sup>1,5</sup>.

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## Continuing Education Quiz

Diabetes Dispatch: Winter 2008

1. Which patient is most appropriate to treat with Symlin®?

- a. a 12 year old recently diagnosed with type 2 diabetes
- b. a patient with gestational diabetes
- c. a patient with type 1 diabetes on multiple daily insulin injection regimen whose blood glucose is still above goal
- d. a patient with type 2 diabetes on metformin

2. What is the recommended Symlin® starting dose for a patient with type 1 diabetes?

- a. initial dose, 15 mcg subcutaneously immediately prior to major meals and titrate at 15 mcg increments to 30-60mcg SC as tolerated
- b. initial dose, 60 mcg subcutaneously immediately prior to major meals and increase as tolerated to 120mcg SC as tolerated.
- c. initial dose, 30 mcg subcutaneously immediately prior to major meals and increase as tolerated to 120mcg SC as tolerated.

3. What is the recommended Symlin® starting dose for a patient with type 2 diabetes?

- a. initial dose, 15 mcg subcutaneously immediately prior to major meals and titrate at 15 mcg increments to 30-60mcg SC as tolerated
- b. initial dose, 60 mcg subcutaneously immediately prior to major meals and increase as tolerated to 120mcg SC as tolerated.
- c. initial dose, 30 mcg subcutaneously immediately prior to major meals and increase as tolerated to 120mcg SC as tolerated.

4. What oral diabetes medication is FDA approved for the treatment of type 2 diabetes in children over 10 years of age?

- a. nateglinide
- b. glyburide
- c. glimiperide
- d. metformin

5. Criteria for use of insulin as initial therapy in children with type 2 diabetes includes which of the following

- a. fasting blood glucose  $\geq 200$
- b. HbA1c  $\geq 8.5\%$
- c. overt diabetic symptoms
- d. all of the above

6. What is the recommended starting dose of insulin in children with type 2 diabetes?

- a. 2.0-4.0 units/kg/day
- b. 0.1-0.2 units/kg/day
- c. 0.5-1.0 units/kg/day

7. For a woman with gestational diabetes, what is her blood glucose goal before a meal?

- a. 80-120 mg/dl
- b. <95 mg/dl
- c. <140 mg/dl
- d. <120 mg/dl

8. For a woman with gestational diabetes, what is her blood glucose goal 2 hours after a meal?

- a. 80-120 mg/dl
- b. <95 mg/dl
- c. <140 mg/dl
- d. <120 mg/dl



### LESSON EVALUATIONS

To obtain C.E. credit for this lesson you must answer the questions on the quiz (70% correct required) and return the quiz. Should you score less than 70%, you will be asked to repeat the quiz. In May and November of each year we will mail a statement of credit, unless otherwise arranged with the AkPhA office.

This program furnishes 1.0 credit per lesson.

EXPIRATION FOR CREDIT: Pharmacist and technicians may receive credit for completing this course if returned by January 1, 2011. The ALASKA PHARMACISTS ASSOCIATION is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education.

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