



## Therapeutic Class Review<sup>SM</sup>

### Diabetes - Pramlintide acetate (Symlin<sup>®</sup>)

November 2005

#### New Product(s) for Review

Pramlintide acetate (Symlin<sup>®</sup>) [Amylin Pharmaceuticals, Inc.]

**Dossier Provided by Manufacturer: yes**

**Dossier Evaluation: 3**

- 1 - Dossier w/missing components
- 2 - All components, except pharmacoeconomic model
- 3 - All components present

#### Executive Summary

- Pramlintide (Symlin) is used as adjunctive treatment in patients with Type 1 or Type 2 diabetes currently on insulin and who are unable to achieve adequate glycemic control, despite optimal insulin therapy.
- There is no evidence to support the use of pramlintide (Symlin) as monotherapy in patients with Type 1 or Type 2 diabetes.
- There is no useful evidence to support that adding pramlintide (Symlin) to existing insulin therapy results in clinically relevant decreases in HbA<sub>1c</sub>.
- Risk of hypoglycemia limits the overall usefulness of pramlintide (Symlin) and carries a Black Box warning in product labeling.
- Benefits from weight loss with pramlintide (Symlin) are unsubstantiated by current evidence.
- There is no useful evidence showing pramlintide (Symlin) with insulin results in clinically relevant weight loss or maintenance of weight that results in improved health.

#### Decision

Maintain non-preferred/non-formulary status for pramlintide (Symlin) because:

- There is no useful evidence to conclude any additional clinical value for pramlintide (Symlin) when added to insulin in patients with Type 1 diabetes or Type 2 diabetes.
- Risk of hypoglycemia with pramlintide (Symlin) has the potential to outweigh any modest benefit in improving glycemic control.

## Products

<b>Drug Product</b> <sup>1,2</sup>	<b>Date of FDA Approval</b> <sup>2</sup>	<b>FDA Approved Indication(s)</b>	<b>Dose/Route</b>	<b>Potential Off-Label Use(s)</b>
pramlintide acetate <sup>3</sup> (Symlin <sup>®</sup> )	03/2005	Diabetes mellitus, Type 1 and Type 2 as adjunct to insulin therapy.	<u>Type I Diabetes:</u> 15 - 60 mcg SQ before major meals. <u>Type II Diabetes:</u> 60 - 120mcg SQ before major meals.	Weight loss
<b>INSULIN</b>				
regular human insulin: (Humulin <sup>®</sup> R)	10/1982	Diabetes mellitus – Type 1, Type 2, gestational, pregnancy, diabetic ketoacidosis, hyperglycemic-hyperosmolar nonketotic coma	SQ. Individualized per patient’s needs.	Diabetic ketoacidosis; hyperglycemic-hyperosmolar nonketotic coma
regular human insulin: (Novolin <sup>®</sup> R)	06/1991	Diabetes mellitus – Type 1, Type 2, gestational, pregnancy, diabetic ketoacidosis, hyperglycemic-hyperosmolar nonketotic coma	SQ. Individualized per patient’s needs.	Diabetic ketoacidosis; hyperglycemic-hyperosmolar nonketotic coma
insulin aspart: (Novolog <sup>®</sup> )	06/2000	Diabetes mellitus, Type 1 and Type 2	SQ. Individualized per patient’s needs.	
insulin lispro: (Humalog <sup>®</sup> )	06/1996	Diabetes mellitus, Type 1 and Type 2	SQ. Individualized per patient’s needs.	
isophane (NPH): (Humulin <sup>®</sup> N)	10/1982	Diabetes mellitus – Type 1, Type 2, gestational, pregnancy, diabetic ketoacidosis, hyperglycemic-hyperosmolar nonketotic coma	Individualized per patient’s needs.	Hyperkalemia, diabetic neuropathy, diabetic macrovascular disease, latent autoimmune diabetes in adults, myocardial infarction
isophane (NPH): (Novolin <sup>®</sup> N)	07/1991	Diabetes mellitus – Type 1, Type 2, gestational, pregnancy, diabetic ketoacidosis, hyperglycemic-hyperosmolar nonketotic coma	SQ. Individualized per patient’s needs.	Hyperkalemia, diabetic neuropathy, diabetic macrovascular disease, latent autoimmune diabetes in adults, myocardial infarction
zinc suspension (Lente <sup>®</sup> ): (Humulin <sup>®</sup> L)	09/1985	Diabetes mellitus – Type 1, Type 2, gestational, pregnancy, diabetic ketoacidosis, hyperglycemic-hyperosmolar nonketotic coma	SQ. Individualized per patient’s needs.	Hyperkalemia, diabetic neuropathy, diabetic macrovascular disease, latent autoimmune diabetes in adults, myocardial infarction
glargine: (Lantus <sup>®</sup> )	04/2000	Diabetes mellitus Type 1 in adults and pediatric 6 yrs and older, Type 2 in adults	SQ. Individualized per patient’s needs.	
zinc extended (Ultralente <sup>®</sup> ): Humulin <sup>®</sup> U Ultralente	06/1987	Diabetes mellitus – Type 1, Type 2, gestational, pregnancy, diabetic ketoacidosis, hyperglycemic-hyperosmolar nonketotic coma	SQ. Individualized per patient’s needs.	Hyperkalemia, diabetic neuropathy, diabetic macrovascular disease, latent autoimmune diabetes in adults, myocardial infarction
lispro 75/25: (Humalog <sup>®</sup> Mix)	12/1999	Diabetes mellitus, Type 1 and Type 2	SQ. Individualized per patient’s needs.	
aspart 70/30: (NovoLog <sup>®</sup> Mix)	11/2001	Diabetes mellitus, Type 1 and Type 2	SQ. Individualized per patient’s needs.	

Drug Product <sup>1,2</sup>	Date of FDA Approval <sup>2</sup>	FDA Approved Indication(s)	Dose/Route	Potential Off-Label Use(s)
<b>ORAL ANTI-DIABETIC AGENTS</b>				
Glipizide (generic)	05/1984	Diabetes mellitus, Type 2 (Used alone or in combination)	5 - 40mg PO daily	Diabetic microangiopathy; Gestational diabetes
Glipizide and Metformin HCl (Metaglip®)	10/2002	Diabetes mellitus, Type 2	<u>Monotherapy:</u> 2.5 mg/250 mg PO daily up to 10 mg/2000 mg per day in divided doses <u>Combination therapy:</u> 2.5 mg/500 mg or 5mg/500mg BID; max. 20 mg/2000 mg daily	
Glyburide (generic)	05/1984	Diabetes mellitus, Type 2 (Used alone or in combination)	2.5 - 5 mg PO daily	Gestational diabetes
Glyburide and Metformin HCl (Glucovance®)	07/2000	Diabetes mellitus, Type 2	1.25 mg/250 mg PO once or twice daily <u>Previously treated:</u> 2.5 mg/500 mg to 5 mg/500 mg PO twice daily; max. 20 mg/2000 mg once daily	
Metformin (generic)	03/1995	Diabetes mellitus, Type 2 (Used alone or in combination)	500 mg PO twice daily or 850 mg once daily	
Pioglitazone (Actos®)	07/1999	Diabetes mellitus, Type 2 (Used alone or in combination)	<u>Monotherapy:</u> 15-30 mg PO once daily; max. 45 mg daily <u>Combination therapy:</u> max. 30 mg PO daily	
Rosiglitazone maleate (Avandia®)	05/1999	Diabetes mellitus, Type 2  Diabetes mellitus, Type 2 in combination with insulin, metformin, or sulfonylurea.  (Used alone or in combination)	<u>Monotherapy:</u> 4 mg PO once daily or 2mg twice daily; max. 8 mg daily <u>Concomitant with insulin:</u> 4 mg PO daily; max. 4 mg/day <u>Concomitant with metformin or sulfonylureas:</u> 4 mg orally once daily or 2 mg twice daily	
Rosiglitazone maleate and Metformin HCl (Avandamet®)	10/2002	Diabetes mellitus, type 2 (NIDDM) (not to be given as initial therapy.	2mg/500mg – 4mg/1000mg PO twice daily	

## References

1. Thomson Micromedex © 1974-2005. Micromedex Healthcare Series, Vol 120.
2. Center for Drug Evaluation and Research. Approval package for application number N021332. <http://www.fda.gov/cder/rdmt/nmecy2005.htm> (assessed August 11, 2005)

3. Symlin<sup>®</sup> (pramlintide) Product Information. Amylin Pharmaceuticals, Inc. website: [www.symlin.com](http://www.symlin.com) (assessed August 11, 2005)
4. Product Dossier: Symlin<sup>®</sup> (pramlintide), Amylin Pharmaceuticals, Inc; San Diego, CA. Data reviewed August 8, 2005.
5. American Diabetes Association: Standards of Medical Care in Diabetes. *Diabetes Care*. 2005;28:S4-S36. (assessed August 2, 2005)
6. American Diabetes Association Clinical Practice Recommendations. ADA Clinical Practice Guidelines. *Diabetes Care* 2004;27:S1-S142 (Supplement 1). [http://care.diabetesjournals.org/content/vol27/suppl\\_1/](http://care.diabetesjournals.org/content/vol27/suppl_1/)
7. American Association of Clinical Endocrinologists Medical Guidelines for the Management of Diabetes Mellitus: the AACE System of Intensive Diabetes Self Management – 2002 Update. *Endocrine Practice* 2002 January/February; 8 (Suppl 1): 40-62 (assessed August 2, 2005)
8. Whitehouse F, Kruger DF, Fineman M, Shen L, Ruggles JA, Maggs DG, Weyer C, Kolterman OG. A randomized study and open-label extension evaluating the long-term efficacy of pramlintide as an adjunct to insulin therapy in type 1 diabetes. *Diabetes Care*. 2002 Apr;25(4):724-30.
9. Ratner RE, Dickey R, Fineman M, Maggs DG, Shen L, Strobel SA, Weyer C, Kolterman OG. Amylin replacement with pramlintide as an adjunct to insulin therapy improves long-term glycaemic and weight control in Type 1 diabetes mellitus: a 1-year, randomized controlled trial. *Diabet Med*. 2004 Nov;21(11):1204-12.
10. Ratner RE, Want LL, Fineman MS, Velte MJ, Ruggles JA, Gottlieb A, Weyer C, Kolterman OG. Adjunctive therapy with the amylin analogue pramlintide leads to a combined improvement in glycemic and weight control in insulin-treated subjects with type 2 diabetes. *Diabetes Technol Ther*. 2002;4(1):51-61.
11. Hollander PA, Levy P, Fineman MS, Maggs DG, Shen LZ, Strobel SA, Weyer C, Kolterman OG. Pramlintide as an adjunct to insulin therapy improves long-term glycemic and weight control in patients with type 2 diabetes: a 1-year randomized controlled trial. *Diabetes Care*. 2003 Mar;26(3):784-90.