



Therapeutic Class ReviewSM

Diabetes - Insulin glulisine (Apidra[®])

February 2006

New Product(s) for Review

Insulin glulisine (Apidra[®]) [Sanofi Aventis]

Dossier Provided by Manufacturer: yes

Dossier Evaluation: 3

1 - Dossier with missing components

2 - Dossier with all components, except pharmacoeconomic model

3 - All components present (comprehensive)

Executive Summary

- Insulin glulisine (Apidra) is a rapid-acting human insulin analog¹ indicated for adults with diabetes mellitus for the control of hyperglycemia.
- After subcutaneous injection, the effect of insulin glulisine (Apidra) is more rapid in onset and of shorter duration compared to regular human insulin.
- Insulin glulisine (Apidra) may also be infused subcutaneously by external insulin infusion pumps.

Evidence

- Trials with insulin glulisine (Apidra) compared to regular human insulin or insulin lispro used an open label design, making it difficult to determine whether the results from the trials were due to the different insulin products or other unknown factors.
 - There is no useful evidence that insulin glulisine (Apidra) provides a clinically relevant therapeutic advantage to insulin products currently available for use in either type 1 or type 2 diabetes.
 - There is no useful evidence that insulin glulisine (Apidra) has a side-effect profile significantly different from comparable insulin products currently available for use in either type 1 or type 2 diabetes.
- Caution is urged regarding the uncertain evidence in making health care decisions.

¹ Insulin glulisine differs from human insulin in that the amino acid asparagine at position B3 is replaced by lysine and the lysine in position B29 is replaced by glutamic acid. See appendix G.

Decision

Maintain insulin glulisine (Apidra) as non-preferred/non-formulary because there is no useful evidence that Apidra provides additional clinical value over existing insulin products for the treatment/management of type-1 or type-2 diabetes.

Products

Drug Product ^{1,2}	Date of FDA Approval ²	FDA Approved Indication(s)	Dose/Route	Potential Off-Label Use(s)
INSULIN				
regular human insulin: (Humulin® R)	10/1982	Diabetes mellitus – Type 1, Type 2, gestational, pregnancy, diabetic ketoacidosis, hyperglycemic-hyperosmolar nonketotic coma	Individualized per patient's needs.	Diabetic ketoacidosis; hyperglycemic-hyperosmolar nonketotic coma
regular human insulin: (Novolin® R)	06/1991	Diabetes mellitus – Type I, Type 2, gestational, pregnancy, diabetic ketoacidosis, hyperglycemic-hyperosmolar nonketotic coma	Individualized per patient's needs.	Diabetic ketoacidosis; hyperglycemic-hyperosmolar nonketotic coma
insulin aspart: (Novolog®)	06/2000	Diabetes mellitus, Type 1 and Type 2	Individualized per patient's needs.	
insulin lispro: (Humalog®)	06/1996	Diabetes mellitus, Type 1 and Type 2	Individualized per patient's needs.	
insulin glulisine (Apidra®)	04/2004	Diabetes mellitus, Type 1 and Type 2	Individualized per patient's needs.	
isophane (NPH): (Humulin® 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® N)	07/1991	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
detemir : (Levemir®) ³	6/2005	Diabetes mellitus, Type 1 and Type 2	Individualized per patient's needs.	
glargine: (Lantus®)	04/2000	Diabetes mellitus Type 1 in adults and pediatric 6 yrs and older, Type 2 in adults	Individualized per patient's needs.	
lispro 75/25: (Humalog® Mix)	12/1999	Diabetes mellitus, Type 1 and Type 2	Individualized per patient's needs.	
aspart 70/30: (NovoLog® Mix)	11/2001	Diabetes mellitus, Type 1 and Type 2	Individualized per patient's needs.	

References

1. Thomson Micromedex © 1974-2005. Micromedex Healthcare Series, Vol. 120.
2. Center for Drug Evaluation and Research. Approval package for application number N021629. <http://www.fda.gov/cder/rdmt/nmecy2005.htm> (assessed November 10, 2005)
3. Apidra (insulin glulisine) Product Information. Aventis Pharmaceuticals Inc. ©2004 Accessed at <http://www.sanofi-aventis.us/>. (assessed November 18, 2005)
4. Garg SK, Rosenstock J, Ways K. Optimized Basal-bolus insulin regimens in type 1 diabetes: insulin glulisine versus regular human insulin in combination with Basal insulin glargine. *Endocr Pract.* 2005 Jan-Feb;11(1):11-7. Erratum in: *Endocr Pract.* 2005 Mar-Apr;11(2):145.

5. Dreyer M, Prager R, Robinson A, Busch K, Ellis G, Souhami E, et al. Efficacy and safety of insulin glulisine in patients with type 1 diabetes. *Horm Metab Res.* 2005 Nov;37(11):702-7.
6. Product Dossier: Apidra (insulin glulisine). Aventis Study #3006. Aventis Pharmaceuticals, Bridgewater NJ. Data reviewed November 18, 2005.
7. Dailey G, Rosenstock J, Moses RG, Ways K. Insulin glulisine provides improved glycemic control in patients with type 2 diabetes. *Diabetes Care.* 2004 Oct;27(10):2363-8.
8. Product Dossier: Apidra (insulin glulisine). Aventis Study #3005. Aventis Pharmaceuticals, Bridgewater NJ. Data reviewed November 18, 2005.
9. American Diabetes Association: Standards of Medical Care in Diabetes. *Diabetes Care.* 2005;28:S4-S36. (assessed November 10, 2005)
10. 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/
11. 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 November 10, 2005)