



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

### Insulin glulisine (Apidra<sup>®</sup>) [Sanofi Aventis]

February 2006

**New Product(s) for Review:**

Insulin glulisine (Apidra<sup>®</sup>) [Sanofi Aventis]

**Dossier Provided by Manufacturer:** yes

**Available Therapeutic Alternatives**

Preferred/Formulary	Non-Preferred/Non-Formulary
<i>Rapid-Acting Insulin</i>	
insulin aspart: (Novolog <sup>®</sup> ) [Novo Nordisk ]	insulin glulisine: (Apidra <sup>®</sup> ) [Sanofi Aventis]
insulin lispro: (Humalog <sup>®</sup> ) [Eli Lilly]	
<i>Short-Acting Insulin</i>	
regular human insulin: (Humulin <sup>®</sup> R) [Eli Lilly]	
regular human insulin: (Novolin <sup>®</sup> R) [Novo Nordisk ]	
<i>Intermediate/Long-Acting Insulin</i>	
isophane (NPH): (Humulin <sup>®</sup> N) [Eli Lilly]	
isophane (NPH): (Novolin <sup>®</sup> N) [Novo Nordisk ]	
insulin glargine: (Lantus <sup>®</sup> ) [Aventis]	insulin detemir: (Levimer <sup>®</sup> ) [Novo Nordisk]
<i>Pre-Mixed Insulin</i>	
lispro 75/25: (Humalog <sup>®</sup> Mix) [Eli Lilly]	
aspart 70/30: (NovoLog <sup>®</sup> Mix) [Novo Nordisk ]	

**Reason for Review**

Insulin glulisine (Apidra<sup>®</sup>) is a new, rapid-acting, insulin analog indicated for the treatment of adult patients with type 1 or type 2 diabetes mellitus.

**Executive Summary**

- Insulin glulisine (Apidra) is a rapid-acting human insulin analog\* indicated for adults with diabetes mellitus for the control of hyperglycemia.

\* 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.

- 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.

### **Marketing**

- In 2002, the worldwide diabetes market was worth about \$18 billion of which \$4.4 billion was for insulin products.
- By 2007, the total market share of rapid-acting insulins is expected to be approximately \$2.25 billion worldwide.
- Insulin glulisine (Apidra) is likely to be promoted as an alternative to regular human insulin or other rapid-acting insulins.
- The FDA recognized open-label trials as sufficient to support approval for insulin glulisine (Apidra) because of differences in absorption and onset of action between insulin glulisine (Apidra) and regular human insulin that made blinding impractical and potentially unsafe.

### **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 over 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.

### **Conclusion**

Insulin glulisine (Apidra) is 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 <sup>1,2</sup>	Date of FDA Approval <sup>2</sup>	FDA Approved Indication(s)	Dose/Route	AWP Cost or MAC*	Potential Off-Label Use(s)
<b>INSULIN</b>				<b>Cost of insulin per 10 mL vial</b>	
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.	\$35	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.	\$35	Diabetic ketoacidosis; hyperglycemic-hyperosmolar nonketotic coma
insulin aspart: (Novolog®)	06/2000	Diabetes mellitus, Type 1 and Type 2	Individualized per patient’s needs.	\$81	
insulin lispro: (Humalog®)	06/1996	Diabetes mellitus, Type 1 and Type 2	Individualized per patient’s needs.	\$81	
insulin glulisine (Apidra®)	04/2004	Diabetes mellitus, Type 1 and Type 2	Individualized per patient’s needs.	\$81	
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.	\$35	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.	\$35	Hyperkalemia, diabetic neuropathy, diabetic macrovascular disease, latent autoimmune diabetes in adults, myocardial infarction
detemir : (Levemir®) <sup>3</sup>	6/2005	Diabetes mellitus, Type 1 and Type 2	Individualized per patient’s needs.	Not yet established	
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.	\$91	
lispro 75/25: (Humalog® Mix)	12/1999	Diabetes mellitus, Type 1 and Type 2	Individualized per patient’s needs.	\$81	
aspart 70/30: (NovoLog® Mix)	11/2001	Diabetes mellitus, Type 1 and Type 2	Individualized per patient’s needs.	\$81	

\*AWP (average wholesale price) based on First Data Bank as of January 2006 for 1 month of therapy.

## References

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