



Therapeutic Class ReviewSM

Diabetes - Insulin detemir (Levemir[®])

February 2007

New Product(s) for Review

Insulin detemir (Levemir[®]) [Novo Nordisk]

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 detemir (Levemir) is an intermediate to long-acting insulin analog with up to 24 hours duration of action. Structural differences from human insulin¹ and significant binding to albumin² allow slower absorption from the injection site and prolonged release from albumin-binding sites.
- Insulin detemir (Levemir) is indicated for once- or twice-daily subcutaneous administration for the treatment of adult and pediatric patients with type 1 diabetes mellitus or adult patients with type 2 diabetes mellitus who require basal (long acting) insulin for the control of hyperglycemia.

Evidence

- Evidence from the February 2006 review:
 - There is no useful evidence that insulin detemir (Levemir) provides a clinically relevant therapeutic advantage or disadvantage relative to insulin products currently available for use in either type 1 or type 2 diabetes.
 - There is no useful evidence that insulin detemir (Levemir) has a side-effect profile significantly different from comparable insulin products currently available for use in either type 1 or type 2 diabetes.
- New data since February 2006 is similar to and consistent with this assessment, and adds no useful new evidence for safety or efficacy².

¹ Insulin detemir differs from human insulin in that the amino acid threonine in position B30 has been omitted, and a C14 fatty acid chain has been attached to the amino acid B29.

² More than 98% insulin detemir in the bloodstream is bound to albumin.

- Several external practitioners were contacted to share their clinical experience with insulin detemir (Levemir):
 - Most practitioners reported:
 - Lantus was the product of first choice when selecting a long-acting basal insulin.
 - Insulin detemir (Levemir) appears to have a role as a replacement/ improvement to NPH.
 - They are aware of the difference in dosing/bioavailability (up to a 40% decrease in bioavailability) and compensate when prescribing.
 - Insulin detemir (Levemir) is most commonly dosed twice daily.
 - Some physicians felt that insulin detemir (Levemir) has an advantage in select patients where its unique absorption characteristics (shorter time to peak than Lantus) might be of benefit.
 - One endocrinologist equated insulin detemir (Levemir) as an “improved NPH” insulin, in the same way that Lantus is “an improved Ultralente” insulin.

Decision

Maintain insulin detemir (Levemir) as non-preferred/non-formulary because there is no useful evidence that it 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.	

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