



Therapeutic Class ReviewSM

Diabetes - Exenatide (Byetta[®])

November 2005

New Product for Review

Exenatide (Byetta[®]) [Amylin Pharmaceuticals, Inc.]

Dossier Provided by Manufacturer: yes

Executive Summary

- Exenatide (Byetta) is advertised as a new diabetes medication that has several unique mechanism of actions to lower blood glucose, less hypoglycemia, convenient fixed dosing for subcutaneous administration, and potential for weight loss in patients with Type 2 diabetes.
- Exenatide (Byetta) is indicated as add-on treatment to existing oral diabetes therapy with a sulfonylureas and/or metformin in Type 2 diabetes.
 - There is uncertain evidence that the addition of exenatide (Byetta) to sulfonylureas and/or metformin results in clinically meaningful reduction in HbA_{1c}.
 - There is no evidence to prove the clinical benefits using exenatide (Byetta) as monotherapy or as add-on treatment to thiazolidinediones (TZDs) or insulin.
 - Exenatide (Byetta) is not a substitute for insulin and has not been proven to provide better glycemic control than insulin, halt the disease progression, or prevent a patient's need for insulin long-term.
- Nausea and hypoglycemia are the most prevalent adverse effects observed with exenatide (Byetta).
 - Nausea with exenatide (Byetta) generally occurs early in treatment and accounts for the majority of therapy discontinuation.
 - Hypoglycemia is less frequent when used with metformin than with a sulfonylurea or sulfonylurea/metformin combination therapy.
 - There is no evidence to differentiate the hypoglycemic risk of exenatide (Byetta) versus insulin.
- There is no evidence that any weight loss or weight maintenance with exenatide (Byetta) is clinically meaningful or results in improved long-term health outcomes.

Decision

Exenatide (Byetta) is non-preferred/non-formulary because the evidence is uncertain to support additional benefit over less costly and better established options for glycemic control in diabetes.

Products

Drug Product ^{1,2}	Date of FDA Approval ²	FDA Approved Indication(s)	Dose/Route	Potential Off-Label Use(s)
Exenatide (Byetta) ³	04/2005	Diabetes mellitus, Type 2 patients with inadequate glycemic control on metformin, sulfonylurea, combination of metformin + sulfonylurea. (Used as adjunctive therapy only)	5 - 10mcg SQ twice daily	Weight loss
Glipizide (generic)	05/1984	Diabetes mellitus, Type 2 (Used alone or in combination)	5 - 40mg orally daily	Diabetic microangiopathy; Gestational diabetes
Glipizide and Metformin HCl (Metaglip®)	10/2002	Diabetes mellitus, Type 2	<u>Monotherapy:</u> 2.5 mg/250 mg 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 daily	Gestational diabetes
Glyburide and Metformin HCl (Glucovance®)	07/2000	Diabetes mellitus, Type 2	1.25 mg/250 mg orally once or twice daily <u>Previously treated:</u> 2.5 mg/500 mg to 5 mg/500 mg orally twice daily; max. 20 mg/2000 mg once daily	
Metformin (generic)	03/1995	Diabetes mellitus, Type 2 (Used alone or in combination)	500 mg orally 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 orally once daily; max. 45 mg daily <u>Combination therapy:</u> max. 30 mg orally 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 once daily or 2mg twice daily; max. 8 mg daily <u>Concomitant with insulin:</u> 4 mg orally 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 (not to be given as initial therapy)	2mg/500mg – 4mg/1000mg orally twice daily	

References

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7. Product Dossier: Byetta[®] (exenatide), Amylin Pharmaceuticals, Inc; San Diego, CA. Data reviewed 08/01/05.
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