



**BYETTA® (exenatide) Injection and
BYDUREON™ (exenatide extended-release for injectable suspension)**

U.S. Fact Sheet

Exenatide	
<p>Exenatide is marketed as BYETTA® (exenatide) injection, a twice-daily injectable treatment for type 2 diabetes, and BYDUREON™ (exenatide extended-release for injectable suspension), a once-weekly injectable treatment for type 2 diabetes.</p> <p>Exenatide is an established treatment for type 2 diabetes. As BYETTA, exenatide has been available in the U.S. since 2005 and in the EU since 2006. It is used in nearly 80 countries worldwide to improve glycemic control in adults with type 2 diabetes.</p> <p>BYDUREON received its first regulatory approval in the EU in June 2011, and it was approved in the U.S. in January 2012.</p>	
GLP-1 Class	
<p>BYETTA and BYDUREON are compounds in a class of drugs known as glucagon-like peptide-1 (GLP-1) receptor agonists. BYDUREON and BYETTA mimic several of the actions of a naturally occurring hormone in the body called GLP-1. GLP-1 stimulates insulin release from the pancreas, regulates glucagon levels, reduces food intake and slows the rate of gastric emptying.</p>	
Indication	
<p>BYETTA is indicated in combination with diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. It can also be used with metformin, a sulfonyleurea, a thiazolidinedione or Lantus® (insulin glargine), which is a long-acting insulin.</p>	<p>BYDUREON is indicated in combination with diet and exercise to improve glycemic control in adults with type 2 diabetes. It can also be used with metformin, a sulfonyleurea, or a thiazolidinedione. It is not recommended as first-line therapy.</p>
FDA Approvals and Clinical Trial Experience	
<p>BYETTA was approved in the U.S. in April 2005 as adjunctive therapy with certain oral medications. In 2009, the FDA approved an expanded use for BYETTA as a stand-alone therapy (monotherapy) along with diet and exercise. It was approved as an add-on therapy to insulin glargine in 2011, expanding the indication for the use of BYETTA across the continuum of type 2 diabetes care.</p> <p>The initial approval of BYETTA was based on three, 30-week controlled clinical studies</p>	<p>BYDUREON was approved in the U.S. in January 2012 as the first and only once-weekly treatment for type 2 diabetes.</p> <p>The approval of BYDUREON was based on efficacy data from the DURATION-5 clinical study, safety data from five studies in the DURATION series and clinical and post-marketing experience with BYETTA.³</p>

<p>in the AMIGO program. The approval of BYETTA as a monotherapy treatment and as an add-on therapy to insulin glargine was based on two additional clinical studies.^{1,2}</p>	
<p>Background</p>	
<p>BYETTA was the first GLP-1 receptor agonist to be approved by FDA for the treatment of type 2 diabetes, and it is the first and only GLP-1 receptor agonist approved for use in the U.S. as an adjunct to insulin glargine with or without metformin and/or a thiazolidinedione. For patients not at goal on insulin glargine, adding BYETTA can deliver a complementary approach to glycemic control. BYETTA provides sustained A1C control with potential weight loss (BYETTA is not a weight-loss product).</p> <p>In 2008, the American Diabetes Association and the European Association for the Study of Diabetes (EASD) consensus panel updated treatment guidelines to include GLP-1 receptor agonists, acknowledging the approach of treating diabetes with glucose control therapies that promote weight loss without increasing hypoglycemia. In addition, the American Association of Clinical Endocrinologists (AACE) and the American College of Endocrinology (ACE) consensus treatment panel in 2009 issued a new type 2 diabetes algorithm in which GLP-1 receptor agonists are recommended for use earlier in the treatment continuum based on effectiveness and overall safety profile.⁴</p>	<p>BYDUREON is the first and only once-weekly treatment for type 2 diabetes. BYDUREON provides continuous glycemic control in a single weekly dose. BYDUREON uses proprietary technology for long-acting medications developed by Alkermes plc to provide a controlled release of exenatide.</p>
<p>Dosing</p>	
<p>BYETTA is available in a simple-to-use, twice-a-day, fixed-dose pen. Two prefilled pens are available to deliver unit doses of 5 micrograms or 10 micrograms. Each prefilled pen will deliver 60 doses to provide 30 days of twice-daily administration.</p>	<p>BYDUREON is taken once a week via subcutaneous injection. BYDUREON is provided in a straightforward single-dose tray so that patients can self-administer the medicine each week. Each tray contains one vial of exenatide 2 mg, one vial connector, one prefilled diluent syringe and two custom needles (one provided as a spare). BYDUREON is supplied in cartons of four single-dose trays, representing a four-week supply.</p>

Important Safety Considerations	
<p>BYETTA has a bolded warning for pancreatitis. Alternative therapy should be considered in patients with a history of pancreatitis.</p> <p><i>These are not all the safety considerations for BYETTA. Please see the accompanying BYETTA Prescribing Information and Medication Guide.</i></p>	<p>BYDUREON has an important warning regarding possible risk of thyroid tumors including thyroid cancer and a bolded warning for risk of acute pancreatitis. Patients should be counseled regarding risk and symptoms of thyroid tumors, and other antidiabetic therapies should be considered in patients with a history of pancreatitis.</p> <p><i>These are not all the safety considerations for BYDUREON. Please see the accompanying BYDUREON Prescribing Information and Medication Guide.</i></p>
Marketing	
<p>In the U.S., BYETTA and BYDUREON are marketed by Amylin Pharmaceuticals, Inc.</p>	

About BYETTA® (exenatide) injection

BYETTA was the first glucagon-like peptide-1 (GLP-1) receptor agonist to be approved by the FDA for the treatment of type 2 diabetes. BYETTA exhibits many of the same effects as the human incretin hormone GLP-1. GLP-1 improves blood sugar after food intake through multiple effects that work in concert on the stomach, liver, pancreas and brain.

BYETTA is an injectable prescription medicine that may improve blood sugar (glucose) control in adults with type 2 diabetes mellitus, when used with a diet and exercise program. It can also be used with metformin, a sulfonylurea, a thiazolidinedione or Lantus® (insulin glargine), which is a long-acting insulin.

BYETTA is not insulin and should not be taken instead of insulin. BYETTA should not be taken with short- and/or rapid-acting insulin. BYETTA is not for people with type 1 diabetes or people with diabetic ketoacidosis. BYETTA has not been studied in patients with a history of pancreatitis. Other antidiabetic therapies should be considered for these patients.

BYETTA provides sustained A1C control with potential weight loss (BYETTA is not a weight-loss product). BYETTA was approved in the U.S. in April 2005 and in Europe in November 2006 and has been used by more than 1.8 million patients since its introduction. See important safety information below. Additional information about BYETTA is available at www.BYETTA.com.

Important Safety Information for BYETTA® (exenatide) injection

Based on post-marketing data, BYETTA has been associated with acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis. Patients should be observed for signs and symptoms of pancreatitis after initiation or dose escalation of BYETTA.

The risk of getting low blood sugar is higher if BYETTA is taken with another medicine that can cause low blood sugar, such as a sulfonylurea or insulin. The dose of sulfonylurea or insulin may need to be lowered while BYETTA is used. BYETTA should not be used in people who have severe kidney problems and may cause or worsen problems with kidney function, including kidney failure. Patients should talk with their healthcare provider if they have severe problems with their stomach, such as delayed emptying of the stomach (gastroparesis) or problems with digesting food. Antibodies may develop with use of BYETTA. Patients who develop high titers to exenatide could have worsening or failure to achieve adequate glycemic control. Severe allergic reactions can happen with BYETTA. There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with BYETTA or any other antidiabetic drug.

The most common side effects with BYETTA include nausea, vomiting, diarrhea, feeling jittery, dizziness, headache, acid stomach, constipation and weakness. Nausea most commonly happens when first starting BYETTA, but may become less over time.

These are not all the side effects from use of BYETTA. A healthcare provider should be consulted about any side effect that is bothersome or does not go away.

For additional important safety information about BYETTA, please see the full Prescribing Information (www.BYETTA.com/pi) and patient Medication Guide (www.BYETTA.com/mg).

About BYDUREON™ (exenatide extended-release for injectable suspension)

BYDUREON, previously known as exenatide once weekly, is the first and only once-weekly medicine to be approved by the FDA for the treatment of type 2 diabetes. BYDUREON works with the body to help make its own insulin when needed, providing continuous glycemic control with just one dose per week. Each dose of BYDUREON is made up of biodegradable microspheres that provide a controlled release of exenatide throughout the week.

BYDUREON is an injectable prescription medicine that may improve blood sugar (glucose) in adults with type 2 diabetes mellitus, and should be used along with diet and exercise. BYDUREON is not recommended as the first medication to treat diabetes.

BYDUREON is a long-acting form of the medication in BYETTA® (exenatide) injection so both drugs should not be used together. BYDUREON is not insulin and should not be taken instead of insulin. BYDUREON is not for people with type 1 diabetes or people with diabetic ketoacidosis. BYDUREON is not recommended for use in children. It is not known if BYDUREON is safe and effective in people with a history of pancreatitis or severe kidney problems. See important safety information below. Additional information about BYDUREON is available at www.BYDUREON.com.

Important Safety Information for BYDUREON™ (exenatide extended-release for injectable suspension)

In animal studies, BYDUREON caused rats to develop tumors of the thyroid gland. Some tumors were cancers. It is not known if BYDUREON causes thyroid tumors or a type of thyroid cancer called medullary thyroid cancer (MTC) in

people. BYDUREON should not be used if there is a personal or family history of MTC or Multiple Endocrine Neoplasia syndrome type 2.

Based on postmarketing data, exenatide has been associated with acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis. Patients should be observed for signs and symptoms of pancreatitis after initiation of BYDUREON.

The risk of getting low blood sugar is higher if BYDUREON is taken with another medicine that can cause low blood sugar, such as a sulfonylurea. The dose of sulfonylurea may need to be lowered while BYDUREON is used. BYDUREON should not be used in people who have or had severe kidney problems and may cause or worsen problems with kidney function, including kidney failure. Patients should talk with their healthcare provider if they have severe problems with their stomach, such as delayed emptying of the stomach (gastroparesis) or problems with digesting food. Antibodies may develop with use of BYDUREON, which may lead to worsening or failure to achieve adequate glycemic control. Severe allergic reactions can happen with BYDUREON. There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with BYDUREON or any other antidiabetic drug.

The most common side effects with BYDUREON include nausea, diarrhea, headache, vomiting, constipation, itching at injection site, a small bump (nodule) at the injection site, and indigestion. Nausea most commonly happens when first starting BYDUREON, but may become less over time.

These are not all the side effects from use of BYDUREON. A healthcare provider should be consulted about any side effect that is bothersome or does not go away.

For additional important safety information about BYDUREON, please see the full Prescribing Information (www.BYDUREON.com/pi) and patient Medication Guide (www.BYDUREON.com/mg).

###

References

- ¹ Moretto TJ, Milton DR, Ridge TD, et al. Efficacy and tolerability of exenatide monotherapy over 24 weeks in antidiabetic drug-naïve patients with type 2 diabetes: a randomized, double-blind, placebo-controlled, parallel-group study. *Clin Ther.* 2008;30:1448-60.
- ² Buse JB, Bergenstal RM, Glass LC, et al. Use of twice-daily exenatide in basal insulin-treated patients with type 2 diabetes: A randomized, controlled trial. *Ann Intern Med.* 2011;154:103-112.
- ³ Drucker DJ, Buse JB, Taylor K, Kendall DM, Trautmann M, Dongliang Z, Porter L. Exenatide once weekly versus twice daily for the treatment of type 2 diabetes: a randomised open-label, non-inferiority study. *The Lancet.* 2008;372,9645:1240–1250.
- ⁴ Rodbard H, Jellinger P, Davidson J, Einhorn D, Garber A, Grunberger G, Handelsman Y, Horton E, Lebovitz H, Levy P, Moghissi E, Schwartz S. Statement by an American Association of Clinical Endocrinologists/American College of Endocrinology Consensus Panel on Type 2 Diabetes Mellitus: An Algorithm for Glycemic Control. *Endocrine Practice.* 2009; 15(6): 540-559.

06-11-12762-A ©2012 AMYLIN PHARMACEUTICALS, INC. PRINTED IN USA. ALL RIGHTS RESERVED.
BYETTA is a registered trademark of Amylin Pharmaceuticals, Inc. BYDUREON is a trademark of Amylin Pharmaceuticals, Inc.