gestation day 7, there were no adverse fetal effects at doses up to 760 mcg/kg/day, systemic exposures up to 148 times the human exposure resulting from the maximum recommended dose of 2 mg/day, based on AUC.

In pregnant mice given twice-daily subcutaneous doses of 6, 68, 460, or 760 mcg/kg/day exenatide, the active ingredient in BYDUREON, from gestation day 6 through 15 (organogenesis), cleft palate (some with holes), and irregular fetal skeletal ossification of rib and skull bones were observed at 6 mcg/kg/day, a systemic exposure equal to the human exposure resulting from the maximum recommended dose of 2 mg/day, based on AUC.

In pregnant rabbits given twice-daily subcutaneous doses of 0.2, 2, 22, 156, or 260 mcg/kg/day exenatide, the active ingredient in BYDUREON, from gestation day 6 through 18 (organogenesis), irregular fetal skeletal ossifications were observed at 2 mcg/kg/day, a systemic exposure 4 times the human exposure resulting from the maximum recommended dose of 2 mg/day, based on AUC.

In pregnant mice given twice-daily subcutaneous doses of 6, 68, or 760 mcg/kg/day exenatide, the active ingredient in BYDUREON, from gestation day 6 through lactation day 20 (weaning), an increased number of neonatal deaths was observed on postpartum days 2 to 4 in dams given 6 mcg/kg/day, a systemic exposure equal to the human exposure resulting from the maximum recommended dose of 2 mg/day, based on AUC.

14 CLINICAL STUDIES

BYDUREON has been studied as monotherapy and in combination with metformin, a sulfonylurea, a thiazolidinedione, a combination of metformin and a sulfonylurea, or a combination of metformin and a thiazolidinedione.

14.1 24-Week Comparator-Controlled Study

A 24-week, randomized, open-label trial was conducted to compare the safety and efficacy of BYDUREON to BYETTA in patients with type 2 diabetes and inadequate glycemic control with diet and exercise alone or with oral antidiabetic therapy, including metformin, a sulfonylurea, a thiazolidinedione, or combination of two of those therapies.

A total of 252 patients were studied: 149 (59%) were Caucasian, 78 (31%) Hispanic, 15 (6%) Black, and 10 (4%) Asian. Patients were treated with diet and exercise alone (19%), a single oral antidiabetic agent (47%), or combination therapy of oral antidiabetic agents (35%). The mean

baseline HbA_{1c} was 8.4%. Patients were randomly assigned to receive BYDUREON 2 mg once every 7 days (weekly) or BYETTA (10 mcg twice daily), in addition to existing oral antidiabetic agents. Patients assigned to BYETTA initiated treatment with 5 mcg twice daily then increased the dose to 10 mcg twice daily after 4 weeks.

The primary endpoint was change in HbA_{1c} from baseline to Week 24 (or the last value at time of early discontinuation). Change in body weight was a secondary endpoint. Twenty-four week study results are summarized in Table 4.

Table 4: Results of 24-Week Trial of BYDUREON

	BYDUREON 2 mg	**BYETTA 10 mcg***
Intent-to-Treat Population (N)	129	123
HbA_{1c} (%)		
Mean Baseline	8.5	8.4
Mean Change at Week 24†	−1.6	−0.9
Difference from BYETTA† [95% CI]	−0.7 [−0.9, −0.4]¶	
Percentage Achieving HbA_{1c} <7% at Week 24 (%)	58¶	30
Fasting Plasma Glucose (mg/dL)		
Mean Baseline	173	168
Mean Change at Week 24	−25	−5
Difference from BYETTA† [95% CI]	−20 [−31, −10]¶	

N = number of patients in each treatment group.

Note: mean change is least squares mean change.

* BYETTA 5 mcg twice daily before the morning and evening meals for 4 weeks followed by 10 mcg twice daily for 20 weeks.

† Least squares (LS) means are adjusted for baseline HbA_{1c} strata, background antihyperglycemic therapy, and baseline value of the dependent variable (if applicable).

¶ $p<0.001$, treatment vs comparator.

Reductions from mean baseline (97/94 kg) in body weight were observed in both BYDUREON (−2.3 kg) and BYETTA (−1.4 kg) treatment groups.

BYDUREON did not have adverse effects on blood pressure. An LS mean increase from baseline (74 beats per minute) in heart rate of 4 beats per minute was observed with BYDUREON treatment and 2 beats per minute with BYETTA treatment. The long-term effects of the increase in pulse rate have not been established [see *Warnings and Precautions (5.8)*].

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

BYDUREON (exenatide extended-release for injectable suspension) for once every 7 days (weekly) subcutaneous administration is supplied as:

BYDUREON single-dose tray, supplied in cartons that contain four single-dose trays (NDC 66780-219-04). Each single-dose tray contains:

- One vial containing 2 mg exenatide (as a white to off-white powder)
- One prefilled syringe delivering 0.65 mL diluent
- One vial connector
- Two custom needles (23G, 5/16") specific to this delivery system (one is a spare needle)

BYDUREON Pen, supplied in cartons that contain four single-dose pens and one spare needle (NDC 0310-6530-04). Each single-dose pen contains:

- One pen containing 2 mg of exenatide (as a white to off-white powder) and delivering 0.65 mL diluent.
- One custom needle (23G, 9/32") specific to this delivery system.

Do **not** substitute needles or any other components provided with BYDUREON.

16.2 Storage and Handling

- BYDUREON should be stored in the refrigerator at 36°F to 46°F (2°C to 8°C), up to the expiration date or until preparing for use. BYDUREON should not be used past the expiration date. The expiration date can be found on the carton, on the cover of the single-dose tray, or on the pen label.
- Do not freeze BYDUREON. Do not use BYDUREON if it has been frozen. Protect from light.
- BYDUREON can be kept at room temperature not to exceed 77°F (25°C) [see USP Controlled Room Temperature] for no more than a total of 4 weeks, if needed.
- Use the diluent only if it is clear and free of particulate matter.
- After suspension, the mixture should be white to off-white and cloudy.
- BYDUREON must be administered immediately after the exenatide powder is suspended in the diluent.

- Use a puncture-resistant container to discard BYDUREON with the needle still attached. Do not reuse or share needles or syringes.
- Keep out of the reach of children.

17 PATIENT COUNSELING INFORMATION

See FDA-approved Medication Guide. **Prior to initiation of BYDUREON, patients should be trained by their healthcare professional.**

Inform patients about the potential risks and benefits of BYDUREON and of alternative modes of therapy. Also inform patients about the importance of diabetes self-management practices, such as regular physical activity, adhering to meal planning, periodic blood glucose monitoring and HbA_{1c} testing, recognition and management of hypoglycemia and hyperglycemia, and assessment for diabetes complications.

17.1 Risk of Thyroid C-cell Tumors

Inform patients that exenatide extended-release causes benign and malignant thyroid C-cell tumors in rats and that the human relevance of this finding is unknown. Counsel patients to report symptoms of thyroid tumors (e.g., a lump in the neck, hoarseness, dysphagia, or dyspnea) [see *Warnings and Precautions (5.1)*].

17.2 Risk of Pancreatitis

Inform patients treated with BYDUREON of the potential risk for pancreatitis. Explain that persistent severe abdominal pain that may radiate to the back, and which may or may not be accompanied by vomiting, is the hallmark symptom of acute pancreatitis. Instruct patients to discontinue BYDUREON promptly and contact their healthcare provider if persistent severe abdominal pain occurs [see *Warnings and Precautions (5.2)*].

17.3 Risk of Hypoglycemia

The risk of hypoglycemia is increased when BYDUREON is used in combination with an agent that induces hypoglycemia, such as a sulfonylurea [see *Warnings and Precautions (5.3)*]. Explain the symptoms, treatment, and conditions that predispose to the development of hypoglycemia. While the patient's usual instructions for hypoglycemia management do not need to be changed, these instructions should be reviewed and reinforced when initiating

BYDUREON therapy, particularly when concomitantly administered with a sulfonylurea [see *Warnings and Precautions (5.3)*].

17.4 Risk of Renal Impairment

Inform patients treated with BYDUREON of the potential risk for worsening renal function and explain the associated signs and symptoms of renal impairment, as well as the possibility of dialysis as a medical intervention if renal failure occurs [see *Warnings and Precautions (5.4)*].

17.5 Risk of Hypersensitivity Reactions

Inform patients that serious hypersensitivity reactions have been reported during postmarketing use of exenatide. If symptoms of hypersensitivity reactions occur, patients must stop taking BYDUREON and seek medical advice promptly [see *Warnings and Precautions (5.7)*].

17.6 Risk of Injection-Site Reactions

Inform patients that there have been postmarketing reports of serious injection-site reactions with or without subcutaneous nodules, with the use of BYDUREON. Isolated cases of injection-site reactions required surgical intervention. Advise patients to seek medical advice if symptomatic nodules occur, or for any signs or symptoms of abscess, cellulitis, or necrosis [see *Warnings and Precautions (5.8)*].

17.7 Use in Pregnancy

Advise patients to inform their healthcare provider if they are pregnant or intend to become pregnant [see *Use in Specific Populations (8.1)*].

17.8 Instructions

Patients should be trained on how to use BYDUREON properly prior to self-administration. Instruct patients on proper mixing and injection technique to ensure the product is adequately mixed and a full dose is delivered. Refer patients to the accompanying Instructions for Use for complete administration instructions with illustrations.

Each dose of BYDUREON should be administered as a subcutaneous injection at any time on the dosing day, with or without meals. Patients should be informed that the day of once every 7 days (weekly) administration can be changed if necessary as long as the last dose was

administered 3 or more days before. If a dose is missed, it should be administered as soon as noticed, provided the next regularly scheduled dose is due at least 3 days later. Thereafter, patients can resume their usual once every 7 days (weekly) dosing schedule. If a dose is missed and the next regularly scheduled dose is due in 1 or 2 days, the patient should not administer the missed dose and instead resume BYDUREON with the next regularly scheduled dose [see *Dosage and Administration (2.1)*].

Counsel patients that they should never share BYDUREON with another person, even if the needle is changed. Sharing of BYDUREON or needles between patients may pose a risk of transmission of infection.

If a patient is currently taking BYETTA, it should be discontinued upon starting BYDUREON. Patients formerly on BYETTA who start BYDUREON may experience transient elevations in blood glucose concentrations, which generally improve within the first 2 weeks after initiation of therapy [see *Dosage and Administration (2.3)* and *Clinical Studies (14.1)*].

Treatment with BYDUREON may also result in nausea, particularly upon initiation of therapy [see *Adverse Reactions (6)*].

Inform patients about the importance of proper storage of BYDUREON, injection technique, and dosing [see *Dosage and Administration (2)* and *How Supplied/Storage and Handling (16)*].

The patient should read the BYDUREON Medication Guide and the Instructions for Use before starting BYDUREON therapy and review them each time the prescription is refilled.

BYDUREON is a registered trademark of the AstraZeneca group of companies.

Manufactured for:
AstraZeneca Pharmaceuticals LP
Wilmington, DE 19850

By:
Amylin Ohio LLC
West Chester, OH 45071

Medication Guide

BYDUREON® (by-DUR-ee-on) (exenatide extended-release for injectable suspension)

Read this Medication Guide before you start using BYDUREON and each time you get a refill. There may be new information. This information does not take the place of talking with your healthcare provider about your medical condition or your treatment.

What is the most important information I should know about BYDUREON?

Serious side effects may happen in people who use BYDUREON, including:

1. **Possible thyroid tumors, including cancer**. During the drug testing process, the medicine in BYDUREON caused rats to develop tumors of the thyroid gland. Some of these tumors were cancers. It is not known if BYDUREON will cause thyroid tumors or a type of thyroid cancer called medullary thyroid cancer in people.
   - Before you start using BYDUREON, tell your healthcare provider if you or any of your family members have had thyroid cancer, especially medullary thyroid cancer, or Multiple Endocrine Neoplasia syndrome type 2. **Do not** use BYDUREON if you or any of your family members have medullary thyroid cancer, or if you have Multiple Endocrine Neoplasia syndrome type 2. People with these conditions already have a higher chance of developing medullary thyroid cancer in general and should not use BYDUREON.
   - While using BYDUREON, tell your healthcare provider if you get a lump or swelling in your neck, hoarseness, trouble swallowing, or shortness of breath. These may be symptoms of thyroid cancer.
2. **Inflammation of the pancreas (pancreatitis),** which may be severe and lead to death.

   Before using BYDUREON, tell your healthcare provider if you have had:

   - pancreatitis
   - stones in your gallbladder (gallstones)

- a history of alcoholism
- high blood triglyceride levels

These medical conditions can make you more likely to get pancreatitis. It is not known if having these conditions will lead to a higher chance of getting pancreatitis while taking BYDUREON.

Stop using BYDUREON and call your healthcare provider right away if you have pain in your stomach area (abdomen) that is severe, and will not go away. The pain may happen with or without vomiting. The pain may be felt going from your abdomen through to your back. This type of pain may be a symptom of pancreatitis.

What is BYDUREON?

- 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 a long-acting form of the medication contained in BYETTA. **Do not** use BYDUREON and BYETTA together.
- BYDUREON is not recommended as the first choice of medication for treating diabetes.
- BYDUREON is not insulin.
- It is not known if BYDUREON is safe and effective when used with insulin.
- BYDUREON is not for use in people with type 1 diabetes or people with a condition caused by very high blood sugar (diabetic ketoacidosis).
- It is not known if BYDUREON is safe and effective in children. BYDUREON is not recommended for use in children.
- It is not known if BYDUREON is safe and effective in people who have a history of pancreatitis.
- BYDUREON has not been studied in people who have severe kidney problems.

Who should not use BYDUREON?

Do not use BYDUREON if:

- you or any of your family members have a history of medullary thyroid cancer.
- you have Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). This is a disease where people have tumors in more than one gland in their body.

- you are allergic to exenatide or any of the ingredients in BYDUREON. See the end of this Medication Guide for a complete list of ingredients in BYDUREON. Symptoms of a severe allergic reaction may include:
  - swelling of your face, lips, tongue, or throat
  - problems breathing or swallowing
  - severe rash or itching
  - fainting or feeling dizzy
  - very rapid heartbeat

Talk to your healthcare provider before using this medicine if you have any of these conditions.

What should I tell my healthcare provider before using BYDUREON?

Before using BYDUREON, tell your healthcare provider if you:

- have any of the conditions listed in the section **"What is the most important information I should know about BYDUREON?"**
- have severe problems with your stomach such as slow emptying of your stomach (gastroparesis) or problems digesting food.
- have or have had kidney problems, or have had a kidney transplant.
- have any other medical conditions.
- are pregnant or are planning to become pregnant. It is not known if BYDUREON may harm your unborn baby. Tell your healthcare provider if you become pregnant while taking BYDUREON.

  Pregnancy Registry: There is a registry for women who use BYDUREON during pregnancy. The purpose of this registry is to collect information about the health of you and your baby. If you use BYDUREON at any time during pregnancy, you may enroll in this registry by calling 1-800-633-9081.

- are breastfeeding or plan to breastfeed. It is not known if BYDUREON passes into your breast milk. You and your healthcare provider should decide if you will use BYDUREON or breastfeed. You should not do both without talking with your healthcare provider first.

Tell your healthcare provider about all of the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. BYDUREON may affect the way some medicines work and some other medicines may affect the way BYDUREON works.

Especially tell your healthcare provider if you take:

- other diabetes medicines, especially insulin or a sulfonylurea
- any medicine taken by mouth
- warfarin sodium (Coumadin®, Jantoven®)

Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist each time you get a new medicine.

How should I use BYDUREON?

For detailed instructions, see the Instructions for Use that comes with your BYDUREON.

- BYDUREON comes as a single-dose tray or as a single-dose pen. Your healthcare provider will prescribe the BYDUREON that is best for you.
- **Your healthcare provider should teach you how to use BYDUREON before you use it for the first time.** If you have any questions or do not understand the instructions, talk with your healthcare provider or pharmacist.
- Pay special attention to mixing BYDUREON well, as shown in the Instructions for Use.
- After injecting with the BYDUREON Pen, make sure you hold the needle in your skin for 10 seconds, to get the full dose.
- Use BYDUREON exactly as your healthcare provider tells you to.
- BYDUREON is injected once every seven days (weekly) any time during the day.
- BYDUREON is a subcutaneous injection. Inject BYDUREON into your skin exactly the way your healthcare provider told you to. You can use the injection in your stomach area (abdomen), your thigh, or the back of your upper arm. Each week you can use the same area of your body. But be sure to choose a different injection site in that area.
- You can use BYDUREON with or without food.
- **If you miss a dose of BYDUREON, it should be used as soon as you remember, provided the next regularly scheduled dose is due at least 3 days later.**
- **If you miss a dose of BYDUREON and the next regularly scheduled dose is due 1 or 2 days later, do not use the missed dose. Use BYDUREON on the next regularly scheduled day.**
- **Do not** use 2 doses of BYDUREON less than 3 days apart.
- If you want to change your dosing day, you can. Your new dosing day must be at least 3 days after your last dose.

- BYDUREON must be injected right after you mix it.
- **If you are taking BYETTA and your healthcare provider prescribed BYDUREON, you should follow your healthcare provider's instructions about when to stop taking BYETTA and when to start taking BYDUREON.** BYETTA is a different form of the same medicine that is in BYDUREON, so do not take BYETTA when you are taking BYDUREON. When you first change from BYETTA to BYDUREON, your blood sugar levels may be higher than usual and should get better in about 2 weeks.
- Inject your dose of BYDUREON under the skin (subcutaneous injection), as you are told to by your healthcare provider. **Do not inject BYDUREON into a vein or muscle.**
- **Do not** share your BYDUREON with another person even if the needle is changed. Sharing your tray or pen with another person can cause you or someone else to get an infection.
- Follow your healthcare provider's instructions for diet, exercise, how often to test your blood sugar, and when to get your HbA_{1c} checked. If you see your blood sugar increasing during treatment with BYDUREON, talk to your healthcare provider because you may need to adjust your current treatment plan for your diabetes.
- Talk to your healthcare provider about how to manage high blood sugar (hyperglycemia) and low blood sugar (hypoglycemia), and how to recognize problems that can happen with your diabetes.

What are the possible side effects of BYDUREON?

BYDUREON can cause serious side effects, including:

- **See "What is the most important information I should know about BYDUREON?"**
- **Low blood sugar (hypoglycemia).** Your risk for getting low blood sugar is higher if you use BYDUREON with another medicine that can cause low blood sugar, such as a sulfonylurea. The dose of your sulfonylurea medicine may need to be lowered while you use BYDUREON. Signs and symptoms of low blood sugar may include:

- shakiness
- headache
- drowsiness
- weakness
- dizziness
- confusion
- sweating
- irritability
- hunger
- fast heartbeat
- feeling jittery

- **Kidney problems (kidney failure).** BYDUREON may cause nausea, vomiting or diarrhea leading to loss of fluids (dehydration). Dehydration may cause kidney failure, which can lead to the need for dialysis. This can happen in people who have never had kidney problems before. Drinking plenty of fluids may reduce your chance of dehydration. Call your healthcare provider right away if you have nausea, vomiting, or diarrhea that will not go away, or if you cannot drink liquids by mouth.
- **Severe allergic reactions.** Severe allergic reactions can happen with BYDUREON. Stop using BYDUREON, and get medical help right away if you have any symptom of a severe allergic reaction. See "**Who should not use BYDUREON?**"
- **Injection-site reactions.** Serious injection-site reactions, with or without bumps (nodules) have happened in some people who use BYDUREON. Some of these injection-site reactions have required surgical intervention. Call your healthcare provider right away if you have any of the following at your injection site:
  - severe pain
  - swelling
  - blisters
  - an open wound
  - a dark scab

The most common side effects of BYDUREON include:

- nausea
- diarrhea
- headache
- vomiting
- constipation
- itching at the injection site
- a small bump (nodule) at the injection site
- indigestion

Nausea is most common when you first start using BYDUREON, but decreases over time in most people as their body gets used to the medicine.

Talk to your healthcare provider about any side effect that bothers you or does not go away.

These are not all the side effects of BYDUREON. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store BYDUREON?

- Store BYDUREON in the refrigerator at 36°F to 46°F (2°C to 8°C).
- **Do not** use BYDUREON past the expiration date printed on the BYDUREON carton, single-dose tray cover, or pen label. The expiration date is labeled *EXP* and can be found on the paper cover of the single-dose tray or single-dose pen.
- **Do not** freeze BYDUREON. **Do not** use BYDUREON if it has been frozen.
- Keep BYDUREON within its sealed tray until ready for use.
- Protect BYDUREON from light until you are ready to prepare and use your dose.
- If needed, you can keep BYDUREON out of the refrigerator at 68°F to 77°F (20°C to 25°C) for up to 4 weeks.
- See the Instructions for Use for information about how to throw away your used BYDUREON parts.

Keep BYDUREON, and all medicines, out of the reach of children.

General information about safe and effective use of BYDUREON

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use BYDUREON for a condition for which it was not prescribed. Do not give your BYDUREON to other people, even if they have the same symptoms you have. It may harm them.

This Medication Guide summarizes the most important information about BYDUREON. If you would like more information, talk with your healthcare provider. You can ask your healthcare provider or pharmacist for information about BYDUREON that is written for healthcare professionals.

For more information about BYDUREON, go to www.BYDUREON.com or call 1-877-700-7365.

What are the ingredients in BYDUREON?

Contents of the powder:

Active Ingredient: exenatide

Inactive Ingredients: polylactide-co-glycolide and sucrose

Contents of liquid (diluent):

Inactive Ingredients: carboxymethylcellulose sodium, polysorbate 20, sodium phosphate monobasic monohydrate, sodium phosphate dibasic heptahydrate, sodium chloride, water for injection. Sodium hydroxide may be added during manufacture of BYDUREON Pen for pH adjustment.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Manufactured for:
AstraZeneca Pharmaceuticals LP
Wilmington, DE 19850

By:
Amylin Ohio LLC
West Chester, OH 45071

Approved: March 2015

Instructions for Use

BYDUREON® (by-DUR-ee-on) Single-Dose Tray

(exenatide extended-release for injectable suspension)

Before using Bydureon, your healthcare provider should show you how to use it the right way.

Read these Instructions for Use before you start using BYDUREON Single-Dose Tray and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.

Getting ready

Never share your BYDUREON vials or needles with anyone else. You may give an infection to them or get an infection from them.

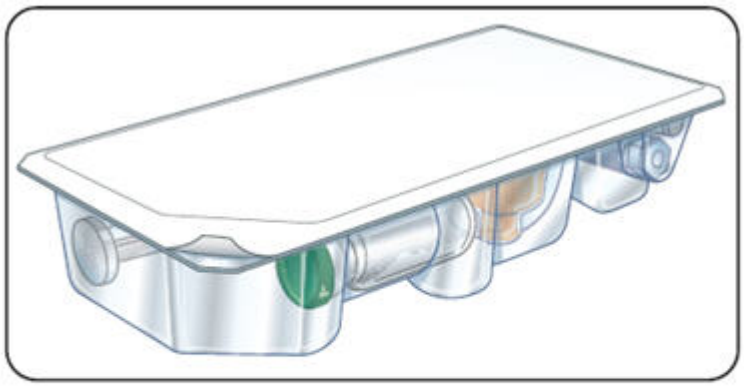
BYDUREON Single-Dose Tray is not for self-injection by people who are blind or cannot see well.

Supplies needed to give your BYDUREON Single-Dose Tray injection (not all supplies are included):

- 1 BYDUREON Single-Dose Tray that contains:
    - 1 BYDUREON vial
    - 1 Syringe
    - 2 Needles
    - 1 Vial connector
- alcohol swab
- a clean flat surface
- sharps container for throwing away used needles, vials, and syringes. See **Step 4h "Disposing of used Needles and Syringes**."

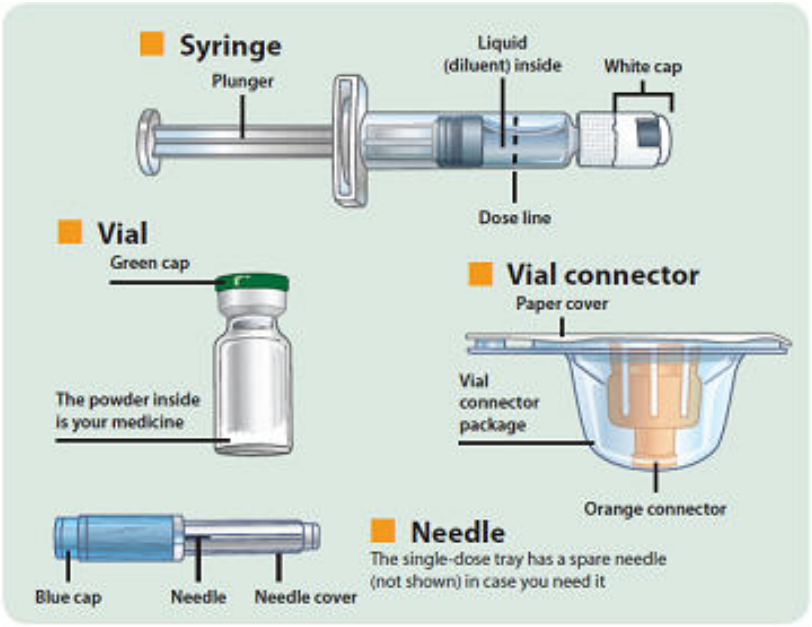
Your guide to your BYDUREON Single-Dose Tray

- Single-dose tray



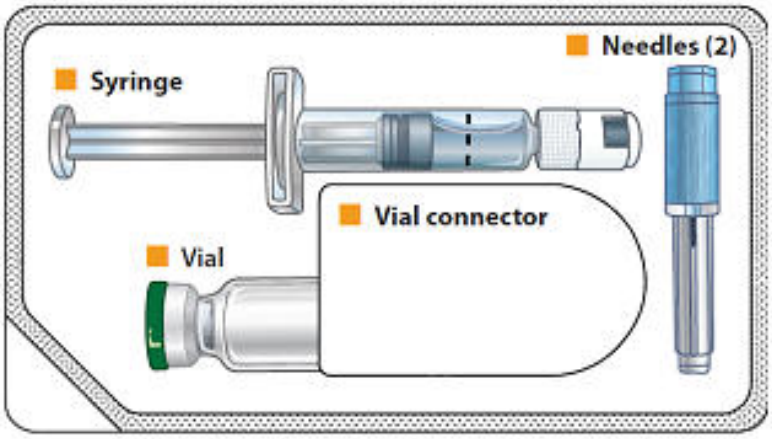
Lift here for a closer look at the parts

Keep this flap open so you can refer to it as you go through the steps.



Your guide to the parts

- Single-dose tray



What's Inside

To take the correct dose, read **each** page so that you do **every** step in order.

This step-by-step guide is divided into 4 sections:

- Getting Started
- Connecting the Parts
- Mixing the Medicine and Filling the Syringe
- Injecting the Medicine

For **Common Questions and Answers,** see page X.

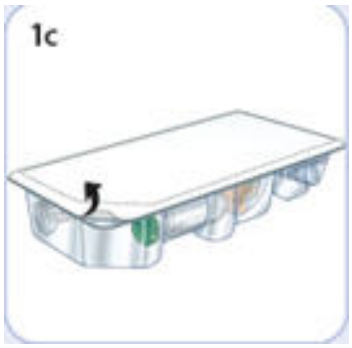
How to store your Single-Dose Trays of BYDUREON

- Store your BYDUREON trays in the refrigerator at 36°F to 46°F (2°C to 8°C).
- If needed, you can keep your BYDUREON tray out of the refrigerator at 68°F to 77°F (20°C to 25°C) for up to 4 weeks.
- Protect BYDUREON from light until you are ready to prepare and use your dose.
- Do not freeze BYDUREON trays.
- Do not use BYDUREON past the expiration date. The expiration date is labeled *EXP* and can be found on the paper cover of each tray.
- Keep BYDUREON, and all medicines, out of the reach of children.

1. Getting Started

1a) Take a Single-Dose Tray from the refrigerator.

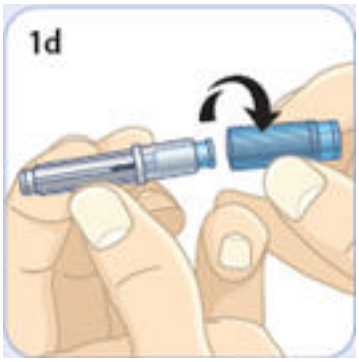
1b) **Wash your hands.** Prepare to clean your injection site with soap and water or an alcohol swab prior to injecting your medicine.



Peel back the paper cover to open.

Remove the syringe. The liquid in the syringe should be clear with no particles in it. It is okay if there are bubbles.

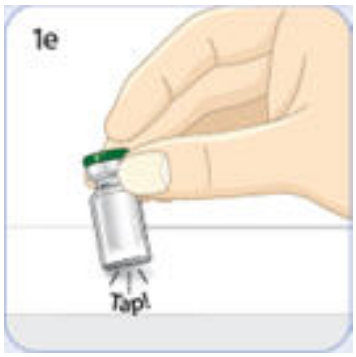
Place the needle, vial connector package, vial, and syringe on a clean, flat surface.



Pick up the needle, and twist off the blue cap.

Set the covered needle aside. You will use it later.

There is a spare needle in the tray if you need it.



Pick up the vial.

Tap the vial several times against a hard surface to loosen the powder.

Use your thumb to remove the green cap.

Put the vial aside.

2. Connecting the Parts

Pick up the vial connector package and peel off the paper cover. Do not touch the orange connector inside.

Hold the vial connector package.

In your other hand, hold the vial.

Press the top of the vial firmly into the orange connector.

Then lift the vial with the orange connector now attached out of the clear package.

This is what the vial should now look like.

Put it aside for later.

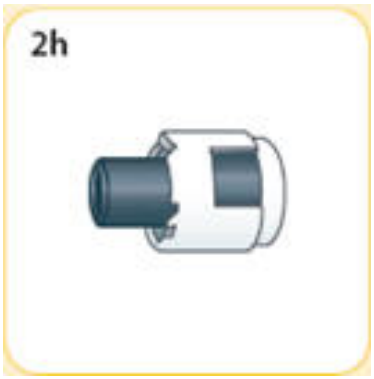
Pick up the syringe.

With your other hand, firmly grasp the 2 gray squares on the white cap.

Break off the cap.

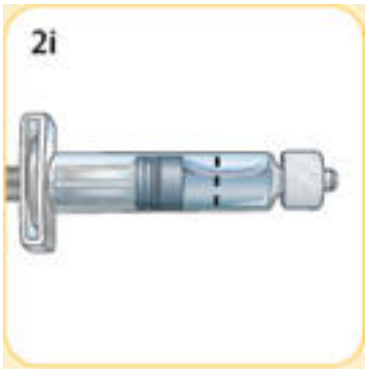
Be careful not to push in the plunger.

Just like you might break a stick, you are breaking off the cap.

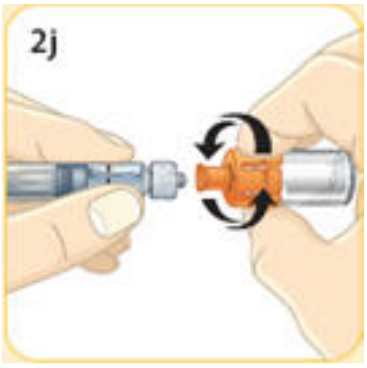


This is what the broken-off cap looks like.

You will not be using the cap and can throw it away.

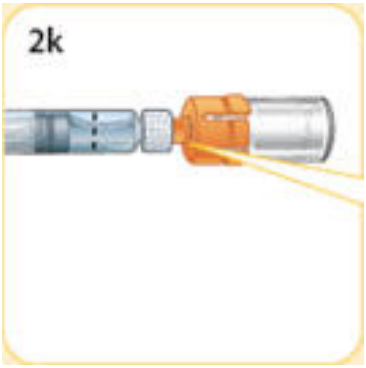


This is what the syringe should now look like.



Now, pick up the vial with the orange connector attached.

Twist the orange connector onto the syringe until snug. While twisting, be sure to grasp the orange connector. Do not over tighten.



This is how the parts should now look when they are connected.

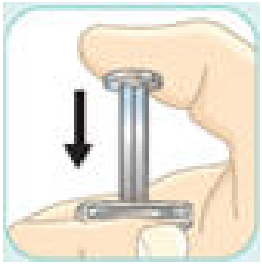
3. Mixing the Medicine and Filling the Syringe

IMPORTANT:

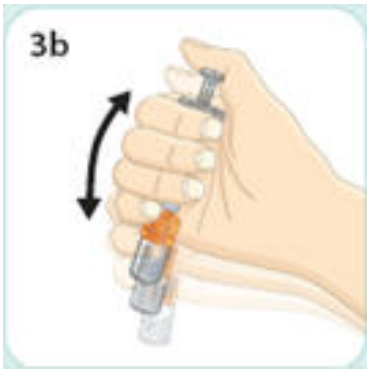
During these next steps, you will be mixing the medicine and filling the syringe. Once you mix the medicine, you must inject it. You cannot save the mixed medicine to inject at a later time.

With your thumb, push down the plunger until it stops.

The plunger may feel like it is springing back a little.



For steps 3a to 3f, keep pushing down on the plunger with your thumb.



Hold the plunger down and shake hard. Keep shaking until the liquid and powder are mixed well.

The vial will not come off. The orange connector will keep it attached to the syringe.

Shake hard like you would shake a bottle of oil-and-vinegar salad dressing.

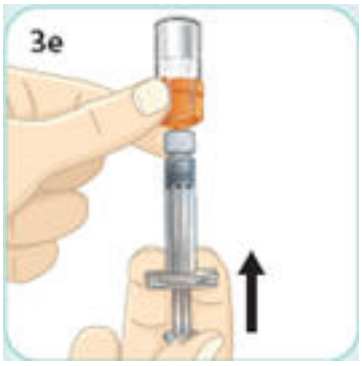
When the medicine is mixed well, it should look cloudy.

If you see clumps of dry powder on the sides or bottom of the vial, the medicine is not mixed well.

Shake hard again until well mixed.

Keep pushing down on the plunger while shaking.

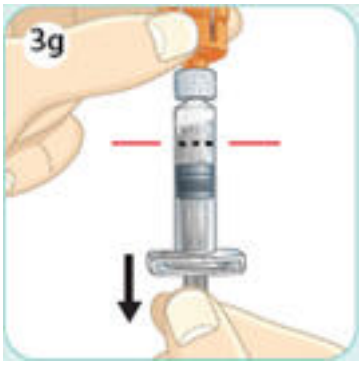
If you have any questions or are not sure if your BYDUREON is mixed well, call 1-877-700-7365 for help.



Now, hold the vial upside down so the syringe is pointing up. Continue to hold the plunger in place with your thumb.

Gently tap the vial with the other hand. Continue to hold the plunger in place.

The tapping helps the medicine drip down. It is okay if there are bubbles.

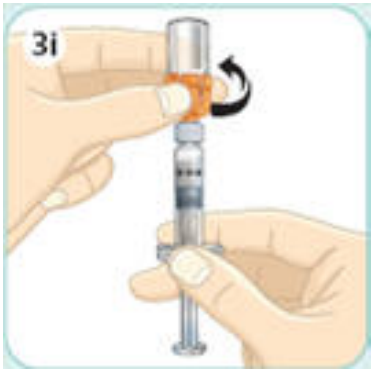


Pull the plunger down beyond the black dashed Dose Line.

This draws the medicine from the vial into the syringe. You may see air bubbles. This is normal.

A little bit of liquid may cling to the sides of the vial.

With 1 hand, hold the plunger in place so it does not move.

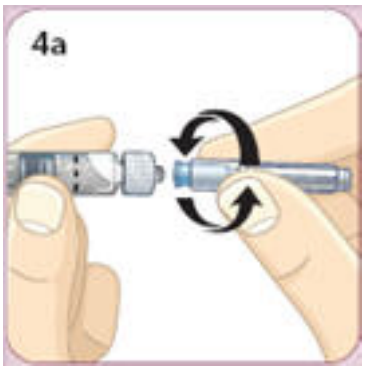


With the other hand, twist the orange connector to remove it from the syringe.

Be careful not to push in the plunger.

This is what the syringe should now look like.

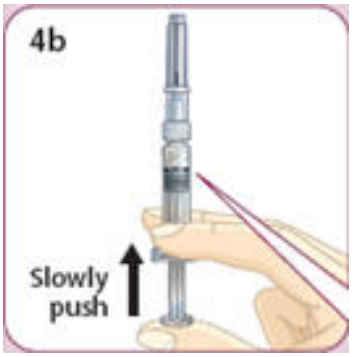
4. Injecting the Medicine



Pick up the needle. Twist the needle onto the syringe until snug. Do not remove the needle cover yet.

IMPORTANT:

Read the next steps carefully and look closely at the pictures. This helps you get the correct dose of medicine.



Slowly push in the plunger so the top of the plunger lines up with the black dashed Dose Line.

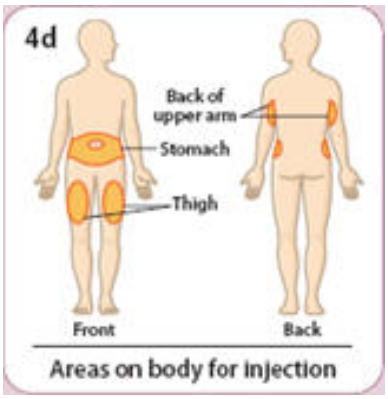
Then, take your thumb off the plunger.

The top of the plunger must stay lined up with the black dashed Dose Line as you go through the next steps. This will help you get the correct dose of medicine.

Put aside the syringe with the needle attached.

IMPORTANT:

It is normal to see a few bubbles in the mixture. The bubbles will not harm you or affect your dose.

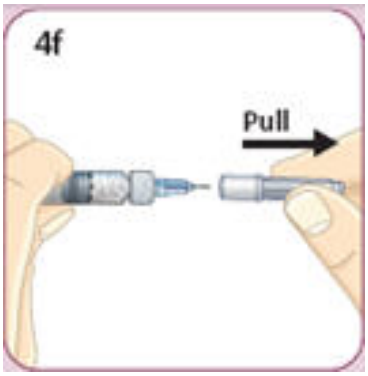


You can inject the medicine in your stomach area (abdomen), your thigh, or the back of your upper arm.

Each week you can use the same area of your body but choose a different injection site in that area.

Gently clean the site you choose with soap and water or an alcohol swab.

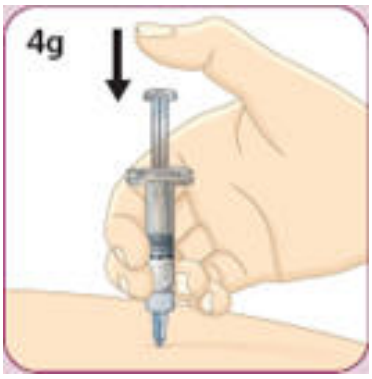
Now, pick up the syringe and hold it near the black dashed Dose Line.



Pull the needle cover straight off. Do not twist.

Be careful not to push in the plunger.

When you remove the cover, you may see 1 or 2 drops of liquid. This is normal.



Insert the needle into your skin (subcutaneously). To inject your full dose, push down on the plunger with your thumb until it stops.

Withdraw the needle.

Be sure to use the injection technique recommended by your healthcare provider.

Disposing of used Needles and Syringes:

- Put your used needles and syringes in a FDA-cleared sharps disposal container right away after use. **Do not** throw away (dispose of) loose needles and syringes in your household trash.
- If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:
    - made of a heavy-duty plastic,
    - can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
    - upright and stable during use,
    - leak-resistant, and
    - properly labeled to warn of hazardous waste inside the container.
- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and pens. For more information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA's website at: http://www.fda.gov/safesharpsdisposal.

Please keep these Instructions for Use for your next dose.

Common Questions and Answers

1. **After I mix the medicine, how long can I wait before taking the injection?**

   You must take your injection of BYDUREON right after mixing it. If you do not inject BYDUREON right away, the medicine will start to form small clumps in the syringe. These clumps can clog the needle when you take the injection (see question 7).

2. **How do I know that the medicine is mixed well?**

   When the medicine is mixed well, it should look cloudy. There should not be any dry powder on the sides or bottom of the vial. **If you do see any dry powder, shake hard while continuing to push down on the plunger with your thumb.** (This question relates to the steps shown on pages X through X.)

3. I'm ready to take the injection. What should I do if I see air bubbles in the syringe?

It is normal for air bubbles to be in the syringe. The air bubbles will not harm you or affect your dose. BYDUREON is injected into your skin (subcutaneously). Air bubbles are not a problem with this type of injection. (This question relates to step 3f shown on page X and step 4c shown on page X.)

4. What should I do if I have trouble attaching the needle?

First, be sure you have removed the blue cap. Then, **twist** the needle onto the syringe until snug. To prevent losing medicine, do not push in the plunger while attaching the needle. (This question relates to step 4a on page X.)

5. What should I do if I have trouble removing the needle cover?

With one hand, hold the syringe near the black dashed Dose Line. With your other hand, hold the needle cover. **Pull the needle cover straight off.** Do not twist it. (This question relates to step 4f on page X.)

6. I am at step 4c. What should I do if the top of the plunger has been pushed past the black dashed Dose Line?

The black dashed Dose Line shows the correct dose. If the top of the plunger has been pushed past the line, you should continue from step 4d and take the injection. Before your next injection in 1 week, carefully review the instructions on pages X through X.

7. When I inject, what should I do if I cannot push the plunger all the way down?

This means the needle has become clogged. Remove the needle from your skin and replace it with the spare needle from your tray. Then choose a different injection site and finish taking the injection.

To review how to:

- Remove the blue cap of the needle, see page X
- Attach the needle, see page X
- Remove the needle cover and give the injection, see pages X and X

If you still cannot push the plunger all the way down, remove the needle from your skin. Use a puncture-resistant container to throw away the syringe with the needle still attached. It is important that you then call 1-877-700-7365.

To help prevent a clogged needle, always mix the medicine very well and inject right after mixing.

Where to learn more about BYDUREON

- **Talk with your healthcare provider**
- **Read the Medication Guide that came with your BYDUREON.** The Medication Guide can help answer your questions about BYDUREON, such as what it is used for, possible side effects, and when to take BYDUREON.
- Enroll in BYDUREON Support for FREE ongoing help managing your diabetes. **Visit www.BYDUREON.com or call 1-877-700-7365.**

These Instructions for Use have been approved by the U.S. Food and Drug Administration.

Manufactured for:
AstraZeneca Pharmaceuticals LP
Wilmington, DE 19850

By:
Amylin Ohio LLC
West Chester, OH 45071

Approved: March 2015

Instructions for Use

BYDUREON® (by-DUR-ee-on) Pen

(exenatide extended-release for injectable suspension)

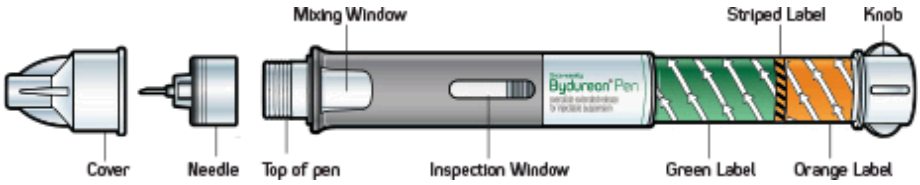


Figure A

Before using Bydureon Pen, your healthcare provider should show you how to use it the right way.

Read the Instructions for Use before you start using Bydureon Pen and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.

Getting ready

Never share your Bydureon Pen or needles with anyone else. You may give an infection to them or get an infection from them.

Bydureon Pen is not for self-injection by people who are blind or cannot see well.

Supplies needed to give your Bydureon Pen injection (not all supplies are included):

- 1 Bydureon single-use "Pen" tray that contains:
  - 1 Bydureon Pen
  - 1 custom needle
- a clean flat surface
- alcohol swab
- sharps container for throwing away used needles and Pens. See "**Disposing of used needles and Pens**" at the end of these instructions.

How should I store Bydureon?

- Store your Bydureon Pens in the refrigerator at 36°F to 46°F (2°C to 8°C).
- Protect pens from light until you are ready to prepare and use your dose.
- **DO NOT** use pens past the expiration date printed on the paper cover of each Bydureon Pen tray.
- **DO NOT** freeze Bydureon. **DO NOT** use Bydureon if it has been frozen.
- Keep Bydureon in its sealed tray until ready for use.
- If needed, you can keep your Bydureon Pen out of the refrigerator at 68°F to 77°F (20°C to 25°C) for up to 4 weeks.

Keep Bydureon Pen, and all medicines, out of the reach of children.

Step 1: Prepare your Bydureon Pen

Let your Pen warm up.

- Remove 1 Pen from the refrigerator and let it stand at room temperature for at least 15 minutes.

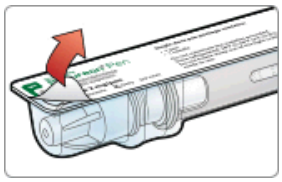
Check the expiration date printed on your Pen tray.

- **Do not** use a Pen past the expiration date printed on your Pen tray.

Wash your hands.

Open the tray.

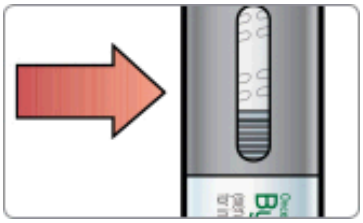
- Pull up on the corner tab.
- Remove the Pen and needle.



- **Do not** use your Pen or needle if any parts are broken or missing.

Check the liquid in your Pen.

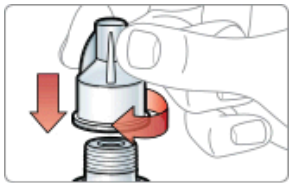
- **Check the liquid** inside the inspection window. It should be clear and free of particles. **Do not** use the Pen if the liquid is colored, has particles, or is not clear. Throw it away and get a new one.
  - You may see bubbles in the liquid, this is normal.



Peel off the paper tab from the needle cover.

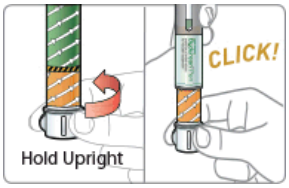
Attach the needle to the Pen.

- Screw the needle onto the Pen by pushing and twisting clockwise until it is tight. **Do not** remove the needle cover yet.



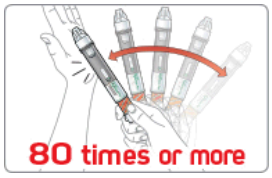
Step 2: Mix your dose

Combine the medicine.



- While holding the pen straight up, **slowly** turn the knob. **Stop** when you hear the click and the green label disappears.

Firmly tap your Pen to mix.



- Hold your Pen by the end with the orange label and **tap the Pen firmly against the palm of your hand**.
  - **DO NOT** twist the white knob.
  - **ROTATE** your Pen every 10 taps.
  - **You may need to tap your Pen 80 times or more.**

Check the Bydureon mix.

- **Hold your Pen up to the light and look through both sides of the mixing window.** The solution should have **NO CLUMPS** and be uniformly cloudy **(see Figure B)**.

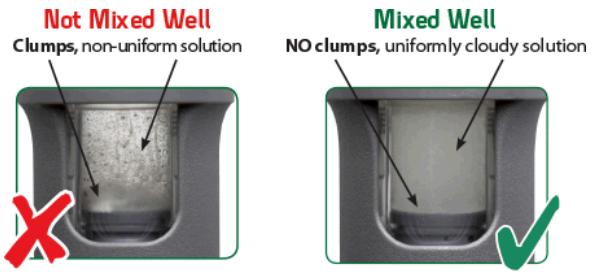


Figure B

- **To get your full dose, Bydureon must be mixed well.**
- **If Bydureon is not mixed well, keep tapping your Pen longer and more firmly until it is mixed well.**
- **Do not give your Bydureon injection unless your Bydureon is mixed well.**

STOP. Do Not proceed unless your medicine is mixed well.

To get your full dose the medicine must be mixed well. If it's not mixed well, tap longer and more firmly.

Check the Bydureon mix again.

- **Compare both sides of the mixing window to the photos below** by holding your Pen against the page. Pay attention to the **bottom surface.** If you **do not see clumps** you are ready to inject **(see Figure C)**.

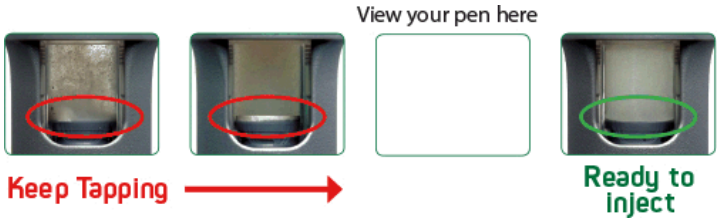


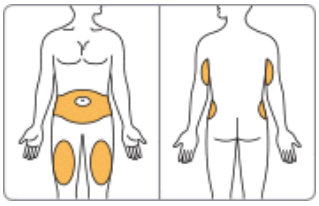
Figure C

If you have any questions or are not sure if your Bydureon is mixed well, call 1-877-700-7365 for help.

Step 3: Inject your dose

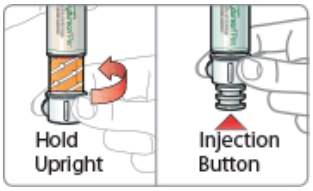
IMPORTANT: After the medicine is mixed well, you must inject your dose right away. You cannot save it for later use.

Choose your injection site.



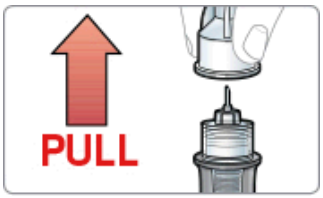
- The recommended injection sites for Bydureon are your stomach (abdomen), thigh, or back of the arm.
  - Each week you can use the same area of your body but choose a different injection site in that area.
  - Gently wipe the site you choose with an alcohol swab (not included).

Twist knob to release injection button.



- Hold your **Pen with the needle pointing straight up** and turn the white knob until the orange label disappears and the injection button is released. **DO NOT** push the injection button yet.

Remove the needle cover.



- Pull the needle cover straight off. **DO NOT** twist the needle cover.
  - You may see a few drops of liquid on the needle or in the cover.

Inject your Bydureon.

- Insert the needle into your skin.
- Press the injection button with your thumb until you hear a "click." Keep holding **the button down and slowly count to 10 to get your full dose.**

Properly dispose of your Pen.

- Put your used needles and Pens in an FDA-cleared sharps disposal container right away after use. **Do not** throw away (dispose of) loose needles and Pens in your household trash. See **Common Questions and Answers** for additional disposal information.

Common Questions and Answers:

1. How do I know that the Bydureon is mixed well?

The Bydureon is mixed well when the liquid looks cloudy from both sides of the window. You should not see any clumps in the liquid. It may help to hold your Pen up to the light to see in the window. If you see clumps of any size keep tapping your Pen firmly against the palm of your hand until mixed.

2. I am having trouble mixing my dose. What should I do?

Remember, before preparing your dose, leave your Pen out of the refrigerator for at least 15 minutes. This will let your Pen warm up to room temperature. It will be easier to mix Bydureon if your Pen is at room temperature.

Be sure you are holding your Pen at the end with the knob and the orange label. This will help you grip your Pen better and tap it more firmly against your palm.

It may also help to tap the mixing window on both sides against your palm. If you see any clumps, keep tapping.

3. After I mix Bydureon, how long can I wait before taking the injection?

You must inject your dose of Bydureon right after mixing it. If you do not inject your Bydureon right away, small clumps of medicine may form in your Pen and you may not get your full dose.

4. I am ready to inject my dose. What should I do if I see air bubbles in the Pen?

It is normal for air bubbles to be in your Pen. Bydureon is injected into your skin (subcutaneously). Air bubbles will not harm you or affect your dose with this type of injection.

5. What should I do if I cannot push the injection button all the way in when trying to inject my dose?

Check that you have fully screwed on the pen needle. Also be sure you twisted the knob until it stopped, the orange label disappeared, and the injection button appears.

If you still cannot push the button in, this may mean that the needle is clogged. Remove the needle from your skin and replace it with the spare needle from the carton. Review how to attach the needle. Then choose a different injection site and finish taking the injection.

If you still cannot push the button all the way in, remove the needle from your skin. Use a puncture-resistant container to throw away the pen with the needle still attached.

If you have problems giving your Bydureon Pen injection or have any questions call 1-877-700-7365 for more instructions.

6. How do I know if I injected my full dose?

To be sure you get your full dose, press the injection button with your thumb until you hear a "click." After the "click," continue to hold the needle in your skin for 10 seconds. This will allow enough time for you to get your full dose.

7. What if I do not have an FDA-cleared sharps disposal container?

Do not throw away (dispose of) loose needles and Pens in your household trash.

- If you do not have an FDA-cleared sharps disposal container, you may use a household container that is:
  - made of a heavy-duty plastic,
  - can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
  - upright and stable during use,
  - leak-resistant, and
  - properly labeled to warn of hazardous waste inside the container.
- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and Pens. For more

information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA's website at: http://www.fda.gov/safesharpsdisposal

This Instructions for Use has been approved by the U.S. Food and Drug Administration.

BYDUREON® is a registered trademark of the AstraZeneca group of companies.

Manufactured for:
AstraZeneca Pharmaceuticals LP
Wilmington, DE 19850

By:
Amylin Ohio LLC
West Chester, OH 45071

Approved: March 2015