PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986

This medicine is dispensed with a doctor's prescription only

Name of the preparation: **BYDUREON® 2 mg**

Once a week injection pen

Powder and solvent for suspension for injection in pre-filled pen

Composition:

Each pen contains: Exenatide 2 mg

Inactive ingredients and allergens: see Section 6 “Further Information”.

Read this leaflet carefully in its entirety before using this medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.

This medicine has been prescribed for the treatment of your ailment. Do not pass it on to others. It may harm them even if it seems to you that their ailment is similar.

This medicine is not intended for children below 18 years of age.

Essential information about Bydureon:

- Bydureon used in combination with a sulphonylurea may cause a decrease in blood sugar levels (hypoglycemia). Be sure to check your blood sugar level regularly during the course of treatment with the medicine (see below sections 2 “Before using the medicine” and 4 “Side effects”).
- Bydureon is not intended for treatment of type 1 diabetes (insulin dependent diabetes) and diabetic ketoacidosis.
- Bydureon is intended for injection under the skin, once a week, at any hour of the day, and with no relation to meals.

- Treatment with the medicine is not recommended for patients with kidney problems, patients on dialysis, women who are pregnant or breastfeeding (see section 2 below “Before using the medicine”).

1. WHAT IS THE MEDICINE INTENDED FOR?

Bydureon is an injectable medicine used to improve control of blood sugar levels in adult patients with type 2 diabetes (diabetes mellitus). Bydureon is given in combination with additional anti-diabetes medicines: metformin, sulphonylurea, thiazolidinediones, SGLT2 inhibitors and/or a long-acting insulin.

Your doctor prescribed treatment with Bydureon for you as an additional medicine to help control your blood sugar level. Continue to follow your food and exercise plan.

Diabetes occurs when the body does not produce enough insulin to control the level of sugar in your blood or when your body is not able to use the insulin properly. Bydureon helps your body increase the production of insulin when your blood sugar is high.

Therapeutic group: Bydureon belongs to a group of medicines that lower the blood sugar level. The active ingredient of Bydureon, Exenatide, activates a receptor of a protein called GLP-1, thereby activating a number of mechanisms that help lower blood sugar.

2. BEFORE USING THE MEDICINE:

X Do not use the medicine if:

- You are sensitive (allergic) to the active ingredient or to any of the other ingredients the medicine contains (see section 6 “Further Information” below).

! Special warnings regarding use of the medicine:

Talk to your doctor, pharmacist, or diabetes nurse before using Bydureon about the following:

- Combined use of Bydureon with sulphonylurea may cause a decrease in blood sugar levels (hypoglycemia). Check your blood sugar level regularly. Ask your doctor, pharmacist or diabetes nurse if you are not sure if any of the other medicines you are taking contains sulphonylurea.
- Bydureon should not be used if you have type 1 diabetes or diabetic ketoacidosis.
- Bydureon should be injected into the skin (subcutaneous injection) and not into a vein or into the muscle.
- Use of Bydureon is not recommended if you have severe problems with stomach emptying (including gastroparesis) or food digestion. Bydureon slows stomach emptying so food passes more slowly through your stomach.
- Tell your doctor if you have ever had pancreatitis (see section 4 below “Side Effects”).
- If you lose weight too quickly (more than 1.5 kg per week) talk to your doctor about it since this may cause problems such as gallstones.
- There is limited experience with Bydureon in patients with kidney problems. Use of Bydureon is not recommended for patients with severe kidney disease or if you are on dialysis.
- Bydureon is not an insulin and should therefore not be used as a substitute for insulin.

Drug -Induced Thrombocytopenia

During use of exenatide, drug-induced thrombocytopenia has been reported. If symptoms of thrombocytopenia appear, such as bleeding, refer immediately to the doctor. The doctor may instruct you to discontinue treatment.

Since there is no treatment experience with Bydureon in children and adolescents under 18 years of age, use of Bydureon in this age group is not recommended.

! If you are taking other medicines

If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell your doctor or pharmacist, especially if you are taking:

- Warfarin (Coumadin – for treatment of excessive blood clotting). You may require additional monitoring of changes in INR (measurement of blood thinning) during initiation of therapy with this medicine.
- Other medicines for treatment of type 2 diabetes – combined use of Bydureon with other medicines for treatment of type 2 diabetes that work similarly to Bydureon (for example: liraglutide and Byetta [immediate-release exenatide]) is not recommended.
- if you are using insulin, your doctor will tell you how to reduce the dose of insulin and will recommend that you monitor your blood sugar more frequently, in order to avoid hyperglycaemia (high blood sugar levels) and diabetic ketoacidosis (a complication of diabetes that occurs when the body is unable to break down glucose because there is not enough insulin).

! Use of the medicine and food

The medicine can be taken at any hour of the day, with or without food.

! Pregnancy and breastfeeding

Women of childbearing age should use contraception during treatment with Bydureon. It is not known whether use of Bydureon may harm your unborn

child. Tell your doctor if you are pregnant, think you might be pregnant, or are planning to become pregnant, as the medicine should not be used during pregnancy and for at least three months before a planned pregnancy.

It is not known if Bydureon passes into breast milk. The medicine should not be used if you are breastfeeding.

If you are pregnant or breastfeeding, think you may be pregnant, or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

! Driving and using machines

Treatment with Bydureon in combination with a sulphonylurea may cause a reduction in blood sugar levels (hypoglycemia). Hypoglycemia may reduce your ability to concentrate. Please keep this problem in mind in any situation where you might put yourself and others in danger (e.g., driving a car or operating machines).

! Important information about some of the ingredients of the medicine

This medicine contains less than 1 mmol sodium (23 mg) per dose, i.e., “sodium-free”.

Each pen contains 0.8 mg sucrose.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use according to the instructions of the doctor or diabetes nurse only. Check with the doctor, diabetes nurse or pharmacist if you are not sure about the dosage and the treatment regimen. Do not exceed the recommended dose.

The dosage and the treatment regimen will be determined by the doctor only. The recommended dosage is usually one injection per week, at any time of the day, with or without meals.

Bydureon is intended for injection into the skin (subcutaneous injection) in the area of the abdomen, thigh or back of the upper arm.

You can choose the same area of your body each week, but be sure to inject into a different site in that same area.

Never mix insulin and Bydureon together in the same injection. If you need to give yourself both at the same time, use two separate injections. You may give both injections in the same body area (for example, your stomach area), but you should not give the injections next to each other.

Check your blood sugar level regularly. It is especially important to check the blood sugar level if you are concomitantly using a sulphonylurea.

Follow the Instructions for Use provided in the package to prepare and inject Bydureon.

Your health care professional will teach you how to inject the medicine before you use it for the first time.

Check that the liquid in the pen is clear and free of particles before you begin. After mixing the liquid with the powder, use the suspension only if the mixture is white to off-white and cloudy. If you see clumps of dry powder on the sides of the pen, the medicine was NOT mixed well. Tap vigorously again until well mixed.

Inject immediately after mixing the powder with the solvent.

Use a new pen for each injection and dispose of it after use.

If you are not sure you have used the full dose of Bydureon: If you are not sure if you have taken the entire dose, do not inject another dose of Bydureon; just take the next dose the following week, as planned.

If you accidentally take a higher dosage, you may need medical treatment. An overdose of Bydureon can cause nausea, vomiting, dizziness, or signs of a low blood sugar level (see section 4 below “Side Effects”).

If you forget to take the medicine: It is advisable to choose a day that you always plan to inject your Bydureon. If you miss your injection day, take your injection as soon as possible after you remember. For your next injection you can return to your chosen injection day as long as the next injection is at least one day (24 hours) later. You can also change your chosen injection day.
Do not take two injections on the same day.

If you stop using Bydureon: Always adhere to the treatment recommended by the doctor. Even if there is an improvement in your health, or if you feel you should stop using Bydureon, you should first consult your doctor, since this may affect your blood sugar levels.

How can you contribute to the success of the treatment?
Do not take medicines in the dark! Check the label and dose each time you take a medicine. Wear glasses if you need them.

If you have further questions regarding use of the medicine, consult the doctor, diabetes nurse or a pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Bydureon may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not get any of the them.

Severe allergic reactions (anaphylactic shock) have been reported rarely (may affect up to 1 in 1000 people).
You should see your doctor immediately if you notice the following symptoms:

- Swelling of the face, tongue or throat (angioedema).
- Hypersensitivity (rash, itching, rapid swelling of the tissues of the neck, face, mouth or throat).
- Difficulty with swallowing.
- Hives and difficulty with breathing.

Cases of inflammation of the pancreas (pancreatitis) were reported uncommonly (may affect up to 1 in 100 people) in patients who received Bydureon. Pancreatitis is a medical condition which may be serious, and can potentially be life-threatening.

- **Tell your doctor** if you have had pancreatitis, gallstones, alcoholism or very high triglyceride levels. These medical conditions can increase your chance of getting pancreatitis, or of getting it again, whether or not you are taking Bydureon.
- **Stop taking Bydureon and contact your doctor immediately** if you experience **severe** and persistent stomach pain, with or without vomiting, because you could have an inflamed pancreas (pancreatitis).

Very common side effects (more than 1 in 10 patients):

- nausea (nausea is more characteristic when first starting treatment with Bydureon, but decreases over time in most patients).
- Diarrhoea.
- Hypoglycemia.

When Bydureon is used in combination with a medicine that contains **sulphonylurea**, episodes of low blood sugar level (hypoglycemia, generally mild to moderate) can occur. The dosage of your sulphonylurea may need to be reduced during treatment with Bydureon. The signs of low blood sugar levels include: headache, drowsiness, weakness, dizziness, confusion, nervousness, hunger, fast heartbeat, sweating, and feeling jittery. Your doctor will tell you how to treat low blood sugar level.

Common side effects (may affect up to 1 in 10 people):

- Hypoglycaemia (low blood sugar levels) when taken with an insulin
- Dizziness.
- Headache.
- Vomiting
- Loss of energy and strength
- Tiredness.
- Constipation
- Pain in the stomach area.
- Bloating.
- Indigestion.
- Flatulence (passing gas)
- Heartburn.
- Reduced appetite.

Bydureon may reduce your appetite, the amount of food you eat, and your weight. If you lose weight too quickly (more than 1.5 kg per week) talk to your doctor about it since this may cause problems such as gallstones.

- injection site reactions - if you have an injection site reaction (redness, rash, or itching) you may like to ask your doctor for something to help relieve any signs or symptoms. You may see or feel a small bump under the skin at the injection site; it should go away after 4 to 8 weeks. You do not need to stop your treatment.

Uncommon side effects (appear in up to 1 in every 100 patients):

- Decrease in kidney function.
- Dehydration, sometimes with a decrease in kidney function
- Intestinal obstruction (blockage in intestine)
- Burping
- Unusual taste in the mouth
- Increased sweating
- Hair loss
- Sleepiness

Rare side effects (may affect up to 1 in 1,000 people)

- feeling jittery

In addition, some **other side effects** (frequency not known, cannot be estimated from the available data) have been reported

- Bleeding or bruising more easily than normal due to low level of blood platelets (drug-induced thrombocytopenia). Bydureon may cause the number of platelets in your blood to be reduced. Refer immediately to the doctor if you have unusual bleeding or bruising.
- Changes in INR values (measurement of blood thinning) have been reported when used together with warfarin (coumadin).
- Injection site reactions. Skin reactions at the injection site have been reported following injection of exenatide. These include: cavity containing pus (abscess) and swollen, red area of skin that feels hot and tender (cellulitis).

If any of the side effects worsens, or if you notice any side effect not listed in this leaflet, please consult your doctor or pharmacist.

Reporting side effects

Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link:
https://sideeffects.health.gov.il

5. HOW SHOULD THE MEDICINE BE STORED?

Avoid poisoning! This medicine and any other medicine must be kept in a closed place out of the reach of children and/or infants to avoid poisoning. Do not induce vomiting unless clearly indicated by the doctor.

Do not use the medicine after the expiry date (exp. date) appearing on the package. The expiry date refers to the last day of that month.
Storage: Store in the refrigerator (2-8°C). Do not freeze.

The pen may be kept for up to 4 weeks below 30ºC prior to use.

Store in the original package in order to protect from light.

Throw away any pen that has been frozen.

Medicines should not be disposed of via the garbage or household sewage system. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION:

In addition to the active ingredient, the medicine also contains:
Powder:
Poly (D,L-lactide-co-glycolide) and sucrose.

Solvent:
Carmellose sodium, Sodium chloride, Polysorbate 20, Monobasic sodium phosphate monohydrate, Dibasic sodium phosphate heptahydrate, Sodium hydroxide, Water for Injections.

What the medicine looks like and contents of the package:
Powder and solvent for suspension for injection in pen. The powder (2 mg) in one chamber, is white to off-white and the solvent (0.65 ml) in the other chamber, is a clear, colourless to pale yellow to pale brown solution.
Each single-dose pen is provided with one custom needle. Each carton also contains one spare needle.
Bydureon is dispensed as a pack containing 4 single-dose pens.

License holder and its address: AstraZeneca (Israel) Ltd.,
1 Atirei Yeda St., Kfar Saba 4464301.

Manufacturer and its address: AstraZeneca AB., Sodertalje, Sweden.

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 1492733557

Revised in February 2022 according to MoH guidelines.