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

This medicine is to be supplied upon physician's prescription only

SEGLUROMET® 2.5/1000 MG
SEGLUROMET® 7.5/1000 MG
FILM-COATED TABLET

Each Segluromet 2.5/1000 mg film-coated tablet contains:
2.5 mg ertugliflozin (as ertugliflozin L-pyroglutamic acid) and 1000 mg of metformin hydrochloride.

Each Segluromet 7.5/1000 mg film-coated tablet contains:
7.5 mg ertugliflozin (as ertugliflozin L-pyroglutamic acid) and 1000 mg of metformin hydrochloride.

For a list of inactive ingredients see section 6 "FURTHER INFORMATION".
See also section 2.10, "IMPORTANT INFORMATION ABOUT SOME OF THE INGREDIENTS OF THE MEDICINE".

Read this leaflet carefully in its entirety before using the medicine.
- This leaflet contains concise information about the medicine. If you have any further questions, refer to the doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if it seems to you that their ailment is similar.

1. WHAT THE MEDICINE IS INTENDED FOR?

Segluromet is intended, in addition to diet and exercise, to improve the control of sugar levels in the blood in adults aged 18 years and older with type 2 diabetes: which are treated with metformin alone or in combination with other medicines and their sugar levels are not controlled, or for patients that receive a combination of metformin and ertugliflozin as separate tablets.

Therapeutic group:
Segluromet contains two active substances, ertugliflozin and metformin.
- Ertugliflozin belongs to a group of medicines called sodium glucose co-transporter-2 (SGLT2) inhibitors.
- Metformin belongs to a group of medicines called biguanides.

How Segluromet works
- Ertugliflozin works by blocking the SGLT2 protein in your kidneys causing increased excretion of the glucose in the urine.
- Metformin works by inhibiting sugar (glucose) production in the liver.

What is type 2 diabetes?
Type 2 diabetes is a condition in which your body does not make enough insulin or the insulin that your body produces does not work as well as it should. Your body can also make too much sugar. When this happens, sugar (glucose) builds up in the blood. This can lead to serious medical problems, like heart disease, kidney disease, blindness and poor circulation.

2. BEFORE USING THE MEDICINE

2.1 Do not use the medicine if:

- you are allergic to the active ingredients ertugliflozin or metformin, or any of the other ingredients of this medicine (listed in section 6 “FURTHER INFORMATION”).
- you have severely reduced kidney function or need dialysis.
- you have uncontrolled diabetes, with, for example, severe hyperglycaemia (high blood glucose), nausea, vomiting, diarrhoea, rapid weight loss, lactic acidosis (see “Risk of lactic acidosis” below) or ketoacidosis. Ketoacidosis is a condition in which substances called “ketone bodies” accumulate in the blood and which can lead to diabetic pre-coma. Symptoms include stomach pain, fast and deep breathing, sleepiness, or your breath developing an unusual fruity smell.
- you have a severe infection or are dehydrated.
- you have recently had a heart attack or have severe circulatory problems, such as “shock” or breathing difficulties.
- you have liver problems.
- you drink alcohol to excess (either regularly or from time to time).

Do not take Segluromet if any of the above apply to you. If you are not sure, talk to your doctor before taking Segluromet.

2.2 Special warnings regarding use of the medicine

Before and during the treatment with Segluromet tell the doctor if you:

- suffer from kidney problems.
- suffer or suffered in the past from yeast infections of the vagina or penis.
- suffer from serious heart disease or if you have experienced a stroke.
- suffer from type 1 diabetes. Segluromet is not intended to treat people with type 1 diabetes.
- take other diabetes medicines; you are more likely to get low blood sugar with certain medicines.
- might be at risk of dehydration (for example, if you are taking medicines that increase urine production [diuretics], lower blood pressure or if you are over 65 years old). Ask your doctor about ways to prevent dehydration.
- suffer from rapid weight loss, feeling sick or being sick, stomach pain, excessive thirst, fast and deep breathing, confusion, unusual sleepiness or tiredness, a sweet smell to your breath, a sweet or metallic taste in your mouth or a different odour to your urine or sweat, contact a doctor or the nearest hospital straight away. These symptoms could be a sign of “diabetic ketoacidosis” – a problem you can get with diabetes because of increased levels of “ketone bodies” in your urine or blood, seen in tests. The risk of developing diabetic ketoacidosis may be increased with prolonged fasting, excessive alcohol consumption, dehydration, sudden reductions in insulin dose, or a higher need of insulin due to major surgery or serious illness.

It is important to check your feet regularly and adhere to any other advice regarding foot care given by your healthcare professional.

Talk to your doctor immediately if you notice one of the following side effects:
Redness, pain, tenderness or swelling in the area between and around your anus and genitals, accompanied by fever over 38°C or a general bad feeling and weakness. These side effects can indicate about the development of Fournier's gangrene. This is a rare but life-threatening bacterial infection. There are several reports of the incidence of this side effect in women and men who have taken drugs to treat diabetes from the family of drugs to which Segluromet belongs. This side effect can lead to hospitalization, need of surgery, and even death. Fournier's gangrene symptoms can quickly deteriorate, so it's important to seek medical help quickly if you experience any of these symptoms.

When this medicine is used in combination with insulin or medicines that increase insulin release from the pancreas, low blood sugar (hypoglycaemia) can occur. Your doctor may reduce the dose of your insulin or other medicine.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

Risk of lactic acidosis (see details in chapter 4 "SIDE EFFECTS")
Segluromet may cause a very rare, but very serious side effect called lactic acidosis, particularly if your kidneys are not working properly. The risk of developing lactic acidosis is also increased with uncontrolled diabetes, serious infections, prolonged fasting or alcohol intake, dehydration (see further information below), liver problems and any medical conditions in which a part of the body has a reduced supply of oxygen (such as acute severe heart disease).
If any of the above apply to you, talk to your doctor for further instructions.

Stop taking Segluromet for a short time if you have a condition that may be associated with dehydration (significant loss of body fluids) such as severe vomiting, diarrhea, fever, exposure to heat or if you drink less fluid than normal. Talk to your doctor for further instructions.

Stop taking Segluromet and contact a doctor or the nearest hospital immediately if one of the following symptoms of lactic acidosis appear, as this condition may lead to coma.
Symptoms of lactic acidosis include:
- vomiting
- stomach ache (abdominal pain)
- muscle cramps
- a general feeling of not being well with severe tiredness
- difficulty in breathing
- reduced body temperature and heartbeat

Lactic acidosis is a medical emergency and must be treated in a hospital.

If you need to have major surgery, you must stop taking Segluromet during and for some time after the procedure. Your doctor will decide when you must stop and when to restart your treatment with Segluromet.

2.3 Tests and follow-up
During treatment with Segluromet, your doctor will check your kidney function at least once a year or more frequently if you are elderly and/or if you have worsening kidney function.

Urine glucose
Because of how Segluromet works, your urine will test positive for sugar (glucose) while you are on this medicine.

2.4 Children and adolescents
Children and adolescents below 18 years should not take this medicine.
There is no data available regarding the safety and efficacy of the medicine in children and adolescents under 18 years of age**.**

2.5 Interactions with other medicines
If you are taking, or have recently taken, other medicines including non-prescription medicines and nutritional supplements, you should tell the doctor or pharmacist.

You may need more frequent blood glucose and kidney function tests, or your doctor may need to adjust the dose of Segluromet. In particular, tell your doctor if you are taking:
- medicines which increase urine production (diuretics).

- other medicines that lower the sugar levels in your blood, such as insulin or medicines that increase insulin release from the pancreas.
- medicines used to treat pain and inflammation (NSAID and COX-2-inhibitors, such as ibuprofen and celecoxib).
- certain medicines for the treatment of high blood pressure (ACE inhibitors and angiotensin II receptor antagonists).

If any of the above apply to you (or you are not sure), tell your doctor.

If you need to have an injection of a contrast medium that contains iodine into your bloodstream, for example, in the context of an X-ray or scan, you must stop taking Segluromet before or at the time of the injection. Your doctor will decide when you must stop and when to restart your treatment with Segluromet.

2.6 Use of the medicine and food
It is best to take your tablet with a meal.

2.7 Using the medicine and alcohol consumption
Avoid excessive amounts of alcohol while taking thismedicine. Alcohol consumption increases the risk of lactic acidosis (see section 2.2 “SPECIAL WARNINGS REGARDING USE OF THE MEDICINE”).

2.8 Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant, or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

It is not known if Segluromet can harm your unborn baby. If you are pregnant, talk with your doctor about the best way to control your blood sugar while you are pregnant. You should not use Segluromet if you are pregnant.

It is not known if Segluromet passes into breast milk. Talk with your doctor about the best way to feed your baby if you take this medicine. You should not use Segluromet if you are breast-feeding.

2.9 Driving and using machines
This medicine has no or negligible influence on the ability to drive and use machines. Taking this medicine in combination with insulin or medicines that increase insulin release from the pancreas can cause blood sugar levels to drop too low (hypoglycaemia), which may cause symptoms such as shaking, sweating and change in vision, and may affect your ability to drive and use machines. Do not drive or use any tools or machines if you feel dizzy while taking Segluromet.

2.10 Important information about some of the ingredients of the medicine
This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially ‘sodium-free’.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use the preparation according to the doctor’s instructions.
You should check with the doctor or pharmacist if you are not sure regarding the dosage and treatment regimen of the preparation.
The dosage and treatment regimen will be determined by the doctor only.

How much to take
- The recommended dose of Segluromet is one tablet twice a day.
- The dose of Segluromet that you take will depend on your condition and the amount of ertugliflozin and metformin needed to control your blood sugar.

- Your doctor will prescribe the right dose for you. Do not change your dose unless your doctor has told you to.

Do not exceed the recommended dose.

- **Method of administration:** swallowing
- Swallow the tablet;
- Take one tablet twice daily. Try to take it at the same time each day; this will help you remember to take it.
- It is best to take your tablet with a meal. This will lower your chance of having an upset stomach.
- You need to keep following your food and exercise plan while taking Segluromet.

crushing/ splitting/ chewing
- to make the swallowing easier, it is possible, if needed, to split or crush the tablet for immediate use. The two halves need to be taken immediately after the splitting.

If you have accidentally taken a higher dose
If you take too much Segluromet, talk to a doctor or pharmacist straight away.
If you have taken an overdose, or if a child has accidentally swallowed the medicine, proceed immediately to a doctor or to a hospital emergency room and bring the package of the medicine with you.

If you have forgotten to take the medicine
If you forget a dose, take it as soon as you remember. However, if it is nearly time for your next dose, skip the missed dose and go back to your regular schedule.

Do not take a double dose (two doses at the same time) to make up for a forgotten dose.

Adhere to the treatment regimen recommended by the doctor.
Even if there is an improvement in your health, do not discontinue use of this medicine before consulting your doctor.

If you stop taking this medicine
Do not stop taking this medicine without talking to your doctor. Your blood sugar levels may increase if you stop the medicine.

Do not take medicines in the dark! Check the label and the dose <u>each time</u> you take a medicine. Wear glasses if you need them.

If you have further questions on the use of the medicine, consult with a doctor or a pharmacist.

4. SIDE EFFECTS

As with any medicine, the use of Segluromet may cause side effects, in some users.
Do not be alarmed by reading the list of side effects, you may not suffer from any of them.

Contact a doctor or the nearest hospital straight away if you have any of the following serious side effects:

Lactic acidosis (very rare side effect, which may appear in less than one user out of 10,000)
Segluromet may cause a very rare, but very serious side effect called lactic acidosis (see section 2.2 “SPECIAL WARNINGS REGARDING USE OF THE MEDICINE”). If this happens, you must stop taking Segluromet and contact a doctor or the nearest hospital immediately, as lactic acidosis may lead to coma.

Diabetic ketoacidosis (rare side effect, which may appear in 1-10 users out of 10,000)
These are the signs of diabetic ketoacidosis (see also section 2.2 “SPECIAL WARNINGS REGARDING USE OF THE MEDICINE”):

- increased levels of “ketone bodies” in your urine or blood
- rapid weight loss
- feeling sick or being sick
- stomach pain
- excessive thirst
- fast and deep breathing
- confusion
- unusual sleepiness or tiredness
- a sweet smell to your breath, a sweet or metallic taste in your mouth or a different odour to your urine or sweat

This may occur regardless of blood glucose level. Your doctor may decide to temporarily or permanently stop your treatment with Segluromet.

Necrotising fasciitis of the perineum or Fournier’s gangrene (not known, cannot be estimated from the available data)
A serious soft tissue infection of the genitals or the area between and around your anus and genitals (see section 2.2 “SPECIAL WARNINGS REGARDING USE OF THE MEDICINE” for symptoms).

If you notice any of the side effects above, contact a doctor or the nearest hospital straight away.

Contact your doctor as soon as possible if you notice the following side effects:

Urinary tract infection (very common side effect, which may appear in more than 1 user out of 10)
The signs of urinary tract infection are:

- burning sensation when passing urine
- urine that appears cloudy
- pain in the pelvis or mid-back (when kidneys are infected)

Although uncommon, if you have fever or see blood in your urine, tell your doctor immediately.

Dehydration (losing too much water from your body; common side effect, which may appear in 1-10 users out of 100)
Symptoms of dehydration include:

- dry mouth
- feeling dizzy, light-headed, or weak, especially when you stand up
- fainting

You may be more likely to get dehydrated if you:

- have kidney problems
- take medicines that increase your urine production (diuretics) or lower blood pressure
- are 65 years or older

Low blood sugar (hypoglycaemia; common side effect)
Your doctor will tell you how to treat low blood sugar levels and what to do if you have any of the symptoms or signs below. The doctor may lower the dose of your insulin or other diabetes medicine.
Signs and symptoms of low blood sugar levels may include:

- headache
- drowsiness

- irritability
- hunger
- dizziness
- confusion
- sweating
- feeling jittery
- weakness
- fast heartbeat

If you notice any of the side effects above, contact your doctor as soon as possible.

Additional side effects include:

Very common side effects:
- vaginal yeast infection (thrush)
- feeling sick (nausea)
- vomiting
- diarrhoea
- stomach ache
- loss of appetite

Common side effects:
- yeast infections of the penis
- changes in urination, including urgent need to urinate more often, in larger amounts, or at night
- thirst
- vaginal itching
- change in taste
- blood tests may show changes in the amount of urea in your blood
- blood tests may show changes in the amount of total and bad cholesterol (called LDL - a type of fat in your blood)
- blood tests may show changes in the amount of red blood cells in your blood (called haemoglobin)

Uncommon side effects (may appear in 1-10 users out of 1,000):
- blood tests may show changes related to kidney function (such as ‘creatinine’)

Very rare side effects
- decreased vitamin B_{12} levels. This may cause anaemia (low levels of red blood cells).
- liver function test disorders
- hepatitis (a liver problem)
- hives
- redness of the skin
- itching

If a side effect appears, if any of the side effects worsens or if you suffer from a side effect not mentioned in this leaflet, consult with the doctor.

Side effects can be reported to the Ministry of Health by using the link "Adverse Drug Reactions Report" at the home page of the Ministry of Health's web site (www.health.gov.il) which refers to the online side effects reporting form, or by using the link: /https://sideeffects.health.gov.il

5. HOW TO STORE THE MEDICINE

- Avoid Poisoning! This medicine and any other medicine must be stored in a safe place out of the reach and sight of children and/or infants, in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by a doctor.
- Do not use the medicine after the expiry date (exp. date) which is stated on the pack. The expiry date refers to the last day of the indicated month.
- **Storage conditions**:
  Store below 30°C. Store in the original package in order to protect from moisture.
- Medicines should not be disposed of via wastewater or household waste. Ask the pharmacist how to dispose of medicines you no longer use. These measures will help to protect the environment.

Do not use this medicine if the packaging is damaged or shows signs of tampering.

6. FURTHER INFORMATION

- **In addition to the active ingredients the medicine also contains:**

Tablet core:
microcrystalline cellulose, povidone, crospovidone, magnesium stearate, sodium lauryl sulfate.
Film coating:
hypromellose, hydroxypropyl cellulose, titanium dioxide, iron oxide red, carnauba wax.

What the medicine looks like and contents of the pack:

- Segluromet 2.5/1000 mg are pink, 19.1 x 10.6 mm oval, film-coated tablets debossed with “2.5/1000” on one side and plain on the other side.
- Segluromet 7.5/1000 mg are red, 19.05 x 10.57 mm oval, film-coated tablets debossed with “7.5/1000” on one side and plain on the other side.

Pack sizes:
Segluromet is available in Alu/PVC/PA/Alu blisters. The pack sizes are 14, 28, 56, 60, 168, 180 and 196 film-coated tablets in non-perforated blisters.

Not all pack sizes may be marketed.

Marketing authorization holder:
Merck Sharp & Dohme (Israel-1996) Company Ltd., P.O.Box 7121, Petah-Tikva 49170.

Manufacturer:
Merck Sharp & Dohme Corp., New-Jersey, USA.

Revised in February 2022 according to MOHs guidelines.

Drug registration no. listed in the official Registry of the Ministry of Health:
Segluromet 2.5/1000 mg 161-70-35634
Segluromet 7.5/1000 mg 161-71-35635