Glucoset® (Tablets)

30100
Ref. No.:B2130100/24.09

Semaglutide
Glucagon-like peptide-1 (GLP-1) Analogue

GLUCOSET® TABLETS 3MG
GLUCOSET® TABLETS 7MG
GLUCOSET® TABLETS 14MG

PRESENTATION:
Glucoset® Tablets 3mg: White to off-white, oval-shaped tablet, embossed "3mg" on one side and plain on the other side.
Each tablet contains Semaglutide 3mg and other excipients.
Glucoset® Tablets 7mg: White to off-white, oval-shaped tablet, embossed "7mg" on one side and plain on the other side.
Each tablet contains Semaglutide 7mg and other excipients.
Glucoset® Tablets 14mg: White to off-white, oval-shaped tablet, embossed 14mg on one side and plain on the other side.
Each tablet contains Semaglutide 14mg and other excipients

CLINICAL PHARMACOLOGY:
Semaglutide is a GLP-1 analogue with 94% sequence homology to human GLP-1. Semaglutide acts as a GLP-1 receptor agonist that selectively binds to and activates the GLP-1 receptor, the target for native GLP-1.
GLP-1 is a physiological hormone that has multiple actions in glucose and appetite regulation and the cardiovascular system. The glucose and appetite effects are specifically mediated via GLP-1 receptors in the pancreas and the brain.
Semaglutide reduces blood glucose in a glucose-dependent manner by stimulating insulin secretion and lowering glucagon secretion when blood glucose is high. The mechanism of blood glucose lowering also involves a minor delay in gastric emptying in the early postprandial phase. During hypoglycaemia, Semaglutide diminishes insulin secretion and does not impair glucagon secretion. The mechanism of Semaglutide is independent of the route of administration.
Semaglutide reduces body weight and body fat mass through lowered energy intake, involving an overall reduced appetite. In addition, Semaglutide reduces the preference for high-fat foods.
GLP-1 receptors are expressed in the heart, vasculature, immune system and kidneys. Semaglutide has a beneficial effect on plasma lipids, lowers systolic blood pressure and reduces inflammation in clinical studies. In animal studies, Semaglutide attenuates the development of atherosclerosis by preventing aortic plaque progression and reducing inflammation in the plaque.

PHARMACOKINETICS:
Absorption: Orally administered Semaglutide has a low absolute bioavailability and variable absorption. Daily administration according to the recommended posology in combination with a long half-life reduces day-to-day fluctuation of the exposure.
The pharmacokinetics of Semaglutide have been extensively characterized in healthy subjects and patients with type 2 diabetes. Following oral administration, maximum plasma concentration of Semaglutide occurred 1-hour post-dose. Steady-state exposure was reached after 4–5 weeks of once-daily administration. In patients with type 2 diabetes, the average steady-state concentrations were approximately 6.7 nmol/L and 14.6 nmol/L with Semaglutide 7 mg and 14 mg, respectively; with 90% of subjects treated with Semaglutide 7 mg having an average concentration between 1.7 and 22.7 nmol/L and 90% of subjects treated with Semaglutide 14 mg having an average concentration between 3.7 and 41.3 nmol/L. Systemic exposure to Semaglutide increased in a dose-proportional manner.
Distribution: The estimated absolute volume of distribution is approximately 8 L in subjects with type 2 diabetes. Semaglutide is extensively bound to plasma proteins (>99%).
Biotransformation: Semaglutide is metabolized through proteolytic cleavage of the peptide backbone and sequential beta-oxidation of the fatty acid sidechain. The enzyme-neutral endopeptidase (NEP) is expected to be involved in the metabolism of Semaglutide.
Elimination: The primary excretion routes of Semaglutide-related material are via the urine and faeces. Approximately 3% of the absorbed dose is excreted as intact Semaglutide via the urine.
With an elimination half-life of approximately 1 week, Semaglutide will be present in the circulation for about 5 weeks after the last dose. The clearance of Semaglutide in patients with type 2 diabetes is approximately 0.04 L/h.

USES:
Glucoset® is indicated for the treatment of adults with insufficiently controlled type 2 diabetes mellitus to improve glycaemic control as an adjunct to diet and exercise.
- As monotherapy when Metformin is considered inappropriate due to intolerance or contraindications
- In combination with other medicinal products for the treatment of diabetes.

DOSAGE AND ADMINISTRATION:
The starting dose of Semaglutide is 3mg once daily for one month. After one month, the dose should be increased to a maintenance dose of 7mg once daily. After at least one month with a dose of 7mg once daily, the dose can be increased to a maintenance dose of 14 mg once daily to further improve glycaemic control.
The maximum recommended single daily dose of Semaglutide is 14mg. Taking two 7mg tablets to achieve the effect of a 14mg dose has not been studied and is therefore not recommended.
When Semaglutide is used in combination with Metformin and/or a sodium-glucose co-transporter-2 inhibitor (SGLT2i) or thiazolidinedione, the current dose of metformin and/or SGLT2i or thiazolidinedione can be continued.
Self-monitoring of blood glucose is not needed to adjust the dose of Semaglutide. Blood glucose self-monitoring is necessary to adjust the dose of sulfonylurea and insulin, particularly when Semaglutide is started and insulin is reduced. A stepwise approach to insulin reduction is recommended.
Missed dose
If a dose is missed, the missed dose should be skipped and the next dose should be taken the following day.
Special populations
Elderly

No dose adjustment is required based on age.

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CONTRA-INDICATIONS:
Hypersensitivity to the active substance or any of the excipients.

ADVERSE EFFECTS:
Common: Diabetic eye disease (retinopathy), **Rare:** serious allergic reactions (anaphylactic reactions). breathing problems, swelling of face and throat, wheezing, fast heartbeat, pale and cold skin, feeling dizzy or weak, and inflamed pancreas (acute pancreatitis) which could cause severe pain in the stomach and back, **Very common:** feeling sick (nausea), diarrhoea – low blood sugar (hypoglycaemia), **Uncommon:** weight loss, gallstones, burping, fast pulse, allergic reactions like rash, itching or hives, a delay in the emptying of the stomach, change in the way food or drink tastes.

OVERDOSAGE:
Effects of overdose with Semaglutide in clinical studies may be associated with gastrointestinal disorders. In the event of an overdose, appropriate supportive treatment should be initiated according to the patient's clinical signs and symptoms. A prolonged period of observation and treatment of the symptoms may be necessary, considering the long half-life of Semaglutide of approximately 1 week. There is no specific antidote for overdose with Semaglutide.

DRUG INTERACTIONS:
Thyroxine: Total exposure (AUC) of thyroxine (adjusted for endogenous levels) was increased by 33% following administration of a single dose of levothyroxine. Maximum exposure (C_{max}) was unchanged. Monitoring of thyroid parameters should be considered when treating patients with Semaglutide at the same time as levothyroxine.
Warfarin: Semaglutide did not change the AUC or C_{max} of R- and S-warfarin following a single dose of warfarin, and the pharmacodynamic effects of warfarin as measured by the international normalized ratio (INR) were not affected in a clinically relevant manner. However, upon initiation of Semaglutide treatment in patients on warfarin or other coumarin derivatives, frequent monitoring of INR is recommended.
Rosuvastatin: The AUC of rosuvastatin was increased by 41% [90% CI: 24; 60] when co-administered with Semaglutide. Based on the wide therapeutic index of rosuvastatin the magnitude of changes in the exposure is not considered clinically relevant.
Digoxin, oral contraceptives, metformin, furosemide: No clinically relevant change in AUC or C_{max} of digoxin, oral contraceptives (containing ethinylestradiol and levonorgestrel), metformin or furosemide was observed when concurrently administered with Semaglutide.

SPECIAL WARNINGS AND PRECAUTIONS:
General
Semaglutide should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis. Diabetic ketoacidosis has been reported in insulin-dependent patients who had rapid discontinuation or dose reduction of insulin when treatment with a GLP-1 receptor agonist is started.
Gastrointestinal effects and dehydration
Use of GLP-1 receptor agonists may be associated with gastrointestinal adverse reactions that can cause dehydration, which in rare cases can lead to a deterioration of renal function.
Acute pancreatitis
Acute pancreatitis has been observed with the use of GLP-1 receptor agonists. Caution should be exercised in patients with a history of pancreatitis.
Hypoglycaemia
Patients treated with Semaglutide in combination with sulfonylurea or insulin may have an increased risk of hypoglycaemia. The risk of hypoglycaemia can be lowered by reducing the dose of sulfonylurea or insulin when initiating treatment with Semaglutide.
Diabetic retinopathy
In patients with diabetic retinopathy treated with insulin and s.c. Semaglutide, an increased risk of developing diabetic retinopathy complications has been observed.

PREGNANCY AND LACTATION:
Women of childbearing potential
Women of childbearing potential are recommended to use contraception when treated with Semaglutide.
Pregnancy
Studies in animals have shown reproductive toxicity. There is limited data on the use of Semaglutide in pregnant women. Therefore, Semaglutide should not be used during pregnancy. If a patient wishes to become pregnant, or pregnancy occurs, Semaglutide should be discontinued. Semaglutide should be discontinued at least 2 months before a planned pregnancy due to the long half-life.
Breast-feeding
Glucoset® should not be used during breast-feeding.
Fertility
The effect of Semaglutide on fertility in humans is unknown. Semaglutide did not affect male fertility in rats. In female rats, an increase in oestrous length and a small reduction in number of ovulations were observed at doses associated with maternal body weight loss.

PHARMACEUTICAL PRECAUTIONS:
Store in a dry place below 25˚C. Protect from light. Keep all medicines out of the reach of children.

LEGAL CATEGORY:
Prescription Only Medicine (POM)

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