Summary Product Characteristics for pharmaceutical products

1. Name of the Medicinal Product

Glucoset MXR 20 /500 mg Tablets

2. Qualitative and Quantitative Composition

Each tablet contains 20 mg of Teneligliptin and 500 mg Metformin HCl

For a complete list of excipients, see section 6.1.

3. Pharmaceutical Form

Uncoated Tablet

4. Clinical Particulars

4.1 Therapeutic Indications

Type 2 diabetes mellitus

The drug product should be used only in patients who have not sufficiently

responded to either of the following treatments.

(a) Diet and/or exercise therapy alone.

(b) Use of sulfonylureas in addition to diet and/or exercise therapy.

(c) Use of thiazolidinediones in addition to diet and/or exercise therapy.

4.2 Posology and Method of administration

The usual adult dosage is one tablet administered orally once daily. If efficacy is

insufficient, the dose may be increased up to twice daily while closely monitoring.

4.3 Contraindication

Teneligliptin is contraindicated in the following:

- Any patient with a known hypersensitivity to teneligliptin or any of the
- components in the formulation,
- Severe ketosis, diabetic coma or history of diabetic coma, type 1 diabetic
- patients,
- Patients with severe infection, surgery, severe trauma (blood sugar control
- should preferably be done by insulin).
- Metformin is contraindicated in the following:
- Any type of acute metabolic acidosis (such as lactic acidosis, diabetic

ketoacidosis)

- Diabetic pre-coma

• Severe renal failure (GFR< 30 mL/min)

• Acute conditions with the potential to alter renal function such as: Dehydration, Severe infection, Shock

4.4 Special warnings and precautions for use

Teneligliptin should be administered carefully in the following:

- Patients with advanced liver failure (safety has not been established),
- Patients with congestive heart failure (NYHA category III-IV) (safety has not been established),
- Patients with pituitary insufficiency or adrenal insufficiency, poor nutritional state, starvation, an irregular dietary intake, or debilitating condition, intense muscle movement or excessive alcohol intake (may cause low blood sugar),
- Patients with history of abdominal surgery or with a history of bowel obstruction (may cause bowel obstruction),
- Patients with arrhythmia, severe bradycardia or its history, patients with heart disease such as congestive heart failure or patients with low serum potassium, congenital prolonged QT syndrome, history of Torsades de pointes or patients using antiarrhythmic drugs (may cause QT prolongation),
- Patients using an insulin secretagogue (e.g., sulfonylurea) (risk of severe hypoglycaemia).

Metformin should be administered carefully in the following:

- Lactic acidosis, most often occurs at acute worsening of renal function or

cardiorespiratory illness or sepsis. Metformin accumulation occurs at acute

worsening of renal function and increases the risk of lactic acidosis.

- Patients with heart failure are more at risk of hypoxia and renal insufficiency.
- In patients with stable chronic heart failure, metformin may be used with a

regular monitoring of cardiac and renal function.

- GFR should be assessed before treatment initiation and regularly thereafter.
- Patients with renal impairment.

4.5 Interaction with other medicinal products and other forms of interaction

Teneligliptin should be used with caution with drugs that can enhance the blood

glucose lowering effect (like β blockers, MAO inhibitors, etc.) and attenuate the

blood glucose lowering effect (like steroids, thyroid hormones, etc).

Consumption of Alcohol with Metformin is associated with an increased risk of

lactic acidosis, particularly in case of fasting, malnutrition or hepatic impairment.

Co-administration of metformin with

- Inhibitors of OCT1 (such as verapamil) may reduce efficacy of metformin.
- Inhibitors of OCT 2 (such as cimetidine, dolutegravir, trimethoprim affects

elimination of Metformin and therefore affects metformin plasma concentration.

4.6 Pregnancy and lactation

Glucoset MXR should be used during pregnancy only if the potential benefit

justifies the potential risk to the fetus. Safety and effectiveness of teneligliptin in

pediatric patients have not been established. Metformin is excreted into human

breast milk and as only limited data are available, breastfeeding is not

recommended during metformin treatment.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been

performed. Patients who experience dizziness as an adverse reaction should

avoid driving vehicles or using machines.

4.8 Undesirable effects

Gastrointestinal Disorders: Nausea, Intestinal obstruction, abdominal bloating,

abdominal discomfort, nausea, abdominal pain, flatulence, stomatitis, gastric

polyps, colon polyps, duodenal ulcer, reflux esophagitis, diarrhea, loss of appetite,

increased amylase, lipase increased, acute pancreatitis.

Kidney and Urinary system: Proteinuria, urine ketone-positive.

Skin and Subcutaneous Tissue Disorders: Eczema, rash, itching, allergic

dermatitis.

Lactic acidosis

Decrease of vitamin B12 absorption with decrease of serum levels during long term use of Metformin.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org

4.9 Overdose

In the event of an overdose, it is reasonable to employ the usual supportive

measures, e.g., remove unabsorbed material from the gastrointestinal tract, employ

clinical monitoring (including obtaining an electrocardiogram), and institute

supportive therapy as dictated by the patient's clinical status.

5 Pharmacological Properties

5.1 Pharmacodynamic Properties

Teneligliptin

Teneligliptin is a DPP-4 inhibitor, which is believed to exert its actions in patients with type 2 diabetes by slowing the inactivation of incretin hormones. Concentrations of the active intact hormones are increased by teneligliptin, thereby increasing and prolonging the action of these hormones. Incretin hormones, including glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP), are released by the intestine throughout the day, and levels are

increased in response to a meal. These hormones are rapidly inactivated by the enzyme, DPP-4.

The incretins are part of an endogenous system involved in the physiologic regulation of glucose homeostasis. When blood glucose concentrations are normal or elevated, GLP-1 and GIP increase insulin synthesis and release from pancreatic beta cells by intracellular signaling pathways involving cyclic AMP. GLP-1 also lowers glucagon secretion from pancreatic alpha cells, leading to reduced hepatic glucose production. By increasing and prolonging active incretin

levels, teneligliptin increases insulin release and decreases glucagon levels in the

circulation in a glucose-dependent manner.

Metformin

Metformin improves glucose tolerance in patients with type-2 diabetes (NIDDM),

lowering both basal and postprandial plasma glucose. Metformin decreases hepatic

glucose production, decreases intestinal absorption of glucose, and improves

insulin sensitivity by increasing peripheral glucose uptake and utilization.

5.2 Pharmacokinetic Properties

Teneligliptin

After oral administration of a single 20 mg and 40 mg dose to healthy subjects,

teneligliptin was rapidly absorbed, with peak plasma concentrations (mean T max)

occurring at 1.8 hours and 1 hour post dose. Plasma AUC of teneligliptin increased

in a dose-proportional manner. Following a single oral 20 mg and 40 mg dose to

healthy volunteers, mean plasma AUC of teneligliptin was 2028.9 and 3705.1

ng*hr/ml, Cmax was 187.2 and 382.4 ng/ml, and apparent terminal half-life (t1/2)

was 24.2 and 20.8 hours. Co-administration with food reduces the Cmax by 20%,

increases the Tmax from 1.1 to 2.6 hours but does not affect the AUC of

teneligliptin as compared to that in the fasting state. The plasma protein binding rate is 77.6 – 82.2%.In vitro studies indicated that CYP3A4 and flavin-containing

monooxygenase (FMO1 and FMO3) are involved in the metabolism of

teneligliptin Following a 20 mg single oral dose of [14C] teneligliptin, 45.4% of administered radioactivity was excreted in urine and 46.5% in faeces till 216 hours after dose.

Metformin

The absolute bioavailability of a metformin 500 mg tablet given under fasting conditions is approximately 50-60 %. Following a single oral dose of

metformin sustained-release, Cmax is achieved within 4-8 hours. Peak plasma levels are approximately 20 % lower compared to

the same dose of metformin immediate release, however, the extent of absorption (as measured by AUC) is similar to immediate release. Both high and low fat meals had the same effect on the pharmacokinetics of sustained release. Plasma

protein binding is negligible. Metformin is excreted unchanged in urine.

5.3 Preclinical safety data

Not known.

6 Pharmaceutical Particulars

6.1 list of Excipients

FLOCEL 101 USP

Hydroxypropyl cellulose

Partially pregelatinized starch

Yellow iron oxide

Croscarmellose sodium Dried

Aerosil

Magnesium stearate

Sodium starch glycollate

Instamodel Blend I

Instamodel Blend II

Aerosil

6.2 Incompatibilities

Not Applicable

6.3 Shelf life

2 Years

6.4 Special precautions for storage

Store in a dry place below 30˚C. Protect from light.

Keep all medicines out of the reach of children.

6.5 Nature and contents of container

Aluminium/Aluminium blister pack.

6.6 Instructions for use, handling and disposal

No special requirements.

7.Marketing authorization holder

Cosmos Limited

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8. Marketing authorization numbers

H2022/CTD8128/17970

9.Date of first authorization/renewal of the authorization

2022 January 11

10. Date of revision of the text

2022 January 11