SUMMARY OF PRODUCT CHARACTERISTICS OF GLUCOSET 20 MG FILM COATED TABLET (Teneligliptin 20 mg tablet)

1. **Name of the Medicinal Product**
   Glucoset 20 mg film coated Tablets
2. **Qualitative and Quantitative Composition**
   Each film coated tablet contains 20 mg of Teneligliptin.
3. **Pharmaceutical Form**
   Film coated Tablet
4. **Clinical Particulars**

4.1 Therapeutic Indications

Treatment of type 2 diabetes mellitus when patients do not show sufficient improvement after diet control and exercise or a combination of diet control, exercise, and sulfonylurea- or thiazolidine-class drugs.

4.2 Posology and Method of administration

The usual adult dosage is 20 mg of teneligliptin administered orally once daily. If efficacy is insufficient, the dose may be increased up to 40 mg once daily while closely monitoring the clinical course.

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).

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).

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).

4.6 Pregnancy and lactation

Pregnancy
This medicine is not recommended for use in pregnant women unless absolutely necessary. All the risks and benefits should be discussed with the doctor before taking this medicine.
Breast-feeding
This medicine is not recommended for use in breastfeeding women.

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

The most common adverse reactions reported with teneligliptin are hypoglycemia and constipation. Other adverse reactions reported with teneligliptin are:

- **Gastrointestinal Disorders:** 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

5 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.

6 Pharmacological Properties

6.1 Pharmacodynamic Properties

Glucoset 20 mg Tablet 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.

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7.1 Pharmacokinetic Properties

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. Plasma AUC of teneligliptin increased following 20 mg doses at steady-state compared to the first dose. 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%. Following a 20 mg single oral dose of [14C] teneligliptin, 5 metabolites M1, M2, M3, M4 and M5 were observed. In vitro studies indicated that CYP3A4 and flavin-containing monooxygenase (FMO1 and FMO3) are involved in the metabolism of teneligliptin. Teneligliptin does not inhibit CYP1A2, CYP2A6, CYP2B6, CYP2C8, CYP2C8/9, CYP2C19, CYP2E1, is a weak inhibitor of CYP2D6, CYP3A4, and FMO does not induce CYP3A4 and CYP1A2. Following a 20 mg single oral dose of teneligliptin, 45.4% of administered radioactivity was excreted in urine and 46.5% in faeces till 216 hours after dose. The cumulative urinary excretion rates for up to 120 hours for un-metabolized, M1, M2, and M3 were 14.8%, 17.7%, 1.4% and 1.9% respectively while the cumulative faecal excretion rates for un-metabolized, M1, M3, M4 and M5 were 26.1%, 4.0%, 1.6%, 0.3% and 1.3% respectively.

7.2 Preclinical safety data

Teneligliptin was not mutagenic in conventional *in vitro* and *in vivo* tests for genotoxicity.

8 Pharmaceutical Particulars

8.1 list of Excipients

FLOCEL 101 USP
Hydroxypropyl cellulose
Partially pregelatinized starch
Yellow iron oxide
Croscarmellose sodium Dried
Aerosil
Magnesium stearate
Sodium starch glycollate
Opadry II Yellow

7.2 Incompatibilities

Not Applicable

7.3 Shelf life

2 Years

7.4 Special precautions for storage

Store in a dry place below 30˚C. Protect from light.
Keep all medicines out of the reach of children.

7.5 Nature and contents of container

Aluminium/Aluminium blister pack.

7.6 Instructions for use, handling and disposal

No special requirements.

8 REGISTRANT

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9 MANUFACTURER

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