

TEN20[®]

1. Generic Name

Teneligliptin

2. Qualitative and Quantitative Composition

Each Tablet Contains

Teneligliptin 20 mg

3. Dosage form and strength

Ten-20 is available in strength of 20mg tablet.

4. Clinical particulars

4.1 Therapeutic indication

Type 2 diabetes mellitus

The drug product should be used only in patients who have not sufficiently responded to either of the following treatments.

- Diet and/or exercise therapy alone
- Use of sulfonylureas in addition to diet and/or exercise therapy
- Use of thiazolidinedione in addition to diet and/or exercise therapy.

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).



We Impart Health to Life

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 Drug interactions

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). On concomitant therapy with ketoconazole, the geometric least squares mean ratio (concomitant therapy/Teneligliptin monotherapy) of C_{max} and AUC of unchanged plasma Teneligliptin with their two-sided 90% CI is 1.37 [1.25, 1.50] and 1.49 [1.38, 1.60], respectively.

4.6 Use in special population

- Pediatric: Safety and effectiveness of Teneligliptin in Pediatric patients have not been established
- Geriatric: Safety and effectiveness of Teneligliptin in paediatric patients have not been established.
- Liver impairment: Teneligliptin should be used with extreme caution in patients with a known history of severe hepatic impairment since the safety and efficacy of this medicine have not been established for such patients. Close monitoring of liver function is recommended in these patients.
- Renal failure: Safety and effectiveness of Teneligliptin in renal failure patients have not been established.
- Pregnancy and lactation: Teneligliptin should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus. Safe use of



We Impart Health to Life

Teneligliptin during pregnancy has not been established. Teneligliptin should be avoided by breastfeeding mothers (transition to milk has been reported in laboratory animals).

4.7 Effects on ability to drive and use machine

No data available.

4.8 Undesirable effects

The most common adverse reactions reported with Teneligliptin are hypoglycaemia 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, diarrhoea, 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.

Investigations: Increase in AST, ALT, γ -GTP and ALP. Others: Increased CPK, increased serum potassium, fatigue, allergic rhinitis, elevation of serum uric acid.

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 Mechanism of action

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 insulin tropic 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 incretin 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



We Impart Health to Life

pancreatic beta cells by intracellular signalling 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, Tenueligliptin increases insulin release and decreases glucagon levels in the circulation in a glucose-dependent manner.

5.2 Pharmacodynamics properties

Tenueligliptin is a long-acting, orally bioavailable, pyrrolidine-based inhibitor of dipeptidyl peptidase 4 (DPP-4), with hypoglycaemic activity. Tenueligliptin may also reduce plasma triglyceride levels through a sustained increase in GLP-1 levels.

5.3 Pharmacokinetic properties

- After oral administration of a single 20 mg and 40 mg dose to healthy subjects, Tenueligliptin was rapidly absorbed, with peak plasma concentrations (mean T max) occurring at 1.8 hours and 1 hour post dose. Plasma AUC of Tenueligliptin increased in a dose-proportional manner. Following a single oral 20 mg and 40 mg dose to healthy volunteers, mean plasma AUC of Tenueligliptin 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 Tenueligliptin 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 Tenueligliptin 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] Tenueligliptin, 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 Tenueligliptin. Tenueligliptin does not inhibit CYP1A2, CYP2A6, CYP2B6, CYP2C8, CYP2C8/9, CYP2C19, and CYP2E1, is a weak inhibitor of CYP2D6, CYP3A4, and FMO (IC50 value : 489.4, 197.5 and 467.2 µmol/l) and does not induce CYP3A4 and CYP1A2. Following a 20 mg single oral dose of [14C] Tenueligliptin, 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. The single administration of Tenueligliptin at 20 mg in patients with renal impairment revealed no remarkable changes in Cmax and t1/2 corresponding to the level of renal impairment. Compared with healthy adult subjects, the AUC0 of subjects with mild renal impairment (50 ≤ creatinine clearance [Ccr] ≤ 80 mL/minute), moderate renal impairment (30 ≤ Ccr < 50 mL/minute), and severe renal impairment (Ccr < 30 mL/minute) was approximately 1.25 times, 1.68 times, and 1.49 times higher than that of healthy adult subjects, respectively. A single administration of Tenueligliptin 20 mg in patients with hepatic impairment revealed that the Cmax of subjects with mild



hepatic impairment (Child–Pugh classification: total score 5–6) and moderate hepatic impairment (Child–Pugh classification: total score 7–9) was approximately 1.25 times and 1.38 times that of healthy adult subjects, respectively. Compared to healthy adult subjects, the AUC of subjects with mild and moderate hepatic impairments was approximately 1.46 times and 1.59 times higher than that of healthy adult subjects, respectively. There have been no previous clinical studies using Teneligliptin in patients with severe hepatic impairment (Child–Pugh classification: total score was greater than 9).

6. Nonclinical properties

6.1 Animal Toxicology or Pharmacology

NA.

7. Description

Teneligliptin

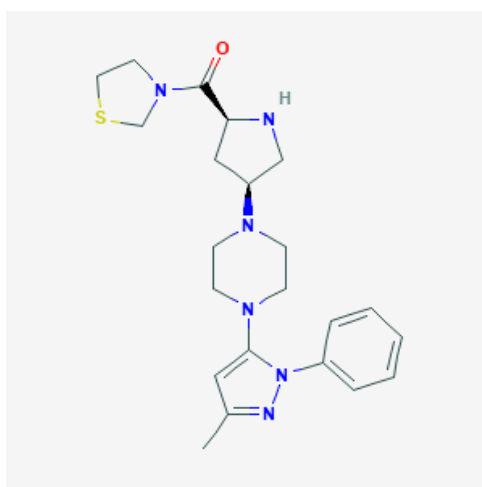
Teneligliptin has been investigated for the treatment of Type 2 Diabetes Mellitus. Teneligliptin is a long-acting, orally bioavailable, pyrrolidine-based inhibitor of dipeptidyl peptidase 4 (DPP-4), with hypoglycemic activity.

Chemical Name - 3 [(2S,4S)-4-[4-(5-methyl-2-phenylpyrazol-3-yl)piperazin-1-yl]pyrrolidin-2-yl]-(1,3-thiazolidin-3-yl)methanone

Molecular Weight- 426.6 g/mol

Molecular Formula- C₂₂H₃₀N₆OS

Structure-



8. Pharmaceutical particulars

8.1 Incompatibilities



We Impart Health to Life

There are no known incompatibilities.

8.2 Shelf-life

24 months.

8.3 Packaging Information

Ten-20 is available in a strip of 10 tablets

8.4 Storage and handling instructions

Store below 25°C away from direct sunlight, heat and moisture.

9. Patient Counselling Information

9.1 Adverse Reactions

Refer part 4.8

9.2 Drug Interactions

Refer part 4.5

9.3 Dosage

Refer part 4.2

9.4 Storage

Refer part 8.4

9.5 Risk Factors

Refer part 4.4

9.6 Self-monitoring information

NA

9.7 Information on when to contact a health care provider or seek emergency help

Patients are advised to be alert for the emergence or worsening of the adverse reactions and contact the prescribing physician.

9.8 Contraindications

Refer part 4.3



We Impart Health to Life

10. Manufactured by SYNOKEM PHARMACEUTICALS LTD

11. Details of permission or license number with date

Permission No. MF/FF/SND/193/2018 – 13.07.2018

12. Date of revision: January 2021



We Impart Health to Life