HOSPIMAX
Maximising Life

Hoslina™-D 5 mg/ 10 mg

Linagliptin 5 mg + Dapagliflozin 10 mg tablet

Product Description:

Each film coated tablet contains Linagliptin 5mg and Dapagliflozin 10mg.

Description:

Linagliptin is an oral inhibitor of dipeptidyl peptidase-4 (DPP-4). It is the first agent of its class to be eliminated predominantly via a nonrenal route.

Dapagliflozin is a sodium-glucose cotransporter 2 inhibitor indicated for managing diabetes mellitus type 2. When combined with diet and exercise in adults, dapagliflozin helps to improve glycaemic control by inhibiting glucose reabsorption in the proximal tubule of the nephron and causing glycosuria.

Indications:

Dapagliflozin and linagliptin are commonly used medications for the treatment of type-2 diabetes mellitus (T2DM).

Dosage:

once in a day, can be taken with or without food any time of the day.

Mode of Action:

Hoslina-D Tablet is a combination of two antidiabetic medications. Linagliptin works by increasing the amounts of certain natural substances that lower blood sugar when it is high.Dapagliflozin works by lowering blood sugar levels in people with type 2 diabetes by excreting extra sugar from the body through urine.

Pharmacokinetics:

Linagliptin:

Absorption:
The absolute bioavailability of linagliptin is approximately 30%. Co-administration of a high-fat meal with linagliptin prolonged the time to reach Cmax by 2 hours and lowered Cmax by 15% but no influence on AUC 0-72h was observed. No clinically relevant effect of Cmax and Tmax changes is expected; therefore linagliptin may be administered with or without food.

Distribution:
As a result of tissue binding, the mean apparent volume of distribution at steady-state following a single 5 mg intravenous dose of linagliptin to healthy subjects is approximately 1,110 litres, indicating that linagliptin extensively distributes to the tissues. Plasma protein binding of linagliptin is concentration-dependent, decreasing from about 99% at 1 nmol/l to

75-89% at ≥30 nmol/l, reflecting saturation of binding to DPP-4 with increasing concentration of linagliptin. At high concentrations, where DPP-4 is fully saturated, 70-80% of linagliptin was bound to other plasma proteins than DPP-4, hence 30-20% were unbound in plasma.

Biotransformation:
Following linagliptin oral 10 mg dose, approximately 5% of the radioactivity was excreted in urine. Metabolism plays a subordinate role in the elimination of linagliptin. One main metabolite with a relative exposure of 13.3% of linagliptin at steady-state was detected which was found to be pharmacologically inactive and thus does not contribute to the plasma DPP-4 inhibitory activity of linagliptin.

Elimination: Following administration of an oral linagliptin dose to healthy subjects, approximately 85% of the administered radioactivity was eliminated in faeces (80%) or urine (5%) within 4 days of dosing. Renal clearance at steady-state was approximately 70 ml/min.

Dapagliflozin:

Absorption

Oral dapagliflozin reaches a maximum concentration within 1 hour of administration when patients have been fasting. When patients have consumed a high fat meal, the time to maximum concentration increases to 2 hours and the maximum concentration decreases by half though a dose adjustment is not necessary. Oral dapagliflozin is 78% bioavailable

Metabolism

Dapagliflozin is primarily glucuronidated to become the inactive 3-O-glucuronide metabolite (60.7%). Dapagliflozin also produces another minor glucuronidated metabolite (5.4%), a de-ethylated metabolite. Metabolism of dapagliflozin is mediated by cytochrome p-450(CYP)1A1, CYP1A2, CYP2A6, CYP2C9, CYP2D6, CYP3A4, uridine diphosphate glucuronyltransferase(UGT)1A9, UGT2B4, and UGT2B72 . Glucuronidation to the major metabolite is mediated by UGT1A9

Route of elimination

75.2% of dapagliflozin is recovered in the urine with 1.6% of the dose unchanged by metabolism. 21% of the dose is excreted in the feces with 15% of the dose unchanged by metabolism

Method Of Administration:

Hoslina-D Tablet may be taken with or without food. Take it at the same time every day to help you remember to take it. The dose and duration of the treatment will be decided by your doctor. Do not stop taking it without asking your doctor. If you do, your blood sugar levels may increase and put you at risk of serious complications like kidney damage and

blindness. This medicine is only part of a treatment program that should include a healthy diet, regular exercise, and weight reduction as advised by your doctor.

Contraindications:

Before taking this medicine, inform your doctor if you have any kidney or liver problems or a urinary tract infection or if you are on water pills (diuretics). Pregnant or breastfeeding women should also consult their doctor before taking it. Avoid excessive alcohol intake while taking it as this may increase the risk of developing some side effects. Monitor your blood sugar levels regularly while taking this medicine.

Drug Interaction:

Dapagliflozin

Diuretics

Dapagliflozin may add to the diuretic effect of thiazide and loop diuretics and may increase the risk of dehydration and hypotension Insulin and insulin secretagogues Lower dose of insulin or an insulin secretagogue such as sulphonylureas, may be required to reduce the risk of hypoglycaemia when used in combination with dapagliflozin in patients with type 2 diabetes mellitus

Rifampicin: With rifampicin (an inducer of various active transportersand drug-metabolising enzymes) a 22% decrease in dapagliflozin systemic exposure (AUC) wasobserved, but with no clinically meaningful effect on 24-hour urinary glucose excretion. No doseadjustment is recommended.

Following coadministration of dapagliflozin with mefenamic acid (an inhibitor of UGT1A9), a 55% increase in dapagliflozin systemic exposure was seen, but with no clinically meaningful effect on 24-hour urinary glucose excretion. No dose adjustment is recommended Dapagliflozin 20 mg and simvastatin (a CYP3A4 substrate) resulted in a 19% increase in AUC of simvastatin and 31% increase in AUC of simvastatin acid. The increase in simvastatin and simvastatin acid exposures are not considered clinically relevant.

Linagliptin

Sulphonylureas: co-administration of multiple oral doses of 5 mg linagliptin and a single oral dose of 1.75 mg glibenclamide (glyburide) resulted in clinically not relevant reduction of 14% of both AUC and Cmax of glibenclamide. Because glibenclamide is primarily metabolised by CYP2C9, these data also support the conclusion that linagliptin is not a CYP2C9 inhibitor. Clinically meaningful interactions would not be expected with other sulphonylureas (e.g., glipizide, tolbutamide, and glimepiride) which, like glibenclamide, are primarily eliminated by CYP2C9.

Digoxin: co-administration of multiple daily doses of 5 mg linagliptin with multiple doses of 0.25 mg digoxin had no effect on the pharmacokinetics of digoxin in healthy volunteers. Therefore, linagliptin is not an inhibitor of P-glycoprotein-mediated transport in vivo.

Warfarin: multiple daily doses of 5 mg linagliptin did not alter the pharmacokinetics of S(-) or R(+) warfarin, a CYP2C9 substrate, administered in a single dose.

Simvastatin: multiple daily doses of linagliptin had a minimal effect on the steady-state pharmacokinetics of simvastatin, a sensitive CYP3A4 substrate, in healthy volunteers. Following administration of a supratherapeutic dose of 10 mg linagliptin concomitantly with 40 mg of simvastatin daily for 6 days, the plasma AUC of simvastatin was increased by 34%, and the plasma Cmax by 10%.

Adverse Reactions:

It may cause hypoglycemia (low blood sugar level) when used with other antidiabetic medicines, alcohol or if you delay or miss a meal. Nausea, Urinary tract infection, Genital fungal infection, Diarrhea, Increased urination, Rash are the adverse effect of Hoslina-D.