For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only

(Saxagliptin / Metformin HCl extended-release) tablets.

KOMBIGLYZE™ XR

Abbreviated Prescribing Information

INDICATIONS AND USAGE:

Kombiglyze™ XR is indicated as an adjunct to diet and exercise to improve glycaemic control in adults with type 2 diabetes mellitus when treatment with both saxagliptin and metformin is appropriate.

IMPORTANT LIMITATIONS OF USE:

Kombiglyze™ XR should not be used for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis; it has not been studied in patients with a history of pancreatitis.

DOSAGE AND ADMINISTRATION:

Generally should be administered once daily with the evening meal, with gradual dose titration to reduce the gastrointestinal side effects associated with metformin.

• The recommended starting dose in patients who need 5 mg of saxagliptin and who are not currently treated with metformin is 5 mg saxagliptin/500 mg metformin extended-release. In patients treated with metformin, the dose should provide metformin at the dose already being taken, or the nearest therapeutically appropriate dose.

• Patients who need 2.5 mg saxagliptin in combination with metformin extended-release may be treated with Kombiglyze™ XR 2.5 mg/1000 mg.

• The maximum daily recommended dose is 5 mg for saxagliptin and 2000 mg for metformin extended-release. When co-administered with strong CYP3A4/5 inhibitors, limit the dose to 2.5 mg/1000 mg once daily.

• When KOMBIGLYZE™ XR is used in combination with an insulin secretagogue (e.g. sulphonylurea) or with insulin, a lower dose of the insulin secretagogue or insulin may be required to minimise the risk of hypoglycaemia.

CONTRAINDICATIONS:

Renal impairment, hypersensitivity to metformin hydrochloride, acute or chronic metabolic acidosis (including diabetic ketoacidosis), history of a serious hypersensitivity reaction to Kombiglyze™ XR or saxagliptin (such as anaphylaxis, angioedema, or exfoliative skin conditions).

WARNINGS AND PRECAUTIONS FOR USE:

Lactic acidosis - It is a rare, but serious complication that can occur due to metformin accumulation during treatment with Kombiglyze^{TM}XR. If acidosis is suspected, Kombiglyze^{TM} XR should be discontinued and the patient hospitalised immediately.

Pancreatitis – There have been postmarketing reports of acute pancreatitis in patients taking saxagliptin. After initiation of KOMBIGLYZE^{TM} XR, observe patients for signs and symptoms of pancreatitis. If pancreatitis is suspected, Kombiglyze^{TM}XR should promptly be discontinued and appropriate management should be initiated. It is unknown whether patients with a history of pancreatitis are at increased risk for the development of pancreatitis while using KOMBIGLYZE.

Heart Failure patients- Consider the risks and benefits of KOMBIGLYZE XR prior to initiating treatment in patients at a higher risk for heart failure. Observe patients for signs and symptoms of heart failure during therapy. Advise patients of the characteristic symptoms of heart failure, and to immediately report such symptoms. If heart failure develops, evaluate and manage according to current standards of care and consider discontinuation of KOMBIGLYZE XR.

Kombiglyze^{TM} XR is contraindicated in patients with renal impairment and not recommended in patients with hepatic impairment.

Use with Medications Known to Cause Hypoglycemia - Insulin or insulin secretagogues, such as sulphonylureas, cause hypoglycaemia. Therefore, when used in combination with saxagliptin, a lower dose of the insulin or insulin secretagogue may be required to reduce the risk of hypoglycaemia.

Hypersensitivity Reactions - There have been postmarketing reports of serious hypersensitivity reactions in patients treated with saxagliptin which include anaphylaxis, angioedema, and exfoliative skin conditions. If a serious hypersensitivity reaction is suspected, discontinue Kombiglyze^{TM} XR, assess for other potential causes for the event, and institute alternative treatment for diabetes.

ADVERSE REACTIONS:

Diarrhoea, nausea/vomiting, upper respiratory tract infection, urinary tract infection, headache, nasopharyngitis, hypersensitivity reactions, infections, dose-related mean decrease in absolute lymphocyte count, acute pancreatitis. Hypoglycaemia was seen in patients on insulin, insulin secretagogues such as sulphonylureas, and in renally impaired patients.

USE IN SPECIAL POPULATIONS:

Pregnancy Category B: Kombiglyze^{TM} XR, like other antidiabetic medications, should be used during pregnancy only if clearly needed. •

Nursing Mothers: Because many drugs are secreted in human milk, caution should be exercised when Kombiglyze^{TM} XR is administered to a nursing woman.

Paediatric Use: Safety and effectiveness of Kombiglyze^{TM} XR in paediatric patients have not been established.

Geriatric Use: Because metformin is contraindicated in patients with renal impairment, carefully monitor renal function in the elderly and use Kombiglyze^{TM} XR with caution as age increases.

PATIENT COUNSELING INFORMATION

Heart Failure Patients should be informed of the signs and symptoms of heart failure. Before initiating KOMBIGLYZE XR, patients should be asked about a history of heart failure or other risk factors for heart failure including moderate to severe renal impairment. Patients should be instructed to contact their healthcare provider as soon as possible if they experience symptoms of heart failure, including increasing shortness of breath, rapid increase in weight or swelling of the feet

PRESENTATION:

Each carton contains 4 blister cards of 7 film-coated tablets in Alu/Alu blisters.

STORAGE: Store below 30ºC.

KOMBIGLYZE™ XR is an applied trademark of AstraZeneca group of companies.

For further information, please contact:

AstraZeneca Pharma India Limited
Block N1, 12th Floor
Manyata Embassy Business Park
Rachenahalli, Outer Ring Road
Bangalore – 560045.
www.astrazenecaindia.com

For more information, refer full prescribing information version 8 dated 18th October 2016.

.