ZIGLIM PLUS 1/ 2 TABLET

This is to inform all concerned that the Ministry of Health and Family Welfare vide their Notification No. 4711(E) dated 7th September, 2018 has cleared the manufacturing, sale and distribution of Fixed dose Combination of Glimepiride 1mg/2mg + Pioglitazone 15mg + Metformin 500 mg.

Kindly note that in view of the above notification, our products as given below stands cleared by the Ministry of Health and Family Welfare.

ZIGLIM PLUS 1

ZIGLIM PLUS 2

However, there is an advice for the Healthcare Professionals that the said drugs shall be used for treatment of type-2 diabetes mellitus (T2DM) when diet, exercise along with monotherapy and dual therapy does not achieve glycaemic target.

Also, the following precautions/ warnings to be considered while administering Ziglim Plus 1/ 2 Tablet:

GLIMEPIRIDE

Hypoglycemia

- All sulfonylureas, including glimepiride, can cause severe hypoglycemia. The patient's ability to concentrate and react may be impaired as a result of hypoglycemia. These impairments may present a risk in situations where these abilities are especially important, such as driving or operating other machinery. Severe hypoglycemia can lead to unconsciousness or convulsions and may result in temporary or permanent impairment of brain function or death.

METFORMIN:

Lactic Acidosis

- Post-marketing cases of metformin-associated lactic acidosis have resulted in death, hypothermia, hypotension, and resistant bradyarrhythmias. Symptoms included malaise, myalgias, respiratory distress, somnolence, and abdominal pain. Laboratory abnormalities

included elevated blood lactate levels, anion gap acidosis, increased lactate/pyruvate ratio; and metformin plasma levels generally greater than 5 mcg/mL.

- Risk factors include renal impairment, concomitant use of certain drugs, age ≥65 years old, radiological studies with contrast, surgery and other procedures, hypoxic states, excessive alcohol intake, and hepatic impairment. Steps to reduce the risk of and manage metformin-associated lactic acidosis in these high risk groups are provided in the Full Prescribing Information.
- If lactic acidosis is suspected, discontinue ZIGLIM PLUS 1/2 and institute general supportive measures in a hospital setting. Prompt hemodialysis is recommended.

PIOGLITAZONE

Congestive Heart Failure

- Thiazolidinediones, including pioglitazone, which is a component of ZIGLIM PLUS 1/2, cause or exacerbate congestive heart failure in some patients.
- After initiation of ZIGLIM PLUS 1/2, and after dose increases, monitor patients carefully for signs and symptoms of heart failure (e.g., excessive, rapid weight gain, dyspnea, and/or edema). If heart failure develops, it should be managed according to current standards of care and discontinuation or dose reduction of ZIGLIM PLUS 1/2must be considered.
- ZIGLIM PLUS 1/2 is not recommended in patients with symptomatic heart failure.
- Initiation of ZIGLIM PLUS 1/2 in patients with established New York Heart Association (NYHA) Class III or IV heart failure is contraindicated.

Urinary bladder cancer

- Patients with active bladder cancer or with a history of bladder cancer, and those with uninvestigated haematuria, should not receive pioglitazone.
- Prescribers should review the safety and efficacy of pioglitazone in individuals after 3-6 months of treatment to ensure that only patients who are deriving benefit continue to be treated. Pioglitazone should be stopped in patients who do not respond adequately to treatment (e.g. reduction in glycosylated haemoglobin HbA1c).
- Before starting pioglitazone, the following known risk factors for development of bladder cancer should be assessed in individuals: age, current or past history of smoking, exposure to some occupational or chemotherapy agents such as cyclophosphamide, or previous irradiation of the pelvic region.

- Use in elderly patients should be considered carefully before and during treatment because the risk of bladder cancer increases with age. Elderly patients should start on the lowest possible dose and be regularly monitored because of the risks of bladder cancer and heart failure associated with pioglitazone.