METRIDE PLUS

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

Abbreviated Prescribing information for **METRIDE PLUS** [Metformin Hydrochloride (PR), Glimepiride and Pioglitazone Bilayer Tablets.]

[Please refer the complete prescribing information available at www.torrentpharma.com]

PHARMACOLOGICAL PROPERTIES:

MECHANISM OF ACTION*: Metformin:* Metformin may act via 3 mechanisms: • reduction of hepatic glucose production by inhibiting gluconeogenesis and glycogenolysis • in muscle, by increasing insulin sensitivity, improving peripheral glucose uptake and utilization • and delay of intestinal glucose absorption. Metformin stimulates intracellular glycogen synthesis by acting on glycogen synthase. Metformin increases the transport capacity of all types of membrane glucose transporters (GLUT). *Glimepride:* Glimepiride acts mainly by stimulating insulin release from pancreatic beta cells. As with other sulfonylureas this effect is based on an increase of responsiveness of the pancreatic beta cells to the physiological glucose stimulus. In addition, glimepiride seems to have pronounced extra pancreatic effects also postulated for other sulfonylureas. Pioglitazone: Pioglitazone effects may be mediated by a reduction of insulin resistance. Pioglitazone appears to act via activation of specific nuclear receptors (peroxisome proliferator activated receptor gamma) leading to increased insulin sensitivity of liver, fat and skeletal muscle cells in animals. Treatment with pioglitazone has been shown to reduce hepatic glucose output and to increase peripheral glucose disposal in the case of insulin resistance.

INDICATIONS For treatment of type-2 diabetes mellitus (T2DM) when diet, exercise along with monotherapy and dual therapy does not achieve glycaemic target.

DOSAGE AND ADMINISTRATION: As directed by Physician. The total daily doses of Metride plus should not exceed the maximum recommended total daily doses of pioglitazone (45mg) or metformin (2000mg for extended-release metformin) or glimepiride (8 mg). Patients should be informed that Metride plus must be swallowed whole and not chewed, cut or crushed, and that the inactive ingredients may occasionally be eliminated in the feces as a soft mass that resemble the original tablet.

CONTRAINDICATION: Hypersensitivity to the active substances or to any of the excipients. Patients with established NYHA class III or IV heart failure. Acute or chronic disease which may cause tissue hypoxia such as cardiac or respiratory failure, recent myocardial infarction, shock, Hepatic impairment, Acute alcohol intoxication, alcoholism, Diabetic ketoacidosis or diabetic pre-coma, Renal failure or renal dysfunction (creatinine clearance<60ml/min), Acute conditions with the potential to alter renal function such as: Dehydration Severe infection Shock Intravascular administration of iodinated contrast agents, Lactation.

WARNINGS & PRECAUTIONS: Pioglitazone can cause fluid retention, weight gain, oedema, and may precipitate or worsen heart failure—especially in the elderly or when combined with insulin or NSAIDs—so patients should start at low doses and be closely monitored; it also carries risks of bladder cancer (higher with long duration/high dose), liver dysfunction (requiring liver enzyme monitoring), bone fractures (notably in women), macular oedema, hypoglycaemia when combined with insulin or sulfonylureas, and possible ovulation/pregnancy in PCOS. Metformin is generally safe but carries a rare, serious risk of lactic acidosis, particularly with renal impairment, hypoxia, dehydration, contrast media, surgery, or acute illness; renal function must be monitored regularly, and

metformin temporarily stopped in high-risk situations. Glimepiride mainly risks hypoglycaemia—especially with missed meals, alcohol, renal/hepatic impairment, or in the elderly—requiring regular glucose monitoring, adherence to meals, and caution in G6PD deficiency, with insulin preferred in severe renal or liver disease.

DRUG INTERACTIONS: Pioglitazone has few clinically relevant interactions, but gemfibrozil markedly increases its exposure (↑ adverse effects, dose reduction may be needed) while rifampicin reduces its levels (dose increase may be required), with close glycaemic monitoring in both cases. Metformin should not be used with alcohol, iodinated contrast media, or in situations that impair renal function due to increased lactic acidosis risk and requires temporary discontinuation around contrast studies and caution with hyperglycaemic drugs or loop diuretics. Glimepiride has numerous interactions via CYP2C9, with many drugs and alcohol either increasing hypoglycaemia risk or reducing glycaemic control, beta-blockers masking hypoglycaemia symptoms, and colesevelam reducing absorption—so glimepiride should be taken at least 4 hours before colesevelam and blood glucose monitored closely.

ADVERSE REACTIONS: Upper respiratory tract infection, bronchitis, sinusitis, bladder cancer, anaemia, hypersensitivity, allergic reaction, hypoglycemia, appetite increased, hypo-aesthesia, headache, dizziness, insomania, visual disturbance, macular oedema, vertigo, heart failure, dyspnoea, flatulence, sweating, fracture bone, arthralgia, back pain, haematuria, glycosuria, proteinuria, erectile dysfunction, oedema, fatigue, weight decrease, blood creatine phosphokinase increased, increased lactic dehydrogenase, alanine aminotransferase increased, nausea, vomiting, diarrhoea, abdominal pain, lactic acidosis, taste disturbance, erythema, pruritus, urticaria, thrombocytopenia, leukopenia, granulocytopenia, agranulocytosis, erythropenia, hemolytic anaemia and pancytopenia, blood sodium decrease.

MARKETED BY:

torrent PHARMA

TORRENT PHARMACEUTICALS LTD.

IN/METRIDE PLUS 1,2,15,500mg/SEP-2018/01/ABPI

(Additional information is available on request)