MET-FORTE 850
Metformin Tablets B.P.

COMPOSITION
Each film coated tablet contains Metformin Hydrochloride BP 850mg.

THERAPUTIC CATEGORY
Met-Forte containing Metformin Hydrochloride (1,1-Dimethyl-biguanide hydrochloride) is an oral antihyperglycemic drug used in the management of non-insulin-dependent diabetes mellitus. (type 2 diabetes)

INDICATIONS
Met-Forte tablets, as monotherapy, is indicated as an adjunct to diet to lower blood glucose in patients with type 2 diabetes whose hyperglycemia cannot be satisfactorily managed on diet alone. Metformin Hydrochloride may be used concomitantly with sulfonylurea or insulin to improve glycemic control.

SIDE EFFECTS
Lactic Acidosis : This is very rare but potentially fatal side effect of Metformin which usually occurs when the contraindications to the use of Metformin are not adhered to.
Gastrointestinal Reactions : Gastrointestinal symptoms (diarrhea, nausea, vomiting, abdominal bloating, flatulence and anorexia) are the most common reactions to Metformin. These symptoms are generally transient and resolve spontaneously during continued treatment. Occasionlly, temporary dose reduction may be useful. Because gastrointestinal symptoms during therapy initiation appear to be dose-related, they may be decreased by gradual dose escalaration and by having patients take Metformin with meals. During initiation of Metformin therapy. Approximately 3% of patients may complain of an unpleasant or metalic taste, which usually resolves spontaneously.

CONTRAINDICATIONS
Met-Forte (Metformin Hydrochloride) is contraindicated in patients with:
Renal disease or renal dysfunction (e.g. as suggested by serum creatinine levels $\geq$ 1.5 mg/dL (males), $\geq$ 1.4 mg/dL (females) or abnormal creatinine clearance) which may also result from conditions such as cardiovascular colapse (shock), acute myocardia infraction, and septicemia.
Congestive heart failure requiring pharmacologic treatment.
Metformin should be temporarily discontinued in patients undergoing radiologic studies involving intravascular administration of iodinated contrast materials, because use of such products may result in acute alteration of renal function.
Known hypersensitivity of Metformin Hydrochloride.
Acute or chronic metabolic acidosis, including diabetic ketoacidosis, with or without coma. Diabetic ketoacidosis should be treated with insulin.

WARNINGS and PRECAUTIONS
Lactic Acidosis:
Lactic acidosis is a rare, but serious, metabolic complication that can occur due to Metformin accumulation during treatment with Metformin; when it occurs, it is fatal in approximately 50% of cases. Lactic acidosis is characterized by elevated blood lactate levels (>5 mmol/L), decreased blood pH, electrolyte disturbances with an increased anion gap, and an increased lactate/pyruvate ratio.
The reported incidence of lactic acidosis in patients receiving Metformin is very low (approximately 0.03 cases/1000 patients years). Reported cases have occurred primarily in diabetic patients with significant renal insufficiency, including both intrinsic renal disease and renal hypoperfusion, often in the setting of multiple concomitant medical/surgical problems and multiple concomitant medications.
Patients with congestive heart failure requiring pharmacolgic management, in particular those with unstable or acute congestive heart failure who are at risk of hypoperfusion and hypoxemia are at increased risk of lactic acidosis.
The risk of lactic acidosis increases with the dgree of renal dysfunction and the patients age. The risk of lactic acidosis may, therefore, be significantly decreased by regular monitoring of renal function in patients taking Metformin. Because impaired hepatic function may significantly limit the ability to clear lactate, Metformin should generally be avoided in patients with clinical or laboratory evidence of hepatic disease. Patients should be cautioned against excessive alcohol intake, either acute or chronic, when taking Metformin, since alcohol potentiates the effects of Metformin on lactate metabolism. In addition, Metformin should be temporarily discontinued prior to any intramuscular radiocontrast study and for any surgical procedure. Cardiovascular collapse (shock) from whatever cause, acute

congestive heart failure, acute myocardial infarction and other conditions characterized by hypoxemia have been associated with lactic acidosis and may also cause prerenal azotemia. When such events occur in patients on Metformin therapy, the drug should be promptly discontinued. Lactic acidosis is a medical emergency that must be treated in a hospital setting. In a patient with lactic acidosis who is taking Metformin the drug should be discontinued immediately and general supportive measures promptly instituted. Because Metformin hydrochloride is dialyzable, prompt hemodialysis is recommended to correct the acidosis and remove the accumulated metformin. Such management often results in prompt reversal of symptoms and recovery.

Hypoglycemia:

Hypoglcemia does not occur in patients receiving Metformin alone under usual circumstances of use, but could occur when caloric intake is deficient, when strenuous exercise is not compensated by caloric supplementation, or during concomitant use with other glucose lowering agents (such as sulfonylureas and insulin) or ethanol. Elderly debilitated or malnourished patients, and those with adrenal or pituitary insufficiency or alcohol intoxication are particularly susceptible to hypoglycemic effects. Hypoglycemia may be difficult to recognize in the elderly, and in people who are taking beta-adrenergic blocking drug Loss of control of blood glucose.When a patient stabilized on any diabetic regimen is exposed to stress such as fever, trauma, infection, or surgery,a temporary loss of glycemic control may occur. At such times, it may be necessary to withhold Metformin and temporarily administer insulin. Metformin may be reinstituted after the acute episode is resolved. The effectiveness of oral antidiabetic drugs in lowering blood glucose to a targeted level decreases in many patients over a period of time.

This phenomenon which may be due to progression of the underlying disease or to diminished responsiveness to the drug, is known as secondary failure, to distinguish it from primary failure in which the drug is ineffective during initial therapy. Should secondary failure occur with Metformin or sulfonylurea monotherapy, combined therapy with Metformin and sulfonylurea may result in a response. Should secondary failure occur with combined Metformin/sulfonylurea therapy, it may be necessary to initiate insulin therapy.

DOSAGE and ADMINISTRATION

There is no fixed dosage regimen for the management of hyperglycemia in diabetes mellitus with Metformin. Dosage of Metformin must be individualized on the basis of both effectiveness and tolerance, while not exceeding the maximum recommended daily dose of 2550mg. Metformin should be given in divided doses with meals and should be started at a low dose, with gradual dose escalation, both to reduce gastrointestinal side effects and to permit identification of the minimum required for adequate glycemic control of the patient.

The daily dose of Metformin is 850mg once a day,given with meals. Patients can also be titrated to 850mg twice a day after 2 weeks. For those patients requiring additional glycemic control Metformin may be given to a maximum daily dose of 2550mg per day. Doses above 2000mg may be better tolerated given three times a day with meals.

During treatment initiation and dose titration, fasting plasma glucose should be used to determine the therapeutic response to Metformin. Thereafter glycosylated hemoglobin should be measured at intervals of approximately three months. The therapeutic goal should be to decrease both fasting plasma glucose and glycosylated hemoglobin levels to normal or near normal by using the lowest effective dose of Metformin. Either when used as monotherapy or in combination with sulfonylurea or insulin.

Patients are usually started on 850mg tablet daily taken with the morning or evening meal. The dose is then titrated upward every 1-2 weeks by one tablet/day up to a maximum of 2550mg/day taken in divided doses with food. The dose must be individualized based on the patient response. If the response remains inadequate even at the maximum dose, a sulfonylurea may be gradually added to the regimen.

OVERDOSAGE

Metformin is a dialyzable with a clearance of up to 170ml/min under good hemodynamic conditions. Therefore, hemodialysis may be useful for removal of accumulated drug from patients in whom Metformin overdosage is suspected.

PACKING

Met-Forte 850mg tablet is available in packs of 30.

STORAGE INSTRUCTIONS

Store in a cool dry place, protect from light.

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