**COMPOSITION**

**PHARMACOLOGY**
Metformin is an antihyperglycemic agent that improves glucose tolerance in patients with type 2 diabetes, lowering both basal and postprandial plasma glucose. Metformin decreases hepatic glucose production, decreases intestinal absorption of glucose, and improves insulin sensitivity by increasing peripheral glucose uptake and utilization. Unlike sulfonylureas, Metformin does not produce hypoglycemia in either patients with type 2 diabetes or normal subjects and does not cause hypoinsulinemia.

**INDICATION AND USAGE**
Metformin (Metformin Hydrochloride tablet) is indicated as an adjunct to diet and exercise to improve glycemic control in children and adults with type 2 diabetes mellitus.

**DOSE AND ADMINISTRATION**
Dosage of Comet™ or Comet™ XR must be individualized on the basis of both effectiveness and tolerance, while not exceeding the maximum recommended daily dose. The maximum recommended daily dose of Comet™ or Comet™ XR is 2550 mg in adults and 2000 mg in pediatric patients (10-16 years of age); the maximum recommended daily dose of Comet™ XR is 2000 mg. Comet™ XR should be given in divided doses with meals while Comet™ XR should generally be given once daily with the evening meal. Comet™ XR tablet must be swallowed whole and never be crushed or chewed. Comet™ or Comet™ XR should be started at a low dose, with gradual dose escalation, both to reduce gastrointestinal side effects and to permit identification of the minimum dose required for adequate glycemic control of the patient.

**Recommended Dosing Schedule**

*a) Adults:*
The usual starting dose of Comet™ or Comet™ XR is 500 mg twice a day or 850 mg once a day, given with meals. Dosage increases should be made in increments of 500 mg weekly or 850 mg every 2 weeks, up to a total of 2000 mg per day, given in divided doses. Patients can also be titrated from 500 mg twice a day to 850 mg twice a day after 2 weeks.

Doses above 2000 mg may be better tolerated given three times a day with meals.

The usual starting dose of Comet™ XR is 500 mg once daily with the evening meal. Dosage increases should be made in increments of 500 mg weekly, up to a maximum of 2000 mg once daily with the evening meal. If glycemic control is not achieved on Comet™ XR 2000 mg once daily, a trial of Comet™ XR 1000 mg twice daily should be considered. Patients receiving Comet™ treatment may be safely switched to Comet™ XR once daily at the same total daily dose, up to 2000 mg once daily.

*b) Pediatrics:*
The usual starting dose of Comet™ or Comet™ XR is 500 mg twice a day, given with meals. Dosage increases should be made in increments of 500 mg weekly up to a maximum of 2000 mg per day, given in divided doses. Safety and effectiveness of Comet™ in pediatric patients below 10 years have not been established.

**USE IN PREGNANCY**
Pregnancy Category B. Most experts recommend that insulin should be used during pregnancy to maintain blood glucose levels as close to normal as possible. Both Metformin immediate and extended release tablets should be used during pregnancy unless clearly needed.

**USE IN NURSING MOTHERS**
Because the potential for hypoglycemia in nursing infants may exist, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

**PRECAUTION**
Metformin is known to be substantially excreted by the kidney and the risk of Metformin accumulation and lactic acidosis increases with the degree of impairment of renal function. Thus, patients with serum creatinine levels above the upper limit of normal for their age should not receive Metformin. In patients with advanced age, Metformin should be carefully titrated to establish the minimum dose for adequate glycemic effect, because aging is associated with reduced renal function.

**CONTRAINDICATION**
Metformin is contraindicated in patients with:
1. Renal disease or renal dysfunction (e.g., as suggested by serum creatinine levels > 1.5 mg/dL [males], > 1.4 mg/dL [females] or abnormal creatinine clearance).
2. Known hypersensitivity to Metformin hydrochloride.
3. Acute or chronic diabetic acidosis, including diabetic ketoacidosis, with or without coma.

**ADVERSE EFFECTS**
Diabetes, nausea, vomiting, flatulence, anemia, indigestion, abdominal discomfort, headache, etc.

**WARNINGS**
Lactic acidosis can occur due to Metformin accumulation during treatment with Metformin. The reported incidence of lactic acidosis in patients receiving Metformin is very low.

**DRUG INTERACTION**
No information is available about the interaction of Metformin and furosemide when co-administered chronically. Nifedipine appears to enhance the absorption of Metformin.

**STORAGE**
Store at cool and dry place and keep away from light. Keep out of reach of children.

**HOW SUPPLIED**