PioMet®

Pioglitazone & Metformin Hydrochloride film coated tablet

Description
PioMet® tablets contain two oral antihyperglycemic drugs used in the management of type 2 diabetes: Pioglitazone hydrochloride and Metformin hydrochloride.

Composition
PioMet® is available as a tablet in two-strength: **PioMet®** 500 tab contains 15 mg Pioglitazone as Pioglitazone hydrochloride INN with 500 mg Metformin hydrochloride BP (15 mg/500 mg) and **PioMet®** 850 contains 15 mg Pioglitazone as Pioglitazone hydrochloride INN with 850 mg Metformin hydrochloride BP (15 mg/850 mg).

Indications & Usage
PioMet® is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type2 diabetes who are already treated with a combination of pioglitazone and metformin or whose diabetes is not adequately controlled with metformin alone, or for those patients who have initially responded to pioglitazone alone and require additional glycemic control. Management of type2 diabetes should also include nutritional counseling, weight reduction as needed, and exercise. These efforts are important not only in the primary treatment of type2 diabetes, but also to maintain the efficacy of drug therapy.

Dosage & Administration
General: Maximum recommended daily dose of Pioglitazone 45 mg and Metformin hydrochloride 2550 mg. ***Dosage Recommendations:*** Selecting the starting dose of **PioMet®** should be based on the patient's current regimen of pioglitazone and/or metformin. **PioMet®** should be given in divided daily doses with meals to reduce the gastrointestinal side effects associated with Metformin.

Starting dose for patients inadequately controlled on metformin monotherapy: Based on the usual starting dose of pioglitazone (15-30 mg daily), **PioMet®** may be initiated at either the 15 mg/500 mg (**PioMet®** 500) or 15 mg/850 mg (**PioMet®** 850) tablet strength once or twice daily, and gradually titrated after assessing adequacy of therapeutic response.

Starting dose for patients who initially responded to pioglitazone monotherapy and require additional glycemic control: Based on the usual starting doses of Metformin (500 mg twice daily or 850 mg daily), **PioMet®** may be initiated at either the 15 mg/500 mg (**PioMet®** 500) twice daily or 15 mg/850 mg (**PioMet®** 850) tablet strength once daily, and gradually titrated after assessing adequacy of therapeutic response.

Starting dose for patients switching from combination therapy of pioglitazone plus metformin as separate tablets: **PioMet®** may be initiated with either the 15 mg/500 mg or 15 mg/850 mg tablet strengths based on the dose of pioglitazone and metformin already being taken.

Contraindications
PioMet® (Pioglitazone and Metformin hydrochloride) 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 pioglitazone, metformin.
3. **PioMet®** 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.

Precautions
Pioglitazone exerts its antihyperglycemic effect only in the presence of insulin. Therefore, **PioMet®** should not be used in patients with type1 diabetes or for the treatment of diabetic ketoacidosis. Therapy with combination pioglitazone and metformin should not be initiated if the patient exhibits clinical evidence of active liver disease or the ALT levels exceed 2.5 times the upper limit of normal (ULN). Therapy with combination pioglitazone and metformin should be temporarily discontinued for any major surgical procedure and should not be resumed until the patient's oral intake has resumed and renal function has been evaluated as normal. Combination pioglitazone and metformin therapy should generally be avoided in patients with clinical or laboratory evidence of hepatic disease. The most common adverse events associated with the use of pioglitazone and metformin include upper respiratory tract infection, diarrhea, combined and peripheral edema, and headache. Therapy with combination pioglitazone and metformin should not be initiated if the patient exhibits clinical evidence of active liver disease or the ALT levels exceed 2.5 times the upper limit of normal (ULN). Therapy with combination pioglitazone and metformin should be temporarily discontinued for any major surgical procedure and should not be resumed until the patient's oral intake has resumed and renal function has been evaluated as normal.

Adverse Reactions
The most common adverse events reported in at least 5% of patients in the controlled 16-week clinical trial between placebo plus Metformin and Pioglitazone 30 mg plus Metformin were upper respiratory tract infection, diarrhea, combined edema/peripheral edema and headache. Similar type of adverse events reported in at least 5% of patient in any combined treatment group from the 24-week study comparing pioglitazone 30 mg plus metformin and Pioglitazone 45 mg plus Metformin are shown. Most clinical adverse events were similar between groups treated with pioglitazone in combination with Metformin and those treated with Pioglitazone monotherapy.

Drug Interactions
Pioglitazone hydrochloride:
In vivo drug-drug interaction studies have suggested that Pioglitazone may be a weak inducer of CYP450 isoform 3A4 substrate.
Metformin hydrochloride:
Furosemide, Nifedipine, Cationic drugs (e.g., amiloride, digoxin, morphine, procainamide, quinidine, quinine, ranitidine, triamterene, trimethoprim, and vancomycin) Other: Certain drugs tend to produce hyperglycemia and may lead to loss of glycemic control. These drugs include thiazides and other diuretics, corticosteroids, phenothiazines, thyroid products, estrogens, oral contraceptives, phenytoin, nicotinic acid, sympathomimetics, calcium channel blocking drugs, and isoniazid. Metformin is negligibly bound to plasma proteins and is therefore, less likely to interact with highly protein-bound drugs such as salicylates, sulfonamides, chloramphenicol and probenecid.

Storage
Store at 25˚C (77˚F); excursions permitted to 15˚-30˚C

Commercial pack
Piomet® 500: Box containing 3X10's tablets in blister pack.
Piomet® 850: Box containing 3X10's tablets in blister pack.

Manufactured by :
Silva Pharmaceuticals Limited
Maijdee, Noakhali, Bangladesh