1.3
PRODUCT INFORMATION

1.3.1 SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

Enclosed in the following pages

SUMMARY OF PRODUCT CHARACTERISTICS

1 Name of the medicinal product

Product Name : **PANFOR SR 500 Tablets**
(Metformin Hydrochloride Sustained Release 500 mg)

1.1 Strength : 500 mg

1.2 Pharmaceutical Dosage Form : Oral Tablets

2 Quality and Quantitative composition

Composition :

Sr. No.	Ingredients	Specification	Quantity (mg per tablet)
	Metformin Hydrochloride SR granules 59.88 % w/w		
1.	Metformin Hydrochloride	BP	500.00
2.	Hypromellose (K 100M)	BP/Ph. Eur	75.00
3.	Carboxymethylcellulose Sodium (300 cps) (8M 30)	USP	213.90
4.	Methacrylic Acid and Ethyl Acrylate Copolymer Dispersion	USP-NF	20.00
5.	Polyethylene Glycol 6000	BP/Ph. Eur	4.00
6.	Povidone K90	BP/Ph. Eur	17.10
7.	Magnesium Stearate	BP/Ph. Eur	5.00
8.	^Purified water	USP/Ph. Eur	168.00
	Total Weight		**835.00**

3 Pharmaceutical Form

Oral Tablet

4 Clinical Particulars

4.1 Therapeutic indications

In maturity onset (non-insulin dependent) obese diabetics and juvenile diabetics in whom diet alone has failed as monotherapy or in combination with insulin, glitazones or sulfonylureas. Also as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes.

Glitazones are used in combination with Metformin hydrochloride when glycemic control is poor on Metformin hydrochloride monotherapy and maximum tolerated dose (preferable) of Metformin hydrochloride has been tried. The combination of glitazone plus Metformin hydrochloride is preferred to glitazone plus sulfonylurea, particularly for obese patients.

4.2 Posology and method of administration

Dosage of Panfor SR must be individualized on the basis of both effectiveness and tolerance in patients. The maximum recommended daily dose of 2000 mg should not be exceeded. The drug 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.

During treatment initiation and dose titration, fasting plasma glucose should be used to determine the therapeutic response to the drug and identify the minimum effective dose for the patient. 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.

Short-term administration of the drug may be sufficient during periods of transient loss of blood glucose control in patients usually well-controlled on diet alone.

The usual starting dose of Panfor SR is 500 mg once daily with the evening meal. Dosage increase should be made in increments of 500mg weekly, up to a maximum of 2000mg once daily with the evening meal. If glycemic control is not achieved on 2000mg once daily, trial of 1000mg twice daily should be considered.

The tablet should be swallowed whole and not to be chewed. The tablet should be taken after meals.

4.3 Contraindications

Renal or hepatic failure, alcoholism, NIDDM complicated by severe ketosis and acidosis, diabetic precoma and coma, patients undergoing surgery, after severe trauma or during

infections, chronic obstructive pulmonary disease, coronary heart disease, cardiac failure, peripheral vascular disease, pregnancy, hypoglycemia and know hypersensitivity to Metformin.

4.4 Special warning and precautions for use

Warnings

Lactic acidosis is a rare, but serious metabolic complication that can occur due to Metformin hydrochloride accumulation. The reported incidence of lactic acidosis during Metformin hydrochloride treatment is lower than 0.1 case per 1000 patient years, and the mortality risk is even lower.

Lactic acidosis is a medical emergency that must be treated in a hospital setting. In a patient with lactic acidosis, the drug should be discontinued immediately and general supportive measures promptly instituted.

Precautions

Adjust dose according to blood glucose levels during the first few months.

Lactation: Studies have not been conducted in nursing mothers, but caution should be exercised in such patients, and a decision should be made to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric use: Safety and effectiveness in children has not been established.

Geriatrics: As aging is associated with reduced renal function, care should be taken in dose selection and should be based on careful and regular monitoring of renal functions.

4.5 Interaction with other medicinal products and other forms of interactions

Drug interactions of Metformin hydrochloride is seen with phenprocoumon, hyperglycemic agents (e.g.Thiazides, corticosteroids), alcohol, furosemide, nifedipine and cationic drugs (amiloride, digoxin, morphine, procainamide, quinidine, quinine, ranitidine, triamterene, trimethoprim, cimetidine and vancomycin). Acarbose and guar gum may reduce the absorption of Metformin hydrochloride.

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4.6 Pregnancy and lactation

Pregnancy

Adjust dose according to blood glucose levels during the first few months.

Lactation: Studies have not been conducted in nursing mothers, but caution should be exercised in such patients, and a decision should be made to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

4.7 Effects on ability to drive and use machine

4.8 Undesirable effects

Gastrointestinal disturbances : nausea, diarrhoea, gastric pain, constipation, vomiting, metallic taste in mouth.

Dermatological effects : rash, pruritis, urticaria, erythema and flushing.

Miscellaneous: headache and dizziness. Impaired gastrointestinal absorption of vitamin B12 and folic acid has been associated with long term Metformin hydrochloride therapy.

However if such symptoms occur, please consult with your Physician or pharmacist.

4.9 Management of overdose

Hemodialysis may be useful for removal of accumulating drug from patients in whom Metformin hydrochloride overdosage is suspected.

5 Pharmacological Properties.

5.1 Pharmacodynamic Properties

Metformin hydrochloride is an anti hyperglycemic agent which improves glucose tolerance in NIDDM (type 2 diabetes mellitus) subjects, lowering both basal and postprandial plasma glucose. Its pharmacological mechanisms of action are different from those of sulfonylureas. Metformin decrease hepatic glucose production and improves insulin sensitivity (increases peripheral glucose uptake and utilization). Unlike sulfonylureas, metformin does not produce

hypoglycemia in either diabetic or non diabetic subjects and does not cause hyper insulinemia. With metformin therapy, insulin secretion remains unchanged while fasting insulin levels and day-long plasma insulin levels may actually decrease.

5.2 Pharmacokinetic Properties

Absorption and Bioavailability **:** Following a single oral dose of sustained release Metformin, Cmax is achieved with a median value of 7 hours and a range of 4 hours to 8 hours. After repeated administration of a sustained release formulation, Metformin does not accumulate in plasma. Although the extent of absorption of sustained release Metformin increases by approximately 50% when given with food, there is no effect of food on Cmax and T max of Meformin.

Distribution

The apparent volume of distribution (V/F) of Metformin following single oral doses of 850 mg is 654±375 L. Metformin is negligibly bound to plasma proteins. At usual clinical doses and dosing schedules, steady state plasma concentrations of Metformin are reached within 24-48 hours and are generally < 1 mg/ml.

Metabolism and Elimination

Metformin is excreted unchanged in the urine and does not undergo hepatic metabolism or biliary excretion. Renal clearance is approximately 3.5 times greater than creatinine clearance, which indicates that tubular secretion is the major route of Metformin elimination. Following oral administration, approximately 90% of the absorbed drug is eliminated via the renal route within the first 24 hours, with a plasma elimination half-life of approximately 17.6 hours.

SPECIAL POPULATIONS:

Patients with type 2 *diabetes and Gender:* There are no reported differences in pharmacokinetics of Metformin hydrochloride between patients with type 2 diabetes and normal subjects when analyzed according to gender.

Renal insufficiencv:

In patients with decreased renal function (based on measured creatinine Clearance), the plasma and blood half-life of Metformin Hydrochloride is prolonged and the renal clearance is decreased in proportion to the decrease in creatinine clearance. This increased level may lead to condition of lactic acidosis.

Hepatic insufficiencv:

No pharmacokinetic studies of Metformin hydrochloride have been conducted in patients with hepatic insufficiency.

Geriatrics:

Reported data from controlled pharmacokinetic studies of Metformin hydrochloride in healthy elderly subjects suggest that total plasma clearance is decreased, the half-life is prolonged and Cmax is increased, compared to healthy young subjects. From this data, it appears that the change in Metformin hydrochloride pharmacokinetics with aging is primarily accounted for by a change in renal function.

Pediatrics:

No pharmacokinetic studies of Metformin hydrochloride in pediatric patients have been conducted.

5.3 Preclinical safety Data

Not available

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6 Pharmaceutical Particulars

6.1 List of excipients

Hypromellose (K 100M) BP, Carboxymethylcellulose sodium (KDA 8 M 30) USP, Methacrylic acid copolymer dispersion Drug L 30 NF, Macrogol (PEG 6000) BP, Povidone K 90 BP/Ph.Eur., Magnesium stearate BP.

6.2 Incompatibilities

Not available.

6.3 Shelf-life

36 months

6.4 Special precautions for storage

Store below 25°C. Protect from moisture.

6.5 Nature and contents of container

- 5 blisters of 20 tablets (combipack) in light cardboard carton.

7 Marketing Authorization Holder

MEGA LIFESCIENCES NIGERIA. LTD.

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8. Marketing Authorization Numbers

NAFDAC No. 04-8247

9 Date of first authorization/ renewal of the authorization

June 2016

10 Date of revision of the text

March 2020