1.3.1

Summary of Product Characteristics (SmPC)

1. Name of the medicinal Product

1.1 Name of the medicinal Product

Metformin Hydrochloride Sustained Release Tablets

1.2 Strength

Each Uncoated Sustained Release Tablet contains:

Metformin Hydrochloride BP 1000 mg

Excipients Q.S.

2. Qualitative and Quantitative Composition

2.1 Qualitative Declaration

Metformin Hydrochloride BP

2.2 Quantitative Declaration

Sr. No.	Ingredients	Specifications	Label Claim (mg/tablet)	Function
1	Metformin Hydrochloride	BP	1000.00	Oral Anti-diabetics agent
2	Povidone (PVPK-90)	BP	34.00	Binder
3	Hypromellose (Metolose K-100 M)	BP	300.00	Rate Controlling Polymer
4	Carbomer Homopolymer (Type-A)	USP-NF	105.00	Glidant
5	Purified Talc	BP	3.00	Glidant
6	Magnesium Stearate	BP	15.00	Lubricant
7	Isopropyl Alcohol	BP	520.00	Binding Solvent

3. Pharmaceutical Form

Uncoated Sustained Release Tablet.

White coloured, capsule shaped, uncoated sustained release tablets, plain on one side and embossed “1000” on other side.

4. Clinical Particulars

4.1 Therapeutic Indications

Metformin hydrochloride sustained release tablet is indicated for the management of type 2 diabetes mellitus (noninsulin dependent, NIDDM) as monotherapy when hyperglycemia cannot be managed with diet and exercise alone. In adults, may be used concomitantly with a sulfonylurea or insulin to improve glycaemic control.

4.2 Posology and Method of Administration

Adults: Met form in hydrochloride SR 1000 mg tablet should be taken once daily with evening meal at a maximum recommended dose of 2 tablets per day.

Metformin hydrochloride SR 1000 mg tablet intended for maintenance therapy for patient currently treated with either 1000 mg or 2000 mg of Metformin hydrochloride. On switch, the daily dose of Metformin hydrochloride SR 1000 mg should be equivalent to the current daily dose of Metformin hydrochloride.

For patient new to Metformin hydrochloride SR 1000 mg tablet, the usual starting dose of Metformin SR 500 mg tablet once daily with evening meal. After 10 to 15 days the dose should be adjusted on the basis of blood glucose measurements. A slow increase of dose may improve gastro-intestinal tolerability.

If glycemic control not achieved on once daily dosing of Metformin SR 1000 mg tablet, then twice daily should be considered, with both doses being given with food. If glycemic control is still not achieved, patient may be switched to standard metformin tablets to maximum dose of 3000 mg daily.

Metformin 1000 mg SR tablet is intended for patients who are already treated with metformin tablets (prolonged or immediate release).

Elderly: Due to potential for decreased renal function in elderly subjects, the maximum dose should be adjusted based on renal function.

Pediatrics: It should not be used in children.

4.3 Contraindications

Metformin hydrochloride tablets are contraindicated for patient with:

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), which may also result from conditions such as cardiovascular collapse (shock), acute myocardial infarction, and septicemia.

Known hypersensitivity to Metformin, or any of the ingredients of the Metformin Hydrochloride tablets.

Acute or chronic metabolic acidosis, including diabetic ketoacidosis, with or without coma. Diabetic ketoacidosis should be treated with insulin.

Temporarily discontinue in patients undergoing radiologic studies in which intravascular iodinated contrast media arc utilized, because use of such products may result in acute alteration of renal function.

4.4 Special Warnings and Special Precautions for Use

Use Metformin hydrochloride with caution in patients with Cardiovascular mortality as oral hypoglycemic drugs may be associated with an increased cardiovascular mortality as compared to treatment with diet alone or diet plus insulin.

Lactic acidosis is a rare, but potentially severe consequence of therapy with Metformin.

Hepatic impairment: Avoid use in patients with impaired liver function due to potential for lactic acidosis.

Renal impairment: Metformin is substantially excreted by the kidney; patients with renal function below the limit of normal for their age should not receive therapy.

Elderly: Metformin should not be initiated in patient > 80 years of age unless normal renal function is confirmed.

Stress-related States: It may be necessary to discontinue Metformin and administer insulin if the patient is exposed to stress (fever, trauma, infection, surgery).

Pregnancy: Available information suggests that Metformin use during pregnancy may be safe as long as good glycaemic control is maintained. Metformin Hydrochloride is prescribed unlabeled for the treatment of Gestational diabetes mellitus (GDM); polycystic ovary syndrome (PCOS). However the use of oral agents is generally not recommended as routine management of GDM or type 2 diabetes mellitus during pregnancy. Metformin hydrochloride tablets should not be used unless the potential benefit outweighs the potential risk to fetus.

Lactation: Metformin Hydrochloride tablet is not recommended for use in lactating mothers as it excretes into breast milk.

4.5 Interaction with other medicinal products and other forms of interaction

Amiloride, Digoxin, Morphine, Procainamide, Quinidine, Quinine, Ranitidine, Triamterene, Vancomycin: Compete with Metformin hydrochloride for substantial tubular secretion.

ACE inhibitors: Potential risk of hypoglycemial hyperglycemia when ACE inhibitor therapy is initiated/withdrawn.

Calcium-channel blocking agents, corticosteroids, thiazide diuretics, estrogens and progestins (e.g., oral contraceptives), isoniazid, niacin, phenothiazines, sympathomimetic agents (e.g., albuterol, epinephrine, terbutaline): Antagonize hypoglycemic effects of metformin hydrochloride.

Alcohol: Increased risk of hypoglycemia and lactic acidosis.

Adrenergic blocking agents: Impaired glucose tolerance; Increased frequency or severity of hypoglycemia and hypoglycemia induced complications.

Cimetidine: Possible decreased excretion of metformin hydrochloride.

Clomiphene: Possible resumption of ovulation in premenopausal patients with polycystic ovary syndrome.

Furosemide: Increased plasma concentrations of metformin and furosemide.

Glyburide: Possible resumption of ovulation in premenopausal patients with polycystic ovary syndrome.

Nifedipine: Enhanced absorption and increased urinary excretion of metformin.

Thiazide diuretics: May exacerbate diabetes mellitus.

4.6 Fertility, Pregnancy and Lactation

Pregnancy: Available information suggests that Metformin use during pregnancy may be safe as long as good glycaemic control is maintained. Metformin Hydrochloride is prescribed unlabeled for the treatment of Gestational diabetes mellitus (GDM); polycystic ovary syndrome (PCOS). However the use of oral agents is generally not recommended as routine management of GDM or type 2 diabetes mellitus during pregnancy. Metformin hydrochloride tablets should not be used unless the potential benefit outweighs the potential risk to fetus.

Lactation: Metformin Hydrochloride tablet is not recommended for use in lactating mothers as it excretes into breast milk.

4.7 Effects on ability To Drive and use Machines

No studies on the effects on the ability to drive and use machines have been performed.

4.8 Undesirable Effects

Gastrointestinal: Diarrhea, nausea, vomiting, flatulence indigestion, abdominal discomfort , abdominal distention, abnormal stools, constipation, dyspepsia/heartburn, taste disorder.

New-muscular & Skeletal: Weakness, Myalgia.

Cardiovascular: Chest discomfort, flushing, palpitation.

Central Nervous System: Headache, chills, dizziness, lightheadedness.

Dermatologic: Rash

Endocrine& metabolic: Hypoglycemia

Respiratory: Dyspnea, upper respiratory tract infection.

Miscellaneous: Diaphoresis increased, vitamin B 121cvelsdecreased, nu-like syndrome, nail disorder

4.9 Overdose

Mild hypoglycemic symptoms without loss of consciousness or neurologic findings should be treated aggressively with oral glucose and adjustments in drug dosage and/or meal patterns. Close monitoring should continue until the physician is assured that the patient is out of danger. Severe hypoglycemic reactions with coma, seizure, or other neurological impairment occur infrequently, but constitute medical emergencies requiring immediate hospitalization. If hypoglycemic coma is diagnosed or suspected, the patient should be given a rapid IV injection of concentrated (50%) glucose solution.

This should be followed by a continuous infusion of a more dilute (10%) glucose solution at a rate that will maintain the blood glucose level above 100 mg/dL. Patients should be closely monitored for a minimum of 24 to 48 hours, because hypoglycemia may recur after apparent clinical recovery.

Lactic acidosis is a rare, but serious, metabolic complication that can occur if Metformin accumulates during treatment due to overdosing. Strict monitoring should be continued until the doctor is sure that the patient is out of danger.

5.0 Pharmacological Properties

5.1 Pharmacodynamics Properties

Oral Anti-diabetic Agent

Metformin hydrochloride decreases hepatic glucose production, decreasing intestinal absorption of glucose and improves insulin sensitivity (increases peripheral glucose uptake and utilization).

5.2 Pharmacokinetic Properties

Absorption: After an oral dose of prolonged release tablet, metformin absorption is significantly delayed compared to immediate release tablet with a T max 7 hours (T max for the immediate release tablet is 2.5 hours). Mean metforrnin absorption from the prolonged release formulation is not altered by meal composition.

Distribution: Plasma protein binding is negligible. Metforrnin partitions into erythrocytes. The blood peak plasma lowers than the plasma peak and appears at the approximately same time. The red blood cells most likely represent a secondary compartment of distribution.

Metabolism: Metformin is excreted unchanged in the urine. No metabolites have been identified in humans.

Excretion: Renal clearance of metformin is >400 ml/min, indicating that metformin is eliminated by glomerular filtration and tubular secretion. Following an oral dose the apparent terminal elimination half-life is approximately 6.5 hours.

When renal function is impaired, renal clearance is decreased in proportion to that of creatinine and thus the elimination half-life is prolonged leading to increase the level of metformin in plasma.

5.3 Preclinical Safety Data

Not Applicable

6 Pharmaceutical Particulars

6.1 List of Excipients

Povidone (PVPK-30) BP

Hypromellose (Metolose K- 100 M) BP

Carbomer Homopolymer (Type-A) USP-NF

Purified Talc BP

Magnesium Stearate BP

Purified Water BP

6.2 Incompatibilities

None.

6.3 Shelf Life

36 months

6.4 Special Precautions for Storage

Store below 30^0C. Protect from light.

6.5 Nature and Contents of Container

White coloured, capsule shaped, uncoated sustained release tablets, plain on one side and embossed “1000” on other side. 10 tablets are packed in Alu-PVC blister pack. 3 blisters are packed in printed carton along with packaging insert.

6.6 Special precaution for disposal and other handling

Any unused product or waste material should be disposed of in accordance with local requirements.

7. Registrant (Marketing Authorization Holder And Manufacturing Site Addresses)

7.1 Name and Address of Marketing Authorization Holder

GENERICS AND SPECIALITIES LTD.

31, AWONIYI ELEMO STREET,

OFF LATEEF SALAMI STREET.

AJAO ESTATE, LAGOS,

NIGERIA.

E-mail: info@zolonhealthcare.com

7.2 Name and Address of manufacturing site(s)

Lincoln Pharmaceuticals Limited

Trimul Estate, Khatraj, Taluka: Kalol,

District: Gandhinagar Gujarat, India.

Telephone no.: +91-07949-135000

Fax: +91-07941-078062

Email: info@lincolnpharma.com

Website: www.lincolnpharma.com

7.3 Marketing Authorization Number

To be included after obtaining first registration.

7.4 Date of First <Registration> / Renewal of The <Registration>

It will be applicable after registration of this product.

8. Date of Revision of the Text

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9. Dosimetry (If Applicable)

Not Applicable

10. Instructions for preparation of radiopharmaceuticals (if Applicable)

Not Applicable