AUSTRALIAN PRODUCT INFORMATION
NOUMED METFORMIN (METFORMIN HYDROCHLORIDE) TABLET

Life-threatening lactic acidosis can occur due to accumulation of metformin. Risk factors include renal impairment, old age and the use of high doses of metformin above 2g/day.

1 NAME OF THE MEDICINE

Metformin Hydrochloride.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Noumed Metformin tablet contains 1000 mg metformin hydrochloride.

For the full list of excipients see section **6.1 List of Excipients**

3 PHARMACEUTICAL FORM

Film-coated tablet

Noumed Metformin 1000 mg: white, film-coated, capsule-shaped, biconvex tablet plain on one side and a central breakline on the other.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Metformin is indicated in the treatment of type 2 diabetes mellitus in adults, particularly in overweight patients, when dietary management and exercise alone, does not result in adequate glycaemic control. It may he used as initial treatment. or in sulphonyl urea failures, either alone or in combination with a sulphonylurea and other oral agents or as adjuvant therapy in insulin dependent diabetes.

4.2 DOSE AND METHOD OF ADMINISTRATION

Dosage

Life threatening lactic acidosis can occur due to accumulation of metformin. Risk factors include renal impairment, old age and the use of high doses of metformin above 2 g per day.

Initially 500 mg should be taken once or twice a day and, if necessary, increased over a few weeks up to 1 g three times per day. 500 mg strengths are also available in this brand.

Method of administration

It is important that the tablets are taken in divided doses with meals.

The dose should be titrated with gradual dose increments until the desired effect is obtained. 500 mg three times a day is often sufficient to obtain diabetic control. If necessary, the dose can be increased to 1 g three times daily, which is the maximum recommended daily dose. Control may be attained within a few days but occasionally requires up to two weeks. Once control has been obtained, the dosage should be reviewed and reduced to the lowest maintenance level consistent with good diabetic control. If dose titration has been achieved with one tablet strength, then the patient's response should be reassessed if a different strength or dose schedule is commenced.

Metformin dosage should be frequently reviewed in patients stabilised on metformin, especially if they develop an illness, as they may tolerate the drug less well, particularly if the illness is accompanied by a decrease in renal function. If necessary, metformin should be ceased for a few days during an illness and then restarted at low dosage, as for initial therapy.

The action of metformin is progressive and no final assessment of the patient's real response should be made before the 21st day of treatment. Blood sugar estimations are recommended during the initial 15 days of stabilisation.

Metformin will not produce a hypoglycaemic state when used alone; however, due to its action in increasing insulin effectiveness, care must be taken when metformin is initially administered with parenteral doses of insulin.

Use in the elderly. The initial and maintenance dosing of metformin should be conservative in elderly patients, due to the potential for decreased renal function in this population. Any dosage adjustment should be based on a careful assessment of renal function. Generally, elderly patients should not be titrated to the maximum dose of metformin.

Use in debilitated or malnourished patients.

The dosing should be conservative and based on a careful assessment of renal function.

4.3 CONTRAINDICATIONS

Juvenile diabetes mellitus that is uncomplicated and well regulated on insulin

- Diabetes mellitus regulated by diet alone
- During or immediately following surgery where insulin is essential
- Hypersensitivity to metformin hydrochloride or to any of the excipients
- Any type of metabolic acidosis (such as lactic acidosis, diabetic ketoacidosis),
- diabetic pre-coma
- Renal failure or renal dysfunction (creatinine clearance< 60 mL/min)
- Acute conditions with the potential to alter renal function such as:
    - Dehydration

    - Severe infection
    - Shock
    - Intravascular administration of iodinated contrast agents
- Acute or chronic disease which may cause tissue hypoxia such as:
    - Cardiac failure
    - Recent myocardial infarction
    - Respiratory failure
    - Pulmonary embolism
    - Shock
    - Acute significant blood loss
    - Sepsis
    - Gangrene
    - Pancreatitis
- Elective major surgery (see Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE)
- Severe hepatic insufficiency
    - acute alcohol intoxication
    - alcoholism
- Lactation

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Lactic acidosis.

Lactic acidosis is a rare but serious (high mortality in the absence of prompt treatment), metabolic complication that can occur due to metformin accumulation. Reported cases of lactic acidosis in patients on metformin have occurred primarily in diabetic patients with significant renal failure. The incidence of lactic acidosis can and should be reduced by assessing other associated risk factors such as poorly controlled diabetes, ketosis, prolonged fasting, excessive alcohol intake, hepatic insufficiency and any condition associated with hypoxia.

Diagnosis

The risk of lactic acidosis must be considered in the event of non-specific signs such as muscle cramps with digestive disorders such as abdominal pain and severe asthenia. Lactic acidosis is characterised by acidotic dyspnea, abdominal pain and hypothermia followed by coma. Diagnostic laboratory findings are decreased blood pH, plasma lactate levels above 5 mmol/L, and an increased anion gap and lactate/pyruvate ratio. If metabolic acidosis is suspected, metformin should be discontinued and the patient should be hospitalised immediately (**see Section 4.9 OVERDOSE - Treatment**).

Renal function

As metformin hydrochloride is excreted by the kidney, it is recommended that creatinine clearance and/or serum creatinine levels be determined before initiating treatment and regularly thereafter:

• At least annually in patients with normal renal function,
• At least two to four times a year in patients with serum creatinine levels at the upper limit of normal and in elderly subjects.

Decreased renal function in elderly subjects is frequent and asymptomatic. Special caution should be exercised in situations where renal function may become impaired, for example when initiating antihypertensive therapy or diuretic therapy and when starting therapy with a non-steroidal anti-inflammatory drug (NSAID).

Hypoglycaemia

Hypoglycaemia does not occur in patients receiving metformin hydrochloride alone under usual circumstances of use, but could occur when calorie intake is deficient, when strenuous exercise is not compensated by calorie supplementation, or during concomitant use with other glucose-lowering agents(such as sulphonylureas) or ethanol.

Elderly, debilitated or malnourished patients and those with adrenal pituitary insufficiency or alcohol intoxication are particularly susceptible to hypoglycaemic effects.

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 a 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 HCl or sulphonylurea monotherapy, combined therapy with metformin HCI and sulphonylurea may result in a response. Should secondary failure occur with combined metformin HCI /sulphonylurea therapy, it may be necessary to initiate insulin therapy.

Metformin HCI alone does not usually cause hypoglycaemia, although it may occur when metformin HCl is used in conjunction with oral sulphonylureas. When initiating combination therapy, the risks of hypoglycaemia, its symptoms and treatment, and conditions that predispose to its development should be explained to patients.

Administration of iodinated contrast materials.

Radiological studies involving the use of intravascular iodinated contrast materials (for example intravenous urogram, intravenous cholangiography, angiography, any computed tomography scans with intravascular contrast materials) can lead to acute alteration of renal function and have been associated with lactic acidosis in patients receiving metformin. Therefore, in patients with normal renal function, metformin should be stopped at the time of the study and not recommenced for 48 hours and only after renal function has been reevaluated and found to be normal.

Alcohol use. Alcohol is known to potentiate the effects of metformin on lactate metabolism. Patients should therefore be warned against excessive alcohol intake, acute or chronic, while taking metformin.

Assessment. The risk of lactic acidosis must be considered in the event of nonspecific signs such as muscle cramps with digestive disorders such as abdominal pain and severe asthenia.

Periodic assessment of renal, hepatic and cardiovascular function is recommended during prolonged periods of treatment with metformin. Patients receiving continuous metformin therapy should have an annual estimation of Vitamin B12 levels because of reports of decreased vitamin B_{12} absorption.

Surgery

Metformin hydrochloride must be discontinued 48 hours before elective major surgery. Therapy may be restarted no earlier than 48 hours following surgery and only after renal function has been re-evaluated and found to be normal.

Impaired hepatic function

Since impaired hepatic function has been associated with some cases of lactic acidosis, metformin should be avoided in patients with clinical or laboratory evidence of hepatic disease.

Radiological studies involving the use of intravascular iodinated contrast materials (for example intravenous urogram, intravenous cholangiography, angiography, any computed tomography scans with intravascular contrast materials) can lead to acute alteration of renal function and have been associated with lactic acidosis in patients receiving metformin.

Periodic assessment of renal, hepatic and cardiovascular function is recommended during prolonged periods of treatment with metformin. Patients receiving continuous metformin therapy should have an annual estimation of Vitamin B12 levels because of reports of decreased vitamin B12 absorption.

Use in the elderly.

The risk of lactic acidosis, in association with metformin, is increased in elderly patients on long-term therapy due to the physiological alteration of the renal function and the possible accumulation of metformin. Metformin may be used in the elderly if Contraindications and Precautions are respected, the dosage is frequently reviewed and renal function monitored. Decreased renal function in elderly subjects is frequent and asymptomatic. Special caution should be exercised in situations where renal function may become impaired.

Paediatric use.

Metformin is not recommended for use in children except those with insulin resistant diabetes who are being treated in hospital.

Effects on Laboratory Tests

No information is available.

4.5. INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Contraindicated combinations

Iodinated contrast materials

Metformin must be discontinued either 48 hours before the test when renal function is known to be impaired, or from the time of the test when renal function is known to be normal (**see Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE - Administration of iodinated contrast materials**).

Inadvisable Combinations

Combinations requiring precautions for use

Calcium channel blockers

Calcium channel blockers may affect glucose control in diabetic patients; regular monitoring of glycaemic control is recommended.

Beta-blockers

Coadministration of metformin and β-blockers may result in a potentiation of the anti hyperglycaemic action. In addition, some of the premonitory signs of hypoglycaemia, in particular tachycardia may be masked. Monitoring of blood glucose should be undertaken during dosage adjustment of either agent.

Cimetidine

Reduced clearance of metformin has been reported during cimetidine therapy, so a dose reduction should be considered. Other cationic drugs such as amiloride, digoxin, morphine, procainamide, quinidine, quinine, ranitidine, triamterene, trimethoprim, and vancomycin are eliminated by renal tubular secretion and theoretically have the potential to compete for common renal tubular transport systems with metformin. Careful patient monitoring is recommended in situations where cationic medications which are excreted via the proximal renal tubular secretory system are coadministered with metformin.

Anticoagulants

Metformin increased the elimination rate of vitamin K antagonists. Consequently, the prothrombin time should be closely monitored in patients in whom metformin and vitamin K antagonists are being coadministered. Cessation of metformin in patients receiving vitamin K antagonists can cause marked increases in the prothrombin time.

Nifedipine

A single dose metformin-nifedipine drug interaction study in normal healthy volunteers demonstrated that co-administration of metformin and nifedipine increased plasma metformin C_{max} and AUC by 20 and 9% respectively, and increased the amount of metformin excreted in the urine. T_{max} and half life of metformin were unaffected. Nifedipine appears to enhance the absorption of metformin. Metformin had minimal effects on the pharmacokinetics of nifedipine.

Organic cation transporters (OCT):

Metformin is a substrate of both transporters OCT1 and OCT2.

Co-administration of metformin with:

• Substrates/inhibitors of OCT1 (such as verapamil) may reduce efficacy of metformin.
• Inducers of OCT1 (such as rifampicin) may increase gastrointestinal absorption and efficacy.
• Substrates/inhibitors of OCT2 (such as cimetidine, dolutegravir, crizotinib, olaparib, daclatasvir, vandetanib) may decrease the renal elimination of metformin and thus lead to an increase metformin plasma concentration.

Carbonic anhydrase inhibitors:

Topiramate or other carbonic anhydrase inhibitors (e.g., zonisamide, acetazolamide or dichlorphenamide) frequently cause a decrease in serum bicarbonate and induce non-anion gap, hyperchloremic metabolic acidosis. Concomitant use of these drugs with Metformin hydrochloride tablet may increase the risk for lactic acidosis. Consider more frequent monitoring of these patients.

NSAID:

May increase the risk of lactic acidosis and adversely affect renal function.

Therefore, caution is advised when these drugs are co-administered with metformin and a dose adjustment may be considered, particularly in patients with renal impairment.

ACE inhibitors

Coadministration of metformin and ACE inhibitors may result in a potentiation of the antihyperglycaemic action. Monitoring of blood glucose should be undertaken during dosage adjustment of either agent.

Alcohol

Alcohol may make the signs of hypoglycaemia less clear and delayed hypoglycaemia may occur. The CNS depressant effects of alcohol plus hypoglycaemia can make driving or the operation of dangerous machinery much more hazardous. There is increased risk of lactic

acidosis in acute alcohol intoxication, particularly with fasting, malnutrition or hepatic insufficiency.

Thiazide diuretics

Thiazide therapy may impair glucose tolerance. Dosage adjustment of metformin may be required.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility.

Fertility of male or female rats was unaffected by metformin administration at doses up to 600 mg/kg/day, or approximately twice the maximum recommended daily dose on a body surface area basis.

Use in pregnancy

(Category C) It is important to achieve strict normoglycaemia during pregnancy. Oral hypoglycaemic agents should be replaced by insulin.

Metformin was not teratogenic in rats and rabbits at doses up to 600 mg/kg/day, or about two times the maximum recommended human daily dose on a body surface area basis. Determination of fetal concentrations demonstrated a partial placental barrier to metformin. Because animal reproduction studies are not always predictive of human response, any decision to use this drug should be balanced against the benefits and risks. The safety of metformin in pregnant women has not been established.

Australian Categorisation Definition of Category C: Drugs which, owing to their pharmacological effects, have caused or may be suspected of causing, harmful effects on the human fetus or neonate without causing malformations. These effects may be reversible. Accompanying texts should be consulted for further details. Recent information suggests that abnormal blood glucose levels during pregnancy are associated with a higher incidence of congenital abnormalities. Oral hypoglycaemics may enter the fetal circulation and cause neonatal hypoglycaemia. There is a consensus among experts that insulin be used during pregnancy to maintain blood glucose levels as close to normal as possible.

Use in lactation.

Studies in lactating rats show that metformin is excreted into milk and reaches levels comparable to those in plasma. Similar studies have not been conducted in nursing mothers, but caution should be exercised in such patients, and 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.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Metformin monotherapy does not cause hypoglycaemia and therefore has no effect on the ability to drive or to use machinery.

However, patients should be alerted to the risk of hypoglycaemia when metformin is used in combination with other antidiabetic agents (sulphonylureas, glinides, insulin).

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

The following undesirable effects may occur under treatment with metformin hydrochloride. Frequencies are defined as follows: very common: >1/10; common >1/100, <1/10; uncommon >1/1,000, <1/100; rare >1/10,000, <1/1,000; very rare <1/10,000; not known (cannot be estimated from the available data).

Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Nervous system disorders

Common: Taste disturbance.

Gastrointestinal disorders –

Very common**:** Mild gastrointestinal symptoms (such as diarrhoea, nausea, vomiting, abdominal pain and loss of appetite) are most frequent reactions to metformin (> 1/10), especially during the initial treatment period. These symptoms are generally transient and resolve spontaneously during continued treatment. Gastrointestinal symptoms can possibly be avoided if metformin is taken with meals and the dose is increased slowly. Occasionally a temporary dose reduction can be considered. Occurrence of gastrointestinal symptoms, once a patient is stabilised on any dose of metformin could be due to lactic acidosis or other serious disease.

Metabolism and nutrition disorders –

Very rare.

Lactic acidosis (see **Section 4.4 SPECIAL WARNING AND PRECAUTIONS FOR USE**) is a very rare (< 1/10000) but serious metabolic complication that can occur due to metformin accumulation during treatment with metformin.

The onset of lactic acidosis is often subtle and accompanied by non specific symptoms such as malaise, myalgia, respiratory distress, increasing somnolence and non specific abdominal distress. There may be associated hypothermia, hypotension and resistant bradyarrhythmias with more marked acidosis.

The patient and the patients doctor must be aware of the possible importance of such symptoms and the patient should be instructed to notify the doctor immediately if they occur. Lactic acidosis should be suspected in any diabetic patient with metabolic acidosis lacking evidence of ketoacidosis (ketonuria and ketonaemia). Lactic acidosis is a medical emergency that must be

treated in hospital. In a patient with lactic acidosis who is taking metformin, the drug should be discontinued immediately and general supportive measures should be instituted promptly.

A decrease of Vitamin B12 absorption with a decrease in serum levels has been observed in patients treated long term with metformin, and appears to be generally without clinical significance'(<1/10000). Therefore, serum B12 levels should be appropriately monitored (annually) or periodic parenteral B12 supplementation considered. Initial and periodic monitoring of haematological parameters (e.g. haemoglobin / haematocrit and red blood cell indices) should be performed at least on an annual basis.

Skin and subcutaneous tissue disorders-

Mild erythema, pruritus and urticaria has been reported in some hypersensitive individuals, but the incidence is very rare. (< 1/10,000)

Hepatobiliary Disorders

Very rare: Isolated reports of liver function test abnormalities or hepatitis resolving upon metformin discontinuation.

In clinical trials in children and adolescents with type 2 diabetes, the profile of adverse reactions was similar to that observed in adults.

Reporting suspected adverse effects.

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

Symptoms

Hypoglycaemia has not been seen with ingestion of up to 85 g of metformin alone, although lactic acidosis has occurred in such circumstances. This disorder is a medical emergency and must be treated in hospital. The onset of lactic acidosis is often subtle and accompanied only by non-specific symptoms such as malaise, myalgia, respiratory distress, increasing somnolence and non-specific abdominal distress. There may be associated hypothermia, hypotension and resistant bradyarrhythmias with more marked acidosis. Lactic acidosis should be suspected in any diabetic patient with metabolic acidosis lacking evidence of ketoacidosis, such as ketonuria and ketonaemia).

Treatment –

Lactic acidosis should be feared in diabetic metformin treated patients with overdose. Lactic acidosis is diagnosed and monitored by measuring serum electrolytes, arterial pH and pCO_2 and arterial lactate plasma level.

The aim of treatment is to manage any underlying disorder and in some cases, this will be sufficient to enable the body's homeostatic mechanism to correct the acid-base imbalance. The advantages of more active treatment of the acidosis must be balanced against the risks, including over-alkalinisation with sodium bicarbonate. Because metformin hydrochloride is dialysable (with a clearance of up to 170 mL/min under good haemodynamic conditions), prompt haemodialysis is recommended to correct the acidosis and remove the accumulated metformin

For information on the management of overdose, contact the Poison Information Centre on 131126 (Australia).

5. PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

Metformin is an antihyperglycaemic agent which improves glucose tolerance in NIDDM subjects lowering both basal and post-prandial plasma glucose. Metformin causes an increased peripheral uptake of glucose by increasing the biological efficiency of available exogenous or endogenous insulin. The mode of action of metformin may be linked to increased insulin sensitivity; it does not stimulate insulin release but does require the presence of insulin to exert its antihyperglycaemic effect. Possible mechanisms of action include inhibition of gluconeogenesis in the liver, delay in glucose absorption from the gastrointestinal tract and an increase in peripheral uptake of glucose.

Metformin has an antiketogenic activity which is comparable, though somewhat inferior to insulin itself. Metformin has a modest favourable effect on serum lipids, which are often abnormal in NIDDM patients.

Clinical trials

The prospective randomised (UKPDS) study has established the long-term benefit of intensive blood glucose control in type 2 diabetes. Analysis of the results for overweight patients treated with metformin after failure of diet alone showed:

- a significant reduction of the absolute risk of any diabetes-related complication in the metformin group (29.8 events/1000 patient-years) versus diet alone (43.3 events/1000 patient-years), p = 0.0023, and versus the combined sulfonylurea and insulin monotherapy groups (40.1 events/1000 patient-years), p=0.0034.
- a significant reduction of the absolute risk of diabetes-related mortality: metformin 7.5 events/1000 patient-years, diet alone 12.7 events/1000 patient-years, p = 0.017

- a significant reduction of the absolute risk of overall mortality: metformin 13.5 events/1000 patient-years versus diet alone 20.6 events/1000 patient-years (p = 0.011), and versus the combined sulfonylurea and insulin monotherapy groups 18.9 events/1000 patient-years (p = 0.021);
- a significant reduction in the absolute risk of myocardial infarction: metformin 11 events/1000 patient-years, diet alone 18 events/1000 patient-years (p = 0.01)

5.2 PHARMACOKINETIC PROPERTIES

Absorption.

A randomised, open, balanced, crossover bioequivalence study using Formin tablets 500 mg filmcoated tablets in 26 healthy subjects showed that peak plasma concentrations occurred at between 2 to 3 hours after a single dose of 500 mg. The mean peak plasma concentration was 0.721 mg/mL for the test product. Metformin was detected in plasma for 36 hours post dose in all subjects. The T_{max} values were comparable for both reference and test formulations. The 90% confidence limit for AUC_{0-t} and $AUC_{0-\infty}$ (as a measure of the extent of absorption) of the test product Formin tablets (Metformin-GA 500 mg) compared to the reference product (metformin 500 mg Diabex Alphapharm) was within acceptable limits. No adverse events were reported.

In a bioequivalence study comparing Metformin-GA 1 g tablets with the reference product (Diabex 1 g tablets), the mean C_{max} was 1.4 µg/mL of the test product and 1.5 µg/mL for the reference. The mean Tmax, AUC_{0-t} and $AUC_{0-\infty}$ were comparable for both products and the 90% confidence intervals were within the limits required to demonstrate bioequivalence.

After oral administration, metformin hydrochloride is absorbed along the entire gastrointestinal mucosa. Studies using single oral doses of metformin tablets indicate that there is a lack of dose proportionality with increasing doses, which is due to decreased absorption rather than increase in elimination. At usual clinical doses and dosing schedules of metformin tablets, steady state plasma concentrations are reached in 24 to 48 hours and are generally less than 1 microgram/mL. Food decreases the extent and slightly delays the absorption of metformin. However the clinical relevance of this is unknown. During controlled clinical trials, maximum metformin plasma levels did not generally exceed 5 micrograms/mL even at maximum doses.

Distribution.

Metformin is negligibly bound to plasma proteins.

Metabolism.

Metformin is excreted unchanged in the urine and does not undergo hepatic metabolism.

Excretion.

In patients with decreased renal function (based on measured creatinine clearance), the plasma half-life of metformin is prolonged and renal clearance is decreased in proportion to the decrease

in creatinine clearance, e.g. if creatinine clearance is 10-30 mL/min, renal clearance is reduced to 20% of normal. No pharmacokinetic data are available for hepatic insufficiency.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity. No evidence of a mutagenic potential of metformin was found in the Ames test *(S.* typhimurium), gene mutation test (mouse lymphoma cells), chromosomal aberrations test (human lymphocytes) or in vivo micronuclei formation test (mouse bone marrow).

Carcinogenicity. Long-term carcinogenicity studies have been performed in rats (dosing duration of 104 weeks) and mice (dosing duration of 91 weeks) at doses up to and including 900 mg/kg/day and 1,500 mg/kg/day, respectively. These doses are both approximately two to three times the recommended human daily dose on a body surface area basis. No evidence of carcinogenicity with metformin was found in either male or female mice. Similarly, there was no tumourigenic potential observed with metformin in male rats. However, an increased incidence of benign stromal uterine polyps was seen in female rats treated with 900 mg/kg/day.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Noumed Metformin 1000 mg tablet contains Sodium starch glycollate, maize starch, povidone, colloidal anhydrous silica, magnesium stearate, hypromellose, titanium dioxide, propylene glycol, Macrogol 6000 and purified talc.

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 25°C**.**

6.5 NATURE AND CONTENTS OF CONTAINER

Noumed Metformin 1000 mg is available in PVC/PE/PVDC/Al blister packs of 10, 30, 60 and 90 tablets.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical structure

Metformin hydrochloride

Metformin hydrochloride is a white, crystalline powder which is odourless or almost odourless and hygroscopic. It is freely soluble in water, slightly soluble in ethanol (96%), and practically insoluble in chloroform and in ether.

Chemical Name: 1,1-dimethylbiguanide hydrochloride.

Molecular formula: $C_4H_{11}N_5$,HCl.

Molecular weight: 165.6

CAS number

1115-70-4

7 MEDICINE SCHEDULE (POISONS STANDARD)

S4 – Prescription Only Medicine

8 SPONSOR

Cipla Australia Pty Ltd
Level 1, 132-136 Albert Road
South Melbourne, Vic, 3205
Phone: 1 800 569 074
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Supplier:
Noumed Pharmaceuticals
Adelaide, South Australia
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9 DATE OF FIRST APPROVAL

07.02.2023

10 DATE OF REVISION

TBA

Summary table of changes

Section Changed	Summary of new information
N/A	N/A