AUSTRALIAN PRODUCT INFORMATION – FORMET (METFORMIN HYDROCHLORIDE) TABLETS

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.

1 NAME OF THE MEDICINE

Metformin hydrochloride.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

FORMET tablets come in four strengths:

FORMET 250 contains 250 mg metformin hydrochloride.

FORMET 500 contains 500 mg metformin hydrochloride.

FORMET 850 contains 850 mg metformin hydrochloride.

FORMET 1000 contains 1000 mg metformin hydrochloride.

The tablets are gluten free.

For the full list of excipients, see Section 6.1 List of excipients.

3 PHARMACEUTICAL FORM

Film-coated tablets:

FORMET 250	round, white tablet (approx. 9mm), embossed with MO on one side and the Arrow symbol, “>” on the other.
FORMET 500	oblong, white film-coated tablet, embossed with M | O on one side and the Arrow symbol, “>” on the other.
FORMET 850	round, white film-coated tablet (approx. 13 mm), embossed with MO on one side and the Arrow symbol, “>” on the other.
FORMET 1000	oval, white tablet, embossed with M | O on one side and “> | >” on the other.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Metformin is indicated in the treatment of type 2 diabetes mellitus not satisfactorily controlled by diet, where the risk of lactic acidosis is minimised by excluding predisposing factors, especially impaired renal, hepatic or cardiovascular function.

Metformin may be used as initial therapy or in sulphonylurea failure, either alone or in combination with a sulphonylurea or as adjuvant therapy in insulin-dependent diabetes.

4.2 DOSE AND METHOD OF ADMINISTRATION

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

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

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.

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.

The 250 mg tablet should be used only for the purpose of dose titration. There are no clinical data to support a minimum effective dose lower than 500 mg. 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 FORMET 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 FORMET is initially administered with parenteral doses of insulin.

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.

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/minute)
- Acute conditions with the potential to alter renal function such as:
    - Dehydration
    - Severe infection
    - Shock
    - Intravascular administration of iodinated contrast material (see section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE)
- 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 which can occur due to metformin accumulation during treatment with FORMET. When it occurs, it is fatal in approximately 50% of cases. Lactic acidosis is a medical emergency and must be treated in hospital immediately. The risk of lactic acidosis increases with the degree of renal dysfunction and the patient's age. Reported cases have occurred primarily in diabetic patients with significant renal failure, often in the setting of multiple concomitant medical/surgical problems and

multiple concomitant medications. The incidence of lactic acidosis can and should be reduced by assessing other risk factors such as poorly controlled diabetes, ketosis, prolonged fasting, excessive alcohol intake, hepatic insufficiency and any condition associated with hypoxia.

The reported incidence of lactic acidosis in patients receiving metformin is very low (approximately 0.03 cases per 1,000 patient years, with approximately 0.015 fatal cases per 1,000 patient years). The onset is often subtle and accompanied by nonspecific symptoms such as malaise, myalgia, respiratory distress, increasing somnolence and nonspecific abdominal distress. Lactic acidosis may also occur in association with a number of pathophysiological conditions, including diabetes mellitus, and when there is significant tissue hypoperfusion and hypoxaemia. Lactic acidosis is characterised by acidosis (decreased blood pH), elevated lactate levels with increased lactate/pyruvate ratio and electrolyte disturbances with an increased anion gap.

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).

Administration of iodinated contrast material

The intravascular administration of iodinated contrast materials in radiologic studies can lead to renal failure. This may induce metformin accumulation and may expose to lactic acidosis. Therefore, 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. Metformin may not be reinstituted until 48 hours afterwards, and only after renal function has been re-evaluated and found to be normal (see section 4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS).

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.

Heart failure

Type 2 diabetic patients with heart failure are at an increased risk of hypoperfusion and possible renal insufficiency. Renal insufficiency is a risk factor for systemic accumulation of metformin and consequently lactic acidosis. Careful monitoring of renal function is recommended when metformin is used in patients with cardiac failure. When metformin is implicated as the cause of lactic acidosis, metformin plasma levels greater than 5 μg/mL are generally found (see section 5.2 PHARMACOKINETIC PROPERTIES). Underlying renal disease, or a deterioration in renal function, result in reduced clearance of metformin and drug accumulation and are therefore major risk factors in lactic acidosis. The risk of lactic acidosis may therefore be significantly decreased by regular monitoring of

renal function in patients taking metformin and by the use of the minimum effective dose of metformin. In addition, metformin therapy should be temporarily stopped in the presence of any condition associated with hypoxaemia or dehydration, in patients suffering from serious infections or trauma (particularly if gastrointestinal disturbances are noted or acidosis is suspected) and in those undergoing surgery.

Use in hepatic impairment

Periodic assessment of hepatic and cardiovascular function is recommended during prolonged periods of treatment with metformin.

Use in renal impairment

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).

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

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

The diagnosis of type 2 diabetes mellitus should be confirmed before treatment with metformin is initiated.

No effect of metformin on growth and puberty has been detected during controlled clinical studies of one-year duration but clinical data in relation to the long-term effect of metformin on the development of skeletal and reproductive system in children and adolescents are not available. Therefore, a careful follow-up of the effect of metformin on these parameters in metformin-treated children, especially pre-pubescent children, is recommended.

Effects on laboratory tests

No information is available.

Other precautions

- All patients should continue their diet with a regular distribution of carbohydrate intake during the day. Overweight patients should continue their energy-restricted diet.
- The usual laboratory tests for diabetes monitoring should be performed regularly.
- Metformin hydrochloride alone does not cause hypoglycaemia; however, caution is advised when it is used in combination with other antidiabetic agents (sulphonylureas, glinides, insulin).
- Patients receiving continuous metformin therapy: It is recommended that serum vitamin B_{12} levels be measured prior to initiation treatment with metformin, after 6 months treatment and thereafter annually because of reports of decreased vitamin B_{12} absorption associated with metformin administration.
- Alcohol is known to potentiate the effect of metformin on lactate metabolism. Patients should therefore be warned against excessive alcohol intake, acute or chronic, while taking metformin.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Pharmacokinetic interactions.

Cimetidine: Reduced clearance of metformin has been reported during cimetidine therapy, so a dose reduction should be considered.

Anticoagulants: Metformin increases 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 co-administered. 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.

Pharmacodynamic interactions.

Sulfonylureas: During concomitant therapy with sulfonylureas, blood glucose should be monitored because combined therapy may cause hypoglycaemia.

Beta-blockers: Co-administration of metformin and beta-blockers may result in a potentiation of the hypoglycaemic 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.

ACE inhibitors: ACE-inhibitors may decrease the blood glucose levels. Therefore, dose adjustment of metformin hydrochloride may be necessary when such medicinal products are added or discontinued.

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

Thyroid products: Thyroid products tend to produce hyperglycaemia and may therefore lead to loss of control.

Corticosteroids: Corticosteroids tend to produce hypoglycaemia and may lead to loss of control.

Alcohol: Alcohol may increase the risk of lactic acidosis in acute intoxication, particularly in the case of fasting or malnutrition, and hepatic insufficiency.

Avoid consumption of alcohol and alcohol containing medication. Alcohol may make the signs of hypoglycaemia less clear, and delayed hypoglycaemia can occur. The CNS depressant effects of alcohol plus hypoglycaemia can make driving or the operation of dangerous machinery much more hazardous. Excessive consumption of alcohol while on metformin may result in elevation of blood lactate.

Diuretics, especially loop diuretics: May increase the risk of lactic acidosis due to their potential to decrease renal function.

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

Iodinated contrast media: FORMET should be temporarily withheld in patients undergoing radiological studies involving intravascular administration of iodinated contrast materials, because use of such products may result in acute alteration of renal function. (see section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE)

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 anhydrous 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 tablets may increase the risk for lactic acidosis. Consider more frequent monitoring for these patients.

NSAIDS: 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.

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 human daily dose on a body surface area basis.

Use in pregnancy – Pregnancy Category C

To date, no relevant epidemiological data is available. Animal studies do not indicate harmful effects with respect to pregnancy, embryonal or foetal development, parturition or postnatal development.

Since it is important to achieve strict normoglycaemia during pregnancy, metformin 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 foetal 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.

When the patient plans to become pregnant and during pregnancy, it is recommended that diabetes should not be treated with metformin but insulin should be used to maintain blood glucose levels as close to normal as possible in order to lower the risk of foetal malformations associated with abnormal blood glucose levels.

Use in lactation.

Studies in lactating rats show that metformin is excreted in 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

Very common: Mild gastrointestinal symptoms such as diarrhoea, nausea, vomiting, abdominal pain and loss of appetite, especially during the initial treatment period. These symptoms are generally transient and resolve spontaneously during continued treatment.

Gastrointestinal side effects can possibly be avoided if FORMET is taken with meals and if 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.

Skin and subcutaneous tissue disorders

Very rare: Skin reactions such as erythema, pruritus and urticaria.

Metabolism and nutritional disorder

Very rare.

- Lactic acidosis (see section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE) is a very rare but serious metabolic complication that can occur due to metformin accumulation during treatment with FORMET.

The onset of lactic acidosis is often subtle and accompanied only by nonspecific symptoms such as malaise, myalgia, respiratory distress, increasing somnolence and nonspecific abdominal distress. There may be associated hypothermia, hypotension and resistant bradyarrhythmias with more marked acidosis. The patient and the patient's 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 FORMET, the drug should be discontinued immediately and general supportive measures should be instituted promptly.

Hepatobiliary Disorders

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

Dermatological

Very rare: Mild erythema has been reported in some hypersensitive individuals.

Haematological

Very rare: A decrease of vitamin B_{12} 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. Therefore, serum B_{12} levels should be appropriately monitored and periodic parenteral B_{12} supplementation considered.

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. The onset of lactic acidosis is often subtle and accompanied only by nonspecific symptoms such as malaise, myalgia, respiratory distress, increasing somnolence and nonspecific 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 (ketonuria and ketonaemia).

Treatment

Lactic acidosis should be feared in diabetic metformin treated patients with overdose. Lactic acidosis is diagnosed and monitored by measurement of 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 Poisons Information Centre on 13 11 26 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

FORMET is an oral biguanide hypoglycaemic agent. It 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 an increase of insulin sensitivity. It does not stimulate insulin release but does require the presence of insulin to exert its hypoglycaemic 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 lowers both basal and post-prandial blood glucose in diabetic patients but does not cause hypoglycaemia in either diabetics or normal individuals.

Clinical trials

A randomised, open label bioequivalence study in 18 healthy volunteers showed, on the basis of C_{max} and AUC determinations, that one FORMET 500 mg tablet is bioequivalent to one Diabex 500 mg tablet. The calculated ratio of geometric means and 90% confidence intervals for C_{max} and $AUC_{0-\infty}$ were 0.861 (0.864 - 1.127) and 0.912 (0.918 – 1.103), respectively. The 90% confidence intervals were within the limits 0.80 – 1.25, as required to conclude bioequivalence. Since these two formulations are shown to be bioequivalent, therefore they may be used interchangeably.

5.2 PHARMACOKINETIC PROPERTIES

Absorption

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 an increase in elimination. After oral administration, metformin absorption is saturable and incomplete. It is assumed that the pharmacokinetics of metformin absorption are nonlinear.

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 μg/mL. During controlled clinical trials, maximum metformin plasma levels did not generally exceed 5 μg/mL, even at maximum doses.

Distribution

Metformin is not 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.

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 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 1500 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

The tablets contain the following excipients: povidone, magnesium stearate and Opadry Clear OY-29020.

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 30^{o}C.

6.5 NATURE AND CONTENTS OF CONTAINER

FORMET 250, bottles and blister packs of 10* and 100* tablets.

FORMET 500, bottles of 10* and 100 tablets and PVC/PVDC/Aluminium blister packs of 10*, 20* and 100 tablets.

FORMET 850, bottles* and PVC/PVDC/Aluminium blister packs of 10* and 60 tablets.

FORMET 1000, bottles and blister packs of 10*, 15*, 60*, 90 and 100* tablets.

*These pack sizes are not marketed in Australia

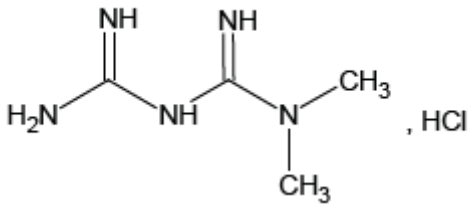
6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

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

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical structure

The chemical name for metformin hydrochloride is 1,1 dimethyl biguanide hydrochloride. Its structural formula is:



$C_4H_{11}N_5.HCl$ Molecular weight: 165.6

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 ether.

CAS number

1115-70-4

7 MEDICINE SCHEDULE (POISONS STANDARD)

S4 – Prescription Only Medicine

8 SPONSOR

Arrow Pharma Pty Ltd
15 – 17 Chapel Street
Cremorne VIC 3121
www.arrowpharma.com.au

9 DATE OF FIRST APPROVAL

16th June 2005.

10 DATE OF REVISION

19 March 2020

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
4.5	Include precautions for use when in combination with carbonic anhydrase inhibitors, topiramate and NSAIDs
2, 3, 6.5	Included 500 mg and 850 mg strengths