SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE FINISHED PHARMACEUTICAL PRODUCT:

BIGOMET 500

(METFORMIN HYDROCHLORIDE TABLETS 500 mg)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

Each uncoated tablet contains:

Metformin Hydrochloride BP 500 mg

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM:

Tablet.

White coloured,oblong,biconvex,uncoated tablets with “Bigomet” embossed on one side and break line on other side.

4. CLINICAL PARTICULARS:

4.1 Therapeutic indications:

Metformin HCl, as monotherapy, is indicated as an adjunct to diet & exercise to lower blood glucose in patients with NIDDM whose hyperglycemia cannot be satisfactorily managed on diet alone.

Metformin HCl may be used concomitantly with a sulfonylurea when diet and Metformin HCl or a sulfonylurea alone do not result in adequate glycemic control.

In initiating treatment for NIDDM, diet should be emphasized as the primary form of treatment. Caloric restriction and weight loss are essential in the obese diabetic patient. Proper dietary management alone may be effective in controlling the blood glucose and symptoms of hyperglycemia. Loss of blood glucose control in diet-managed patients may be transient, thus requiring only short-term pharmacologic therapy. The importance of regular physical activity should also be stressed, and cardiovascular risk factors should be identified and corrective measures taken where possible. If this treatment program fails to reduce symptoms and/or blood glucose, the use of Metformin HCl alone or Metformin HCl plus a sulfonylurea should be considered.

If, after a suitable trial of such treatments, glucose control still has not been achieved, consideration should be given to the use of insulin. Judgements should be based on regular clinical and laboratory evaluations.

4.2 Posology and method of administration:

There is no fixed dosage regimen for the management of hyperglycemia in diabetes mellitus with Metformin HCl or any other pharmacologic agent. Dosage of Metformin HCl must be individualized on the basis of both effectiveness and tolerance, while not exceeding the maximum recommended daily dose of 2550 mg. Metformin HCl should

be given in divided doses with meals and 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.

Usual Starting Dose: In general, clinically significant responses are not seen at doses below 1500 mg per day. However, a lower recommended starting dose and gradually increased dosage is advised to minimize gastrointestinal symptoms.

Metformin HCl 500 mg Tablets: The usual starting dose of Metformin HCl 500 mg tablets is one tablet b.i.d., given with the morning and evening meals. Dosage increases should be made in increments of one tablet every week, given in divided doses, up to a maximum of 2500 mg per day. Metformin HCl can be administered twice a day up to 2000 mg per day (e.g., 1000 mg b.i.d with morning and evening meals). If a 2500 mg daily dose is required, it may be better tolerated given t.i.d. with meals.

Metformin HCl 850 mg Tablets: The usual starting dose of Metformin HCl 850 mg tablets is one tablet daily, given with the morning meal. Dosage increases should be made in increments of one tablet every OTHER week, given in divided doses, up or a maximum of 2550 mg per day. The usual maintenance dose is 850 mg b.i.d. with the morning and evening meals. When necessary, patients may be given 850 mg t.i.d. with meals.

Transfer from Other Antidiabetic Therapy: When transferring patients from standard oral hypoglycemic agents other than chlorpropamide to Metformin HCl, no transition period generally is necessary. When transferring patients from chlorpropamide, care should be exercised during the first two weeks because of the prolonged retention of chlorpropamide in the body, leading to overlapping drug effects and possible hypoglycemia.

Concomitant Metformin HCl and Oral Sulfonylurea Therapy: If patients have not responded to four weeks of the maximum dose of Metformin HCl monotherapy, consideration should be given to gradual addition of an oral sulfonylurea while continuing Metformin HCl at the maximum dose, even if prior primary or secondary failure to a sulfonylurea has occurred. Clinical and pharmacokinetic drug-drug interaction data are currently available only for metformin plus glyburide (glibenclamide). Published clinical information exists for the use of metformin with either chlorpropamide, tolbutamide or glipizide. No published clinical information exists regarding concomitant use of metformin with acetohexamide or tolazamide.With concomitant Metformin HCl and sulfonylurea therapy, the desired control of blood glucose may be obtained by adjusting the dose of each drug.

However, attempts should be made to identify the minimum effective dose of each drug to achieve this goal. With concomitant Metformin HCl and sulfonylurea therapy, the risk of hypoglycemia associated with sulfonylurea therapy continues and may be increased. Appropriate precautions should be taken. If patients have not satisfactorily responded to one to three months of concomitant therapy with the maximum dose of Metformin HCl and the maximum dose of an oral sulfonylurea, institution of insulin therapy and discontinuation of these oral agents should be considered.

Specific Patient Populations: Metformin HCl is not recommended for use in pregnancy or for use in pediatric patients.

The initial and maintenance dosing of Metformin HCl should be conservative in patients with advanced age, 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 HCl.

Monitoring of renal function is necessary to aid in prevention of lactic acidosis, particularly in the elderly.

In debilitated or malnourished patients, the dosing should be conservative and based on a careful assessment of renal function.

4.3 Contraindications:

Metformin HCl is contraindicated in patients with:

-Hypersensitivity to metformin hydrochloride or to any of the excipients.
− Diabetic keto-acidosis, 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 (see section 4.4).

Acute or chronic diseases which may cause tissue hypoxia such as
- cardiac or respiratory failure
- recent myocardial infarction
- shock.
− Hepatic insufficiency, acute alcohol intoxication, alcoholism.
- Lactation

4.4 Special warnings and precautions for use:

PRECAUTIONS:

General:

Monitoring Renal function: Metformin HCl is known to be substantially excreted by the kidney, and the risk of Metformin accumulation and lactic acidosis increases with the degree of impairment of renal function. Thus, patients with serum creatinine levels

above the upper limit of normal for their age should not receive Metformin HCl. In patients with advanced age, Metformin HCL should be carefully titrated to establish the minimum dose for adequate glycemic effect, because aging is associated with reduced renal function. In elderly patients, particularly those 80 years of age, renal function should be monitored regularly and, generally, Metformin HCl should not be titrated to the maximum dose of the Metformin component, i.e., 2,000 mg. Before initiation of therapy with Metformin HCl and at least annually thereafter, renal function should be assessed and verified as normal. In patients in whom development of renal dysfunction is anticipated, renal function should be assessed more frequently and Metformin HCl discontinued if evidence of renal impairment is present.

4.4 Special warnings and precautions for use:[contd]

PRECAUTIONS:

General:

Use of concomitant medications that may affect renal function or Metformin disposition: Concomitant medication(s) that may affect renal function or result in significant hemodynamic change or may interfere with the disposition of Metformin, such as cationic drugs that are eliminated by renal tubular secretion, should be used with caution.

Radiologic studies involving the use of intravascular iodinated contrast materials (For Example, Intravenous Urogram, Intravenous Cholangiography, Angiography, and Computed Tomography (CT) scans with contrast materials): Intravascular contrast studies with iodinated materials can lead to acute alteration of renal function and have been associated with lactic acidosis in patients receiving Metformin. Therefore, in patients in whom any such study is planned, Metformin HCL should be temporarily discontinued at the time of or prior to the procedure, and withheld for 48 hours subsequent to the procedure and reinstituted only after renal function has been re-evaluated and found to be normal.

Hypoxic States: Cardiovascular collapse (shock) from whatever cause, acute congestive heart failure, acute myocardial infarction, and other conditions characterized by hypoxemia have been associated with lactic acidosis and may also cause prerenal azotemia. When such events occur in patients receiving, the drug should be promptly discontinued.

Surgical procedures: Use of Metformin HCL should be temporarily suspended for any surgical procedure (except minor procedures not associated with restricted intake of food and fluids) and should not be restarted until the patient’s oral intake has resumed and renal function has been evaluated as normal.

Alcohol Intake: Alcohol is known to potentiate the effect of Metformin on lactate metabolism. Patients, therefore, should be warned against excessive alcohol intake, acute or chronic, while receiving Metformin HCL.

Impaired Hepatic Function: Since impaired hepatic function has been associated with some cases of lactic acidosis, Metformin HCL should generally be avoided in patients with clinical or laboratory evidence of hepatic disease.

4.4 Special warnings and precautions for use:[contd]

PRECAUTIONS:

Vitamin B_{12} levels: In controlled clinical trials of Metformin hydrochloride of 29 weeks' duration, a decrease to subnormal levels of previously normal serum vitamin B_{12} levels, without clinical manifestations, was observed in approximately 7% of patients. Such decrease, possibly due to interference with B_{12} absorption from the B12-intrinsic factor complex, is, however, very rarely associated with anemia and appears to be rapidly reversible with discontinuation of Metformin or vitamin B_{12} supplementation. Measurement of hematologic parameters on an annual basis is advised in patients on Metformin HCL and any apparent abnormalities should be appropriately investigated and managed. Certain individuals (those with inadequate vitamin B_{12} or calcium intake or absorption) appear to be predisposed to developing subnormal vitamin B_{12} levels. In these patients, routine serum vitamin B12 measurements at 2- to 3-year intervals may be useful.

Change in Clinical Status of Previously Controlled Diabetic: A patient with type 2 diabetes previously well-controlled on Metformin HCL who develops laboratory abnormalities or clinical illness (especially vague and poorly defined illness) should be evaluated promptly for evidence of ketoacidosis or lactic acidosis. Evaluation should include serum electrolytes and ketones, blood glucose and, if indicated, blood pH, lactate, pyruvate, and Metformin levels. If acidosis of either form occurs, Metformin HCL must be stopped immediately and other appropriate corrective measures initiated.

Hypoglycemia: Hypoglycemia does not occur in patients receiving Metformin hydrochloride alone under usual circumstances of use but could occur when caloric intake is deficient, when strenuous exercise is not compensated by caloric supplementation, or during concomitant use with hypoglycemic agents (such as sulfonylureas or insulin) or ethanol. Elderly, debilitated or malnourished patients, and those with adrenal or pituitary insufficiency or alcohol intoxication are particularly susceptible to hypoglycemic effects. Hypoglycemia may be difficult to recognize in the elderly and in people –adrenergic who are taking blocking drugs.

4.4 Special warnings and precautions for use:[contd]

PRECAUTIONS:

Loss of Control of Blood Glucose: When a patient stabilized on any diabetic regimen is exposed to stress such as fever, trauma, infection, or surgery, a temporary loss of glycemic control may occur. At such times, it may be necessary to withhold Metformin HCL and temporarily administer insulin. Metformin HCL may be reinstituted after the acute episode is resolved.

WARNINGS:

Lactic Acidosis: Lactic acidosis is a rare, but serious, metabolic complication that can occur due to Metformin accumulation during treatment with Metformin HCL; when it occurs, it is fatal in approximately 50% of cases. Lactic acidosis may also occur in association with a number of pathophysiologic conditions, including diabetes mellitus, and whenever there is significant tissue hypoperfusion and hypoxemia. Lactic acidosis is characterized by elevated blood lactate levels (>5 mmol/L), decreased blood pH, electrolyte disturbances with an increased anion gap, and an increased lactate/pyruvate ratio. When Metformin is implicated as the cause of lactic acidosis, Metformin plasma levels >5 mcg/mL are generally found.

The reported incidence of lactic acidosis in patients receiving Metformin hydrochloride is very low (approximately 0.03 cases/1,000 patient years of exposure, with approximately 0.015 fatal cases/1,000 patient years of exposure). Reported cases have occurred primarily in diabetic patients with significant renal insufficiency, including both intrinsic renal disease and renal hypoperfusion, often in the setting of multiple concomitant medical/surgical problems and multiple concomitant medications. Patients with congestive heart failure requiring pharmacologic management, in particular those with unstable or acute congestive heart failure who are at risk of hypoperfusion and hypoxemia, are at increased risk of lactic acidosis. The risk of lactic acidosis increases with the degree of renal dysfunction and the patient's age. The risk of lactic acidosis may, therefore, be significantly decreased by regular monitoring of renal function in patients taking Metformin HCL and by use of the minimum effective dose of Metformin HCL. In particular, treatment of the elderly should be accompanied by careful monitoring of renal function. Treatment with Metformin HCL should not be initiated in patients 80 years of age unless measurement of creatinine clearance demonstrates that renal function is not reduced, as these patients are more susceptible to developing lactic acidosis.

WARNINGS:

In addition, Metformin HCL should be promptly withheld in the presence of any condition associated with hypoxemia, dehydration, or sepsis. Because impaired hepatic function may significantly limit the ability to clear lactate, Metformin HCL should generally be avoided in patients with clinical or laboratory evidence of hepatic disease.

Patients should be cautioned against excessive alcohol intake, either acute or chronic, when taking Metformin HCL, since alcohol potentiates the effects of Metformin hydrochloride on lactate metabolism. In addition, Metformin HCL should be temporarily discontinued prior to any intravascular radio contrast study and for any surgical procedure.

The onset of lactic acidosis often is subtle, and accompanied only by nonspecific symptoms such as malaise, myalgias, 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 physician must be aware of the possible importance of such symptoms and the patient should be instructed to notify the physician immediately if they occur. Metformin HCl should be withdrawn until the situation is clarified. Serum electrolytes, ketones, blood glucose and, if indicated, blood pH, lactate levels and even blood metformin levels may be useful. Once a patient is stabilized on any dose level of metformin HCl, gastrointestinal symptoms, which are common during initiation of therapy, are unlikely to be drug related. Later occurrence of gastrointestinal symptoms could be due to lactic acidosis or other serious disease.

Levels of fasting venous plasma lactate above the upper limit of normal but less than 5 mmol/l in patients taking metformin HCl do not necessarily indicate impending lactic acidosis and may be explainable by other mechanisms, such as poorly controlled diabetes or obesity, vigorous physical activity or technical problems in sample handling.

Lactic acidosis should be suspected in any diabetic patient with metabolic acidosis lacking evidence of ketoacidosis (ketonuria and ketonemia).

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

WARNINGS:

Because metformin HCl is dialyzable (with a clearance of up to 170 ml/min under good hemodynamic conditions), prompt hemodialysis is recommended to correct the

acidosis and remove the accumulated metformin. Such management often results in prompt reversal of symptoms and recovery.

SPECIAL WARNING ON INCREASED RISK OF CARDIOVASCULAR MORTALITY:

The administration of oral antidiabetic drugs has been reported to be associated with increased cardiovascular mortality as compared to treatment with diet alone or diet plus insulin. This warning is based on the study conducted by the University Group Diabetes program (UGDP), a long-term prospective clinical trial designed to evaluate the effectiveness of glucose-lowering drugs in preventing or delaying vascular complications in patients with non-insulin-dependent diabetes. The study involved 1027 patients who were randomly assigned to one of five treatment groups (Diabetes, 19 (Suppl.2):747-830, 1970; Diabetes, 24 (Suppl.1):65-184, 1975).

The UGDP reported that patients treated for 5 to 8 years with diet plus a fixed dose of tolbutamide (1.5 g per day) or diet plus a fixed dose of phenformin (100 mg per day), had a rate of cardiovascular mortality approximately 2.5 times that of patients treated with diet alone, resulting in discontinuation of both of these treatments in the UGDP study. Total mortality was increased in both the tolbutamide- and phenformin-treated groups and this increase was statistically significant in the phenformin-treated group. Despite controversy regarding the interpretation of these results, the findings of the UGDP study provide an adequate basis for this warning. The patient should be informed of the potential risks and benefits of metformin HCl and alternative modes of therapy.

Although only one drug in the sulfonylurea category (tolbutamide) and one in the biguanide category (phenformin) were included in this study, it is prudent from a safety standpoint to consider that this warning may also apply to other related oral antidiabetic drugs, in view of the similarities in mode of action and chemical structure among the drugs in each category.

4.5 Interaction with other FPPs and other forms of interaction:

<u>Concomitant use not recommended</u>

<u>Alcohol</u>

Acute alcohol intoxication is associated with an increased risk of lactic acidosis, particularly in case of:

- fasting or malnutrition;
- hepatic insufficiency.

Consumption of alcohol and alcohol-containing medicinal products should be avoided.

<u>Iodinated contrast agents</u>

Intravascular administration of iodinated contrast agents may lead to renal failure, resulting in metformin accumulation and an increased risk of lactic acidosis. Metformin hydrochloride should be discontinued prior to or at the time of the test and not be re-instituted until 48 hours afterwards, and only after renal function has been re-evaluated and found to be normal.

Combinations requiring specific precautions for use:

Glucocorticoids (systemic and local routes), β2-agonists and diuretics have intrinsic hyperglycaemic activity. Patients should be informed and increased glucose monitoring should be performed especially at the beginning of treatment with these medicinal products and dose adjustment of metformin may be required. ACE inhibitors may decrease the blood glucose levels. Therefore, dose adjustments of metformin may be necessary during and after addition or discontinuation of such medicinal products.

4.6 Fertility, Pregnancy and lactation:

To date, no relevant epidemiological data are available. Animal studies do not indicate harmful effects with respect to pregnancy, embryonal or foetal development, parturition or postnatal development (see also section 5.3 "Preclinical safety data").

When the patient plans to become pregnant and during pregnancy, 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:

Metformin is excreted into milk in lactating rats. Similar data are not available in humans and a decision should be made whether to discontinue nursing or to discontinue metformin, taking into account the importance of the compound to the mother.

4.7 Effects on Ability to drive & Use Machines:

Metformin monotherapy does not cause hypoglycaemia and therefore has no effect on the ability to drive or to use machines.
However, patients should be alerted to the risk of hypoglycaemia when Metformin is used in combination with other antidiabetic agents (sulphonylureas, insulin, repaglinide).

4.8 Undesirable effects:

The following undesirable effects may occur under treatment with metformin. 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).

Gastrointestinal disorders :

Very common:

Nausea, vomiting, diarrhoea, abdominal pain and loss of appetite. These occur most frequently during initiation of therapy and resolve spontaneously in most cases. To prevent these gastrointestinal symptoms, it is recommended that metformin hydrochloride be taken in 2 or 3 daily doses during or after meals. A slow increase of the dose may also improve gastro-intestinal tolerability.

Metabolism and nutrition disorders

Very rare:

Lactic acidosis (0.03 cases/1000 patient-years; see section 4.4).

A decrease in vitamin B12 absorption and a decrease in serum levels have been observed in patients on long-term treatment with metformin. Consideration of such aetiology is recommended if a patient presents with megaloplastic anaemia.

Nervous system disorders

Common:

Taste disturbance

Hepatobiliary disorders

Very rare:

Liver function tests abnormalities or hepatitis resolving upon discontinuation.

Skin and subcutaneous tissue disorders

Very rare:

Skin reactions such as erythema, pruritus and urticaria.

Children and adolescents:

For children and adolescents aged 10 – 16 years limited data showed that adverse events reporting was similar in nature and severity to that reported in adults.

4.9 Overdosage and Treatment of Overdosage:

Hypoglycemia has not been seen even with ingestion of up to 85 grams of metformin HCl, although lactic acidosis has occurred in such circumstances. High overdose of metformin or concomitant risks may lead to lactic acidosis. Lactic acidosis is a medical emergency and must be treated in hospital. The most effective method to remove lactate and metformin from the body is haemodialysis.

5. PHARMACOLOGICAL PROPERTIES:

5.1 *Pharmacodynamic properties:*

***Pharmacotherapeutic group*:** Oral blood glucose lowering drugs.

ATC code: A10B A02

Mechanism of action:

Metformin hydrochloride is an antihyperglycemic agent, which improves glucose tolerance in patients with type 2 diabetes, lowering both basal and postprandial plasma glucose. Its pharmacologic mechanisms of action are different from other classes of oral antihyperglycemic agents. Metformin decreases hepatic glucose production, decreases intestinal absorption of glucose, and increases peripheral glucose uptake and utilization. Unlike sulfonylureas, Metformin does not produce hypoglycemia in either patients with type 2 diabetes or normal subjects, except in special circumstances, and does not cause hyperinsulinemia. With Metformin therapy,

insulin secretion remains unchanged while fasting insulin levels and day-long plasma insulin response may actually decrease.

5.2 Pharmacokinetic properties:

Pharmacokinetics:

Absorption and Bioavailability: The absolute bioavailability of a 500 mg Metformin hydrochloride tablet given under fasting conditions is approximately 50% to 60%. Studies using single oral doses of Metformin hydrochloride tablets of 500 mg and 1,500 mg, and 850 mg to 2,550 mg, indicate that there is a lack of dose proportionality with increasing doses, which is due to decreased absorption rather than an alteration in elimination.

5.2 Pharmacokinetic properties: [contd]

Food decreases the extent and slightly delays the absorption of metformin, as shown by approximately a 40% lower peak concentration and 25% lower AUC in plasma and a 35 minute prolongation of time to peak plasma concentration following administration of a single 850 mg tablet of metformin with food, compared to the same tablet strength administered fasting. The clinical relevance of these decreases is unknown.

Distribution:

Plasma protein binding is negligible. Metformin partitions into erythrocytes. The blood peak is lower than the plasma peak and appears at approximately the same time. The red blood cells probably represent a secondary compartment of distribution. The mean volume of distribution (Vd) ranged between 63 and 276 l.

Metabolism:

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

Elimination :

Renal clearance of metformin is > 400 ml/min, indicating that metformin is eliminated by glomerular filtration and tubular secretion. Following an oral dose, the terminal elimination half-life is approximately 6.5 hours. When renal function is impaired, renal clearance decreases in proportion to that of creatinine and thus the apparent elimination half-life is prolonged, leading to increased concentrations of metformin in plasma.

Special Populations:

Children and adolescents:

Single dose study: After single doses of metformin hydrochloride 500 mg, peadiatric patients have shown similar pharmacokinetic profile to that observed in healthy adults. Multiple dose study: Data are restricted to one study. After repeated doses of 500 mg twice daily (BID) for 7 days in paediatric patients the peak plasma

concentration (Cmax) and systemic exposure (AUC0-t) were reduced by approximately 33 % and 40 %, respectively compared to diabetic adults who received repeated doses of 500 mg BID for 14 days. As the dose is individually titrated based on glycaemic control, this is of limited clinical relevance.

5.3 Preclinical safety data:

Preclinical data reveal no special hazard for humans based on conventional studies on safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity reproduction.

6. PHARMACEUTICAL PARTICULARS:

6.1 List of excipients:

Microcrystalline Cellulose, Maize starch, Calcium Hydrogen Phosphate, Purified Talc,Colloidal Anhydrous Silica, Magnesium Stearate & Purified Water.

6.2 Incompatibilities:

Not applicable.

6.3 Shelf life: 36 Months.

6.4 Special precautions for storage:

Store at a temperature not exceeding 30°C.

KEEP OUT OF REACH OF CHILDREN.

PROTECT FROM MOISTURE AND LIGHT.

6.5 Nature and contents of container:

ALU/PVC FILM BLISTER OF 10 TABLETS.10 BLISTER STRIPS PACKED IN A CARTON ALONG WITH AN INSERT.

6.6 Instructions for use and handling:

No special requirements. Any unused product or waste material should be disposed off in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER:

ARISTO PHARMACEUTICALS PRIVATE LIMITED
Gala No. 2, Ground Floor, 23- A Shah Industrial Estate,
Off Veera Desai Road, ANDHERI (W), MUMBAI 400 053, INDIA.
Telephone number: 91 22 2673 9999/26739751/26739749

Fax number : *91 22 2673 4792*
email: *export@aristopharma.co.in*

8. MA number issued by Ethiopian FDA:

06041/07499/REN/2020

9. Date of first authorization/renewal of the authorization:

7/6/2021

10. DATE OF REVISION OF THE TEXT:

05-07-2023