1.3 Product Information

1.3.1 Summary of Product Characteristics (SmPC)

Summary Product Characteristics

1. Name of the proprietary product:

Name of the Medicinal Product: Hydrocortisone Sodium Succinate for Injection BP 100mg

Route of Administration: Intravenous/Intramascular

2. Qualitative and Quantitative composition:
Each vial contains
Hydrocortisone Sodium Succinate(Buffered)
Eq. to Hydrocortisone 100mg

3. Pharmaceutical Form: White or almost white Powder for solution for injection.

4. Clinical Particulars:

4.1 Therapeutic Indications:
Anti-inflammatory agent.
It is indicated for any condition in which rapid and intense corticosteroid effect is required such as:
1. Endocrine disorders :
Primary or secondary adrenocortical insufficiency
2. Collagen diseases :
Systemic lupus erythematosus
3. Dermatological diseases :
Severe erythema multiforme (Stevens-Johnson syndrome)
4. Allergic states :
Bronchial asthma, anaphylactic reactions
5. Gastro-intestinal diseases :
Ulcerative colitis, Crohn's disease
6. Respiratory diseases :
Aspiration of gastric contents
7. Medical emergencies :
Hydrocortisone sodium succinate for injection is indicated in the treatment of shock secondary to adrenocortical insufficiency or shock unresponsive to conventional therapy when adrenocortical insufficiency may be present.

4.2 Posology and method of administration:
Hydrocortisone sodium succinate for injection may be administered by intravenous injection, by intravenous infusion, or by intramuscular injection, the preferred method for initial emergency use being intravenous injection. Following the initial emergency period, consideration should be given to employing a longer-acting injectable preparation or an oral preparation.
Dosage usually ranges from 100 mg to 500 mg depending on the severity of the condition, administered by intravenous injection over a period of one to ten minutes. This dose may be repeated at intervals of 2, 4 or 6 hours as indicated by the patient's response and clinical condition.
In general high-dose corticosteroid therapy should be continued only until the patient's condition has stabilised - usually not beyond 48 to 72 hours. If hydrocortisone therapy must be continued beyond 48 to 72 hours hypernatraemia may occur, therefore it may be preferable to replace Hydrocortisone sodium succinate for injection with a corticosteroid such

as methylprednisolone sodium succinate as little or no sodium retention occurs. Although adverse effects associated with high dose, short-term corticoid therapy are uncommon, peptic ulceration may occur. Prophylactic antacid therapy may be indicated.
Patients subjected to severe stress following corticoid therapy should be observed closely for signs and symptoms of adrenocortical insufficiency.
Corticosteroid therapy is an adjunct to, and not a replacement for, conventional therapy.
In patients with liver disease, there may be an increased effect and reduced dosing may be considered.

Elderly patients: Hydrocortisone sodium succinate for injection is primarily used in acute short-term conditions. There is no information to suggest that a change in dosage is warranted in the elderly. However, treatment of elderly patients should be planned bearing in mind the more serious consequences of the common side-effects of corticosteroids in old age and close clinical supervision is required .
Paediatric population: While the dose may be reduced for infants and children, it is governed more by the severity of the condition and response of the patient than by age or body weight but should not be less than 25 mg daily.
Preparation of solutions: For intravenous or intramuscular injection prepare the solution aseptically by adding not more than 2 ml of sterile water for injections to the contents of one vial of Hydrocortisone sodium succinate for injection 100 mg, shake and withdraw for use.
For intravenous infusion, first prepare the solution by adding not more than 2 ml of sterile water for injections to the vial; this solution may then be added to 100 ml - 1000 ml (but not less than 100 ml) of 5% dextrose in water (or isotonic saline solution or 5% dextrose in isotonic saline solution if patient is not on sodium restriction).
When reconstituted as directed the pH of the solution will range from 6.5 to 8.0.

Method of administration
Hydrocortisone sodium succinate for injection may be administered by intravenous injection, by intravenous infusion, or by intramuscular injection, the preferred method for initial emergency use being intravenous injection.

4.3 Contraindications
Hydrocortisone sodium succinate for injection is contraindicated where there is known hypersensitivity to the active substance or any of the excipients and in systemic fungal infection unless specific anti-infective therapy is employed.
Administration of live or live, attenuated vaccines is contraindicated in patients receiving immunosuppressive doses of corticosteroids.

4.4 Special warnings and precautions for use
Warnings and Precautions:

1. A Patient Information Leaflet is provided in the pack by the manufacturer.
2. Undesirable effects may be minimised by using the lowest effective dose for the minimum period. Frequent patient review is required to appropriately titrate the dose against disease activity.
3. Adrenal cortical atrophy develops during prolonged therapy and may persist for months after stopping treatment. In patients who have received more than physiological doses of systemic corticosteroids (approximately 30 mg hydrocortisone) for greater than 3 weeks, withdrawal should not be abrupt. How dose reduction should be carried out depends largely on whether the disease is likely to relapse as the dose of systemic corticosteroids is reduced. Clinical assessment of disease activity may be needed during withdrawal. If the disease is unlikely to relapse on withdrawal of systemic corticosteroids, but there is uncertainty about HPA suppression, the dose of systemic corticosteroid may be reduced rapidly to physiological doses. Once a daily dose of 30 mg hydrocortisone is reached, dose reduction should be slower to allow the HPA-axis to recover.
   Abrupt withdrawal of systemic corticosteroid treatment, which has continued up to 3 weeks is appropriate if it considered that the disease is unlikely to relapse. Abrupt withdrawal of doses up to 160 mg hydrocortisone for 3 weeks is unlikely to lead to clinically relevant HPA-axis

suppression, in the majority of patients. In the following patient groups, gradual withdrawal of systemic corticosteroid therapy should be considered even after courses lasting 3 weeks or less:

• Patients who have had repeated courses of systemic corticosteroids, particularly if taken for greater than 3 weeks.

• When a short course has been prescribed within one year of cessation of long-term therapy (months or years).

• Patients who may have reasons for adrenocortical insufficiency other than exogenous corticosteroid therapy.

• Patients receiving doses of systemic corticosteroid greater than 160 mg hydrocortisone.

• Patients repeatedly taking doses in the evening.

4. Patients should carry 'Steroid Treatment' cards which give clear guidance on the precautions to be taken to minimise risk and which provide details of prescriber, drug, dosage and the duration of treatment.
5. Corticosteroids may mask some signs of infection, and new infections may appear during their use. Suppression of the inflammatory response and immune function increases the susceptibility to fungal, viral and bacterial infections and their severity. The clinical presentation may often be atypical and may reach an advanced stage before being recognised.
6. Chickenpox is of serious concern since this normally minor illness may be fatal in immunosuppressed patients. Patients (or parents of children) without a definite history of chickenpox should be advised to avoid close personal contact with chickenpox or herpes zoster and if exposed they should seek urgent medical attention. Passive immunization with varicella/zoster immunoglobin (VZIG) is needed by exposed non-immune patients who are receiving systemic corticosteroids or who have used them within the previous 3 months; this should be given within 10 days of exposure to chickenpox. If a diagnosis of chickenpox is confirmed, the illness warrants specialist care and urgent treatment. Corticosteroids should not be stopped and the dose may need to be increased.
7. Exposure to measles should be avoided. Medical advice should be sought immediately if exposure occurs. Prophylaxis with normal intramuscular immuneglobulin may be needed.
8. Live vaccines should not be given to individuals with impaired immune responsiveness. The antibody response to other vaccines may be diminished.
9. The use of Hydrocortisone sodium succinate for injection in active tuberculosis should be restricted to those cases of fulminating or disseminated tuberculosis in which the corticosteroid is used for the management of the disease in conjunction with appropriate antituberculosis regimen. If corticosteroids are indicated in patients with latent tuberculosis or tuberculin reactivity, close observation is necessary as reactivation of the disease may occur. During prolonged corticosteroid therapy, these patients should receive chemoprophylaxis.
10. Rarely anaphylactoid reactions have been reported following parenteral Hydrocortisone sodium succinate for injection therapy. Physicians using the drug should be prepared to deal with such a possibility. Appropriate precautionary measures should be taken prior to administration, especially when the patient has a history of drug allergy.
11. Care should be taken for patients receiving cardioactive drugs such as digoxin because of steroid induced electrolyte disturbance/potassium loss .
12. Hydrocortisone may have an increased effect in patients with liver diseases since the metabolism and elimination of hydrocortisone is significantly decreased in these patients.
13. Corticosteroid therapy has been associated with central serous chorioretinopathy, which may lead to retinal detachment.
14. There have been reports of epidural lipomatosis in patients taking corticosteroids, typically with

long-term use at high doses.

15. Thrombosis including venous thromboembolism has been reported to occur with corticosteroids. As a result corticosteroids should be used with caution in patients who have or may be predisposed to thromboembolic disorders.

Special precautions:

Particular care is required when considering the use of systemic corticosteroids in patients with the following conditions and frequent patient monitoring is necessary.

1. Osteoporosis (post-menopausal females are particularly at risk).
2. Hypertension or congestive heart failure.
3. Existing or previous history of severe affective disorders (especially previous steroid psychosis).
4. Diabetes mellitus (or a family history of diabetes).
5. History of tuberculosis.
6. Glaucoma (or a family history of glaucoma).
7. Previous corticosteroid-induced myopathy.
8. Liver failure or cirrhosis.
9. Renal insufficiency.
10. Epilepsy.
11. Peptic ulceration.
12. Fresh intestinal anastomoses.
13. Predisposition to thrombophlebitis.
14. Abscess or other pyogenic infections.
15. Ulcerative colitis.
16. Diverticulitis.
17. Myasthenia gravis.
18. Ocular herpes simplex, for fear of corneal perforation.
19. Hypothyroidism.
20. Recent myocardial infarction (myocardial rupture has been reported).
21. Kaposi's sarcoma has been reported to occur in patients receiving corticosteroid therapy. Discontinuation of corticosteroids may result in clinical remission.
22. Pheochromocytoma crisis, which can be fatal, has been reported after administration of systemic corticosteroids. Corticosteroids should only be administered to patients with suspected or identified pheochromocytoma after an appropriate risk/benefit evaluation.
23. Hydrocortisone can cause elevation of blood pressure, salt and water retention and increased excretion of potassium. Dietary salt restriction and potassium supplementation may be necessary. All corticosteroids increase calcium excretion.
24. Patients and/or carers should be warned that potentially severe psychiatric adverse reactions may occur with systemic steroids .Symptoms typically emerge within a few days or weeks of starting treatment. Risks may be higher with high doses/systemic exposure that can increase the risk of side effects), although dose levels do not allow prediction of the onset, type, severity or duration of reactions. Most reactions recover after either dose reduction or withdrawal, although specific treatment may be necessary. Patients/carers should be encouraged to seek medical advice if worrying psychological symptoms develop, especially if

depressed mood or suicidal ideation is suspected. Patients/carers should be alert to possible psychiatric disturbances that may occur either during or immediately after dose tapering/withdrawal of systemic steroids, although such reactions have been reported infrequently.

Particular care is required when considering the use of systemic corticosteroids in patients with existing or previous history of severe affective disorders in themselves or in their first degree relatives. These would include depressive or manic-depressive illness and previous steroid psychosis.

Paediatric population: Corticosteroids cause growth retardation in infancy, childhood and adolescence, which may be irreversible. Treatment should be limited to the minimum dosage for the shortest possible time. The use of steroids should be restricted to the most serious indications.

Use in the elderly: The common adverse effects of systemic corticosteroids may be associated with more serious consequences in old age, especially osteoporosis, hypertension, hypokalaemia, diabetes, susceptibility to infection and thinning of the skin. Close clinical supervision is required to avoid life-threatening reactions.

Systemic corticosteroids are not indicated for, and therefore should not be used to treat traumatic brain injury or stroke because it is unlikely to be of benefit and may even be harmful. For traumatic brain injury a multicenter study revealed an increased mortality at 2 weeks and 6 months after injury in patients administered methylprednisolone sodium succinate compared to placebo. A casual association with methylprednisolone sodium succinate treatment has not been established.

4.5 Interaction with other medicinal products and other forms of interaction:

1. Convulsions have been reported with concurrent use of corticosteroids and ciclosporin. Since concurrent administration of these agents results in a mutual inhibition of metabolism, it is possible that convulsions and other adverse effects associated with the individual use of either drug may be more apt to occur.
2. Drugs that induce hepatic enzymes, such as rifampicin, rifabutin, carbamazepine, phenobarbitone, phenytoin, primidone, and aminoglutethimide enhance the metabolism of corticosteroids and its therapeutic effects may be reduced.
3. Drugs which inhibit the CYP3A4 enzyme, such as cimetidine, erythromycin, ketoconazole, itraconazole, diltiazem and mibefradil, may decrease the rate of metabolism of corticosteroids and hence increase the serum concentration.
4. Steroids may reduce the effects of anticholinesterases in myasthenia gravis. The desired effects of hypoglycaemic agents (including insulin), anti-hypertensives and diuretics are antagonised by corticosteroids, and the hypokalaemic effects of acetazolamide, loop diuretics, thiazide diuretics and carbenoxolone are enhanced.
5. The efficacy of coumarin anticoagulants may be enhanced by concurrent corticosteroid therapy and close monitoring of the INR or prothrombin time is required to avoid spontaneous bleeding.
6. The renal clearance of salicylates is increased by corticosteroids and steroid withdrawal may result in salicylate intoxication. Salicylates and non-steroidal anti-inflammatory agents should be used cautiously in conjunction with corticosteroids in hypothrombinaemia.
7. Steroids have been reported to interact with neuromuscular blocking agents such as pancuronium with partial reversal of the neuromuscular block.

4.6 Pregnancy and Lactation:

Pregnancy

The ability of corticosteroids to cross the placenta varies between individual drugs, however, hydrocortisone readily crosses the placenta.

Administration of corticosteroids to pregnant animals can cause abnormalities of foetal development including cleft palate, intra-uterine growth retardation and affects on brain growth and development. There is no evidence that corticosteroids result in an increased incidence of congenital abnormalities, such as cleft palate in man, however, when administered for long periods or repeatedly during pregnancy, corticosteroids may increase the risk of intra-uterine growth retardation. Hypoadrenalism may, in theory, occur in the neonate following prenatal exposure to corticosteroids but usually resolves spontaneously following birth and is rarely clinically important. As with all drugs, corticosteroids should only be prescribed when the benefits to the mother and child outweigh the risks. When corticosteroids are essential, however, patients with normal pregnancies may be treated as though they were in the non-gravid state.

Breast-feeding

Corticosteroids are excreted in breast milk, although no data are available for hydrocortisone. Doses up to 160 mg daily of hydrocortisone are unlikely to cause systemic systemic effects in the infant. Infants of mothers taking higher doses than this may have a degree of adrenal suppression, but the benefits of breast-feeding are likely to outweigh any theoretical risk.

4.7 Effects on the ability to drive and use machines

The effect of corticosteroids on the ability to drive or use machinery has not been systematically evaluated. Undesirable effects, such as syncope, vertigo, and convulsions are possible after treatment with corticosteroids. If affected, patients should not drive or operate machinery.

4.8 Undesirable effects:

Since Hydrocortisone sodium succinate for injection is normally employed on a short-term basis it is unlikely that side effects will occur; however, the possibility of side effects attributable to corticosteroid therapy should be recognised .Such side effects include:

Adverse Reactions table	
System Organ Class	**Frequency Not Known (Cannot be estimated from available data)**
Infections and infestations	Infection masked; Opportunistic infection
Neoplasms benign, malignant and unspecified (including cysts and polyps)	Kaposi's sarcoma (has been reported to occur in patients receiving corticosteroid therapy)
Immune system disorders	Hypersensitivity (including anaphylaxis and anaphylactoid reactions [e.g. bronchospasm, laryngeal oedema, urticaria]); May suppress reactions to skin tests
Blood and lymphatic system disorders	Leucocytosis
Endocrine disorders	Cushingoid; Pituitary-adrenal axis suppression;

	WITHDRAWAL SYMPTOMS - Too rapid a reduction of corticosteroid dosage following prolonged treatment can lead to acute adrenal insufficiency, hypotension and death. However, this is more applicable to corticosteroids with an indication where continuous therapy is given . A 'withdrawal syndrome' may also occur including, fever, myalgia, arthralgia, rhinitis, conjunctivitis, painful itchy skin nodules and loss of weight
Metabolism and nutrition disorders	Sodium retention; Water retention; Alkalosis hypokalaemic; Glucose tolerance impaired; Increased appetite; Weight increased
Psychiatric disorders	Affective disorders (such as irritable, euphoric, depressed and labile mood psychological dependence and suicidal thoughts); Psychotic reactions (including mania, delusions, hallucinations and aggravation of schizophrenia); Behavioural disturbances; Irritability; Anxiety; Sleep disturbances; Cognitive dysfunction including confusion and amnesia
Nervous system disorders	Increased intra-cranial pressure with papilloedema in children (pseudotumour cerebri) has been reported, usually after treatment withdrawal of hydrocortisone; Benign intracranial hypertension; Convulsions; Epidural lipomatosis
Eye disorders	Cataract subcapsular; Glaucoma; Exophthalmos; Increased intra-ocular pressure, with possible damage to the optic nerve; Corneal or scleral thinning; Exacerbation of ophthalmic viral or fungal disease; Central serous chorioretinopathy
Cardiac disorders	Cardiac failure congestive (in susceptible patients); Myocardial rupture following a myocardial infarction
Vascular disorders	Hypertension; Thrombosis including Thromboembolism
Respiratory, thoracic and mediastinal disorders	Hiccups; Pulmonary embolism
Gastrointestinal disorders	Peptic ulcer (with possible perforation and haemorrhage); Gastric haemorrhage; Pancreatitis;

	Abdominal distension; Oesophageal ulceration; Oesophageal candidiasis; Intestinal perforation; Dyspepsia; Nausea
Skin & subcutaneous tissue disorders	Petechiae; Telangiectasia; Ecchymosis; Skin atrophy; Skin striae; Skin hyperpigmentation; Skin hypopigmentation; Hirsutism; Acne; Hyperhidrosis
Musculoskeletal, connective tissue and bone disorders	Myopathy; Muscular weakness; Osteonecrosis; Osteoporosis; Pathological fracture; Growth retardation
Reproductive system and breast disorders	Menstruation irregular; Amenorrhoea
General disorders and administration site conditions	Impaired healing; Abscess sterile; Malaise
Investigations	Carbohydrate tolerance decreased; Increased insulin requirement (or oral hypoglycemic agents in diabetics); Blood potassium decreased; Nitrogen balance negative (due to protein catabolism); Urine calcium increased; Alanine aminotransferase increased; Aspartate aminotransferase increased; Blood alkaline phosphatase increased
Injury, poisoning and procedural complications	Spinal compression fracture; Tendon rupture (particularly of the Achilles tendon)

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation 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.

4.9 Overdose

There is no clinical syndrome of acute overdosage with Hydrocortisone sodium succinate for injection. Hydrocortisone is dialysable.

5. Pharmacological Particulars:

Pharmacodynamic properties Pharmacotherapeutic group: Glucocorticoids, ATC CODE; H02A BO9

Glucocorticoids, naturally occurring and synthetic, are adrenocortical steroids. Naturally occurring glucocorticoids (hydrocortisone and cortisone), which also have salt-retaining properties, are used as replacement therapy in adrenocortical deficiency states. Their synthetic analogs are primarily used for their anti-inflammatory effects in disorders of many organ systems.

Hydrocortisone sodium succinate has the same metabolic and anti-inflammatory actions as hydrocortisone. When given parenterally and in equimolar quantities, the two compounds are equivalent in biologic activity. The highly water-soluble sodium succinate ester of hydrocortisone permits the immediate intravenous administration of high doses of hydrocortisone in a small volume of diluent and is particularly useful where high blood levels of hydrocortisone are required rapidly.

Following the intravenous injection of hydrocortisone sodium succinate, demonstrable effects are evident within one hour and persist for a variable period. Glucocorticoids cause profound and varied metabolic effects. In addition, they modify the body's immune response to diverse stimuli. The relative potency of methylprednisolone sodium succinate and hydrocortisone sodium succinate, as indicated by depression of eosinophil count, following intravenous administration, is five to one. This is consistent with the relative oral potency of methylprednisolone and hydrocortisone.

5.1 Pharmacokinetic properties

The pharmacokinetics of hydrocortisone in healthy male subjects demonstrated nonlinear kinetics when a single intravenous dose of hydrocortisone sodium succinate higher than 20 mg was administered, and the corresponding pharmacokinetic parameters of hydrocortisone are presented in Table 2

Table 2. Mean (SD) hydrocortisone pharmacokinetic parameters following single intravenous doses Page 14 of 17 Healthy Male Adults (21-29 years; N = 6) Dose (mg) 5 10 20 Total Exposure (AUC0-∞; ng·h/mL) 40 410 (80) 790 (100) Clearance (CL; mL/min/m2) 209 (42) 218 (23) 1480 (310) 239 (44) 2290 (260) Volume of Distribution at Steady State (Vdss; L) 294 (34) 20.7 (7.3) 20.8 (4.3) Elimination Half-life (t1/2; hr) 1.3 (0.3) 1.3 (0.2) 26.0 (4.1) 37.5 (5.8) AUC0-∞ = Area under the curve from time zero to infinity. 1.7 (0.2) 1.9 (0.1)

Absorption

Following administration of 5, 10, 20, and 40 mg single intravenous doses of hydrocortisone sodium succinate in healthy male subjects, mean peak values obtained at 10 minutes after dosing were 312, 573, 1095, and 1854 ng/mL, respectively. Hydrocortisone sodium succinate is rapidly absorbed when administered intramuscularly.

Distribution

Hydrocortisone is widely distributed into the tissues, crosses the blood-brain barrier, and is secreted in breast milk. The volume of distribution at steady state for hydrocortisone ranged from approximately 20 to 40 L (Table 2). Hydrocortisone binds to the glycoprotein transcortin (i.e., corticosteroid binding globulin) and albumin. The plasma protein binding of hydrocortisone in

humans is approximately 92%.

Biotransformation
Hydrocortisone (i.e., cortisol) is metabolized by 11β-HSD2 to cortisone, and further to dihydrocortisone and tetrahydrocortisone. Other metabolites include dihydrocortisol, 5α-dihydrocortisol, tetrahydrocortisol, and 5α-tetrahydrocortisol. Cortisone can be converted to cortisol through 11β-hydroxysteroid dehydrogenase type 1 (11β-HSD1). Hydrocortisone is also metabolized by CYP3A4 to 6β-hydroxycortisol (6β-OHF), and 6β-OHF varied from 2.8% to 31.7% of the total metabolites produced, demonstrating large inter-individual variability.

Elimination
Excretion of the administered dose is nearly complete within 12 hours. When hydrocortisone sodium succinate is administered intramuscularly, it is excreted in a pattern similar to that observed after intravenous injection.

5.2 Pre-clinical Safety:
Corticosteroids, a class of steroid hormones that includes hydrocortisone, are consistently negative in the bacterial mutagenicity assay. Hydrocortisone and dexamethasone induced chromosome aberrations in human lymphocytes in vitro and in mice in vivo.

However, the biological relevance of these findings is not clear since hydrocortisone did not increase tumor incidences in male and female rats during a 2-year carcinogenicity study. Adverse reactions not observed in clinical studies, but seen in animals at exposure levels similar to clinical exposure levels and with possible relevance to clinical use were as follows.

Corticosteroids have been shown to reduce fertility when administered to rats. The numbers of implantations and live fetuses were reduced. Corticosteroids have been shown to be teratogenic in many species when given in doses equivalent to the human dose. In animal reproduction studies, glucocorticoids have been shown to increase the incidence of malformations (cleft palate, skeletal malformations), embryo-fetal lethality (e.g., increase in resorptions), and intra-uterine growth retardation. With hydrocortisone, cleft palate was observed when administered to pregnant mice and hamsters during organogenesis

6. Pharmaceutical Particulars:

List of Excipients:
No Excipients are used.

6.2 Incompatibilities:
Not applicable

6.3 Shelf Life:
Unopened – 36 months.
After reconstitution: Use the reconstituted solution immediately. Discard any unused

solution.

6.4 Special Precautions for storage:

Store below 25°C. Protect from light.

No diluents other than those referred to are recommended. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration.

6.5 Nature and contents of container:
10ml flint glass vial with dully rubber capped and yellow colour ed flip off sealed.

6.6 Special precautions for disposal and other handling:
None.

7. Marketing Authorization Holder:
CHEZ RESOURCES PHARMACEUTICAL LIMITED,
NO 7 CALABAR STREET,
FEGGE-ONITSHA, ANAMBRA STATE

8. Manufacturer

Alpa Laboratories LTD.,
32/2, A. B. Road,
Pigdamber-453 446 Dist. Indore-(M.P.)
India.

9. Marketing Authorization Number: ---

10. Date of first Authorization /renewal of the authorization: ---

11. Date of revision of text: