Dexamethasone Médis 4 mg/ml

Summary of Product Characteristics

1. Name of the medicinal product

Dexamethasone Médis 4 mg/ml Solution for Injection

2. Qualitative and quantitative composition

Each ml of solution contains 4 mg of dexamethasone phosphate.
Each ml of solution contains 4.37 mg of dexamethasone sodium phosphate.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Solution for injection

Limpid colourless liquid

4. Clinical particulars

4.1 Therapeutic indications

Dexamethasone Médis Solution for Injection is indicated in acute conditions in which oral glucocorticoid therapy is not feasiblesuch as:

Shock: of haemorrhagic, traumatic, surgical or septic origin; cerebral oedema associated with cerebral neoplasm; inflammatory diseases of joints and soft tissue such as rheumatoid arthritis.

Short term management of acute self-limited allergic conditions such as angioneurotic oedema or acute exacerbations of chronic allergic disorders such as bronchial asthma or serum sickness.

High doses of dexamethasone are intended for the adjunctive treatment of shock where massive doses of corticosteroids are needed. There is a lack of evidence that use of corticosteroids in septic shock affects mortality in the long term. Use must be accompanied by the appropriate concomitant systemic antibiotic treatment and supportive measures which the patient's condition may require.

4.2 Posology and method of administration

N.B. All doses are expressed as mg dexamethasone base.

The lowest effective dose should be used for the minimum period and this should be reviewed frequently to appropriately titrate the dose against disease activity (See Warnings Section).

Dexamethasone Médis 4 mg/ml Solution for Injection may be administered by intramuscular, intraarticular or direct intravenous injection, intravenous infusion or soft tissue infiltration.

Intravenous and Intramuscular Administration: IM or IV dosage of dexamethasone is variable, depending on the condition being treated. It usually ranges from 0.4 to 20 mg (0.1 to 6 ml) daily. The duration of therapy is dependent on the clinical response of the patient and as soon as improvement is indicated, the dosage should be adjusted to the minimum required to maintain the desired clinical response. Withdrawal of the drug on completion of therapy should be gradual.

Shock: A single IV injection of 1.67 to 5 mg/kg (0.5 to 1.5 ml/kg) bodyweight which may be repeated in 2-6 hours if shock persists. High-dose therapy should be continued only until the patient's condition has stabilised and usually for no longer than 48-72 hours. This bolus injection can then be followed by continuous IV infusion of 2.5 mg/kg (0.75 ml/kg) bodyweight per 24 hours. Dexamethasone Médis 4 mg/ml Solution for Injection can be diluted with Sodium Chloride Injection BP or Glucose Injection BP.

Cerebral oedema associated with neoplasm: An initial dose of 8.3 mg (2.5 ml) IV followed by 3.3 mg (1.0 ml) IM every 6 hours until the symptoms of oedema subside (usually after 12 to 24 hours). After 2 to 4 days the dosage should be reduced and gradually stopped over a period of 5 to 7 days. In patients with recurrent or inoperable neoplasms, maintenance therapy may be effective at doses of 1.7 mg (0.5 ml) IM or IV 2-3 times daily.

Life-Threatening Cerebral Oedema:

High Dose Schedule (all doses are expressed as mg dexamethasone base):

	Adults	**Children > 35 kg**	**Children < 35 kg**
Initial dose	41.6 mg (12.5 ml) IV	20.8 mg IV (6.25 ml)	16.7 mg (5.0 ml) IV
1st day	6.6 mg (2.0 ml) IV every 2 hrs	3.3 mg (1.0 ml) IV every 2 hrs	3.3 mg (1.0 ml) IV every 3 hrs

2nd day	6.6 mg (2.0 ml) IV every 2 hrs	3.3 mg (1.0 ml) IV every 2 hrs	3.3 mg (1.0 ml) IV every 3 hrs
3rd day	6.6 mg (2.0 ml) IV every 2 hrs	3.3 mg (1.0 ml) IV every 2 hrs	3.3 mg (1.0 ml) IV every 3 hrs
4th day	3.3 mg (1.0 ml) IV every 2 hrs	3.3 mg (1.0 ml) IV every 4 hrs	3.3 mg (1.0 ml) IV every 6 hrs
5th – 8th day	3.3 mg (1.0 ml) IV every 4 hrs	3.3 mg (1.0 ml) IV every 6 hrs	1.7 mg (0.5 ml) IV every 6 hrs
After 8 days	Decrease by daily reduction of 3.3 mg (1.0 ml)	Decrease by daily reduction of 1.7 mg (0.5 ml)	Decrease by daily reduction of 0.8 mg (0.25 ml)

Note: The intravenous and intramuscular routes of administration of dexamethasone should only be used where acute illness or life-threatening situations exist. Oral therapy should be substituted as soon as possible.

Intraarticular and Soft Tissue Injections

Dosage varies with the degree of inflammation and the size and location of the affected area. Injections may be repeated from once every 3-5 days (e.g. for bursae) to once every 2-3 weeks (for joints).

Site of Injection	Dosage
1. Large Joint	1.7 mg to 3.3 mg (0.5 ml to 1.0 ml)
2. Small Joints	667 micrograms to 0.8 mg (0.2 ml to 0.25 ml)
3. Bursae	1.6 mg to 2.5 mg (0.5 ml to 0.75 ml)
4. Tendon Sheaths	333 micrograms to 0.8 mg (0.1 ml to 0.25 ml)
5. Soft Tissue Infiltration	1.7 mg to 5 mg (0.5 ml to 1.5 ml)
6. Ganglia	0.8 mg to 1.7 mg (0.25 ml to 0.5 ml)

Paediatric population

Dosage requirements are variable and may have to be changed according to individual need. Usually 167 micrograms/kg to 333 micrograms/kg (0.05 ml/kg to 0.1 ml/kg) of body weight daily.

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. In order to minimise suppression of the hypothalamic-pituitary-adrenal axis and growth retardation, treatment should be limited, where possible, to a single dose on alternate days.

Growth and development of infants and children on prolonged corticosteroid therapy should be carefully monitored.

Elderly

Treatment of elderly patients, particularly long-term, should be planned, bearing in mind the more serious consequences in old age. Such effects include osteoporosis, hypertension, hypokalaemia, diabetes, susceptibility to infection, thinning and fragility of the skin. Close clinical supervision is required to avoid life-threatening reactions.

4.3 Contraindications

Unless considered to be life-saving systemic administration of corticosteroids are generally contraindicated in patients with systemic infections, (unless specific anti-infective therapy is employed). Hypersensitivity to any components of the injection.

4.4 Special warnings and precautions for use

A Patient Information Leaflet should be supplied with this product.

In post marketing experience tumour lysis syndrome (TLS) has been reported in patients with haematological malignancies following the use of dexamethasone alone or in combination with other chemotherapeutic agents. Patients at high risk of TLS, such as patients with high proliferative rate, high tumour burden and high sensitivity to cytotoxic agents, should be monitored closely and appropriate precaution taken.

Patients and/or carers should be warned that potentially severe psychiatric adverse reactions may occur with systemic steroids (see section 4.8). Symptoms typically emerge within a few days or weeks of starting the treatment. Risks may be higher with high doses/systemic exposure (see also section 4.5 pharmacokinetic interactions 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 also be alert to possible psychiatric

disturbances that may occur either during or immediately after dose tapering/withdrawal of systemic steroids, although such interactions 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.

The lowest effective dose of corticosteroid should be used to control the condition under treatment for the minimum period. Frequent patient review is required to appropriately titrate the dose against disease activity (See dosage section). When dose reduction is possible, it should occur gradually. Too rapid a reduction of dexamethasone dosage following prolonged treatment can lead to acute adrenal insufficiency, hypotension and death.

A 'withdrawal syndrome' may also occur including fever, myalgia, arthralgia, rhinitis, conjunctivitis, painful itchy skin nodules and loss of weight.

Adrenal suppression: Adrenal cortical atrophy develops during prolonged therapy and may persist for years after stopping treatment. Withdrawal of corticosteroids after prolonged therapy must, therefore, be gradual to avoid acute adrenal insufficiency, being tapered off over weeks or months according to the dose and duration of treatment. During prolonged therapy any intercurrent illness, trauma or surgical procedure will require a temporary increase in dosage; if corticosteroids have been stopped following prolonged therapy they may need to be temporarily re-introduced.

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.

There is a lack of evidence to support the prolonged use of corticosteroids in septic shock. Although they may be of value in the early treatment, the overall survival may not be influenced.

Severe anaphylactoid reactions have occurred after administration of parenteral corticosteroids, particularly in patients with history of allergy. Appropriate precautions should be taken prior to administration.

The slower rate of absorption after intramuscular injection should be noted.

Intraarticular corticosteroids are associated with a substantially increased risk of an inflammatory response in the joint, particularly a bacterial infection introduced with the injection. Great care is required and all intraarticular corticosteroid injections should be undertaken in an aseptic environment. Charcot like arthropathies have been reported particularly after repeated injections.

Prior to intraarticular injection the joint fluid should be examined to exclude a septic process. A marked increase in pain, accompanied by local swelling, further restriction of joint motion, fever and malaise are suggestive of septic arthritis. If this complication occurs and sepsis is confirmed, appropriate antimicrobial therapy should be commenced.

Patients should be impressed strongly with the importance of not overusing joints in which symptomatic benefit has been obtained, but the inflammatory process remains active.

Suppression of the inflammatory response and the immune function increases the susceptibility to infections and their severity. The clinical presentation may be atypical and serious infections, such as septicaemia and tuberculosis, may be masked and may reach an advanced stage before being recognised.

Chickenpox is of particular 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 immunisation with varicella zoster immunoglobulin (VZIG) is needed by exposed non-immune patients who are receiving systemic dexamethasone or who have received it during 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. Dexamethasone should not be stopped and the dose may need to be increased.

Live vaccines should not be given to individuals with impaired immune responsiveness. The antibody response to other vaccines may be diminished.

False negative results may occur with the nitroblue tetrazolium test for bacterial infection.

Extreme caution should be exercised in the treatment of patients with the following conditions and frequent patient monitoring is necessary:

Liver failure, chronic renal failure, congestive heart failure, hypertension, epilepsy, migraine.

Osteoporosis, since corticosteroids increase calcium excretion. Post-menopausal women are at particular risk.

Latent tuberculosis, as corticosteroids can cause reactivation.

Hypothyroidism or cirrhosis, because such patients often show an exaggerated response to corticosteroids.

Latent amoebiasis, as corticosteroids may cause reactivation. Prior to treatment, amoebiasis should be ruled out in any patient with unexplained diarrhoea or who has recently spent time in the tropics.

Ocular herpes simplex, because corticosteroids may cause corneal perforation.

Corticosteroids should also be used with caution in patients with diabetes mellitus (or a family history of diabetes), affective disorders (especially previous steroid psychosis), glaucoma (or a family history of glaucoma), peptic ulceration or previous corticosteroid-induced myopathy.

Visual disturbance

Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.

Dexamethasone has been used 'off–label' to treat and prevent chronic lung disease in preterm infants. Clinical trials have shown a short term benefit in reducing ventilator dependence but no long term benefit in reducing time to discharge, the incidence of chronic lung disease or mortality. Available evidence suggests long-term neurodevelopmental adverse events after early treatment (< 96 hours) of premature infants with chronic lung disease at starting doses of 0.25mg/hg twice daily. Recent trials have suggested an association between the use of dexamethasone in preterm infants and the development of cerebral palsy. In view of this possible safety concern, an assessment of the risk: benefit should be made on an individual patient basis.

Excipient information

Dexamethasone Médis 4 mg/ml Solution for Injection contains less than 1 mmol sodium (23 mg) per 1 ml, that is to say essentially 'sodium-free'.

Paediatric population

Hypertrophic cardiomyopathy

Hypertrophic cardiomyopathy was reported after systemic administration of corticosteroids including dexamethasone to prematurely born infants, therefore appropriate diagnostic evaluation and monitoring of cardiac function and structure should be performed. In the majority of cases reported, this was reversible on withdrawal of treatment. In preterm infants treated with systemic dexamethasone diagnostic evaluation and monitoring of cardiac function and structure should be performed (section 4.8).

4.5 Interaction with other medicinal products and other forms of interaction

Liver enzyme inducing drugs such as barbiturates, ephedrine, rifampicin, rifabutin, carbamazepine, phenytoin, primidone and aminoglutethimide may enhance the metabolism of corticosteroids, resulting in a decrease in pharmacological action, and a need for dosage adjustment.

The efficacy of coumarin anticoagulants may be enhanced by concurrent corticosteroid therapy and close monitoring of prothombin time or INR is required to avoid spontaneous bleeding. Corticosteroids may affect glucose tolerance and increase the dosage requirement for hypoglycaemic drugs (including insulin).

The incidence of gastro-intestinal ulceration is increased in patients receiving concomitant non-steroidal anti-inflammatory drugs and corticosteroids.

The renal clearance of salicylates is increased by corticosteroids and steroid withdrawal may result in salicylate intoxication.

Diuretics are antagonised by corticosteroids and the hypokalaemic effects of acetazolamide, loop diuretics, thiazide diuretics and carbenoxolone are enhanced. Patients receiving corticosteroids and potassium depleting diuretics and/or cardiac glycosides, should be monitored for hypokalaemia. This is of particular importance in patients receiving cardiac glycosides, since hypokalaemia increases the toxicity of these drugs. The effects of anti-hypertensive drugs are also antagonised by corticosteroids.

Co-treatment with CYP3A inhibitors, including cobicistat-containing products, is expected to increase the risk of systemic side effects. The combination should be avoided unless the benefit outweighs the increased risk of systemic corticosteroid side-effects, in which case patients should be monitored for systemic corticosteroid effects.

4.6 Fertility, pregnancy and lactation

Pregnancy

The ability of corticosteroids to cross the placenta varies between individual drugs, however, dexamethasone readily crosses the placenta. Studies have shown an increased risk of neonatal hypoglycaemia following antenatal administration of a short course of corticosteroids including dexamethasone to women at risk for late preterm delivery.

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/lip in man. See also section 5.3 of the SmPC.

However, when administered for prolonged 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

the 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.

There is evidence of harmful effects on pregnancy in animals. Infants born to mothers who have received substantial doses of corticosteroids during the pregnancy should be carefully observed, for signs of adrenal insufficiency.

Patients with pre-eclampsia or fluid retention require close monitoring.

Breast-feeding

Corticosteroids may pass into breast milk, although no data are available for dexamethasone. Infants of mothers taking high doses of systemic corticosteroids for prolonged periods may have a degree of adrenal suppression. Suppression of growth or other adverse effects may occur.

4.7 Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

Adverse Reactions

A wide range of psychiatric reactions including affective disorders (such as irritable, euphoric, depressed and labile mood, and suicidal thoughts). Psychotic reactions (including mania, delusions, hallucinations and aggravation of schizophrenia), behavioural disturbances, irritability, anxiety, sleep disturbances and cognitive dysfunction including confusion and amnesia have been reported. Reactions are common and may occur in both adults and children. In adults the frequency of severe reactions has been estimated to be 5-6%. Psychological effects have been reported on withdrawal of corticosteroids; the frequency is unknown.

The incidence of predictable undesirable effects, including hypothalamic-pituitary-adrenal suppression correlates with the relative potency of the drug, dosage, timing of administration and the duration of treatment (see Other Special Warnings and Precautions).

High doses of dexamethasone sodium phosphate are intended for short term therapy and therefore adverse reactions are uncommon. However, peptic ulceration and bronchospasm may occur.

Except for hypersensitivity, the following adverse effects have been associated with prolonged systemic corticosteroid therapy.

Endocrine disorders:

Suppression of the hypothalamic-pituitary adrenal axis; Cushing-like syndrome.

Metabolism and nutrition disorders:

Hirsuitism and weight gain; suppression of growth in infants, children and adolescents; secondary adrenocortical unresponsiveness, particularly in times of stress, as in surgery or trauma; menstrual irregularities and amenorrhoea; impaired glucose tolerance with increased requirement for anti-diabetic therapy; hyperglycaemia; negative protein/nitrogen and calcium balance; increased appetite.

Electrolyte imbalance (retention of sodium and water with oedema and hypertension); nitrogen depletion; hyperglycaemia; hypokalaemic alkalosis; increased calcium and potassium excretion and hypertension.

Infections and Infestations:

Increased susceptibility to and severity of infection with suppression of clinical symptoms and signs; opportunistic infections; recurrence of dormant tuberculosis. (See Warnings Section).

Musculoskeletal and joint disorders:

Muscular atrophy, proximal myopathy, premature epiphyseal closure, osteoporosis, avascular osteonecrosis, muscle weakness, tendon rupture, vertebral compression and long bone fractures.

Gastro-intestinal disorders:

Dyspepsia, peptic ulceration with perforation and haemorrhage, oesophageal ulcerations, acute pancreatitis and candidiasis.

Skin and subcutaneous disorders:

Impaired wound healing; skin atrophy; bruising; telangiectasia and striae; petechiae and ecchymoses; erythema; increased sweating; possible suppression of skin tests; burning or tingling; bruising; allergic dermatitis; urticaria, candidiasis, acne.

Psychiatric and nervous system disorders:

Mental disturbances, psychological dependence, euphoria, depression, insomnia, headache, convulsions, vertigo. Aggravation of epilepsy and schizophrenia. Increased intra-cranial pressure with papilloedema in children (pseudotumour cerebri), usually after treatment withdrawal.

Eye disorders:

Posterior sub-capsular cataracts or increased intraocular pressure may result in glaucoma or occasionally damage to the optic nerve; exophthalmos papilloedema; corneal or scleral thinning; exacerbation of ophthalmic viral or fungal diseases. Chorioretinopathy, blurred vision though the frequency is unknown (see also section 4.4).

Cardiac disorders:

Hypertrophic cardiomyopathy in prematurely born infants (see section 4.4).

Other:

Hypersensitivity including anaphylaxis, has been reported; blindness associated with intralesional therapy around the face and neck; hyperpigmentation; hypopigmentation; subcutaneous and cutaneous atrophy; sterile abscess; post injection flare (following intraarticular injection): Charcot-like arthropathy, leucocytosis, thromboembolism.

Withdrawal

In patients who have received more than physiological doses of systemic corticosteroids (approximately 1 mg dexamethasone) 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 1 mg dexamethasone 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 is considered that the disease is unlikely to relapse. Abrupt withdrawal of doses up to 6 mg of dexamethasone 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 6 mg daily of dexamethasone,
- Patients repeatedly taking doses in the evening.

Withdrawal symptoms and signs: Too rapid a reduction of corticosteroid dosage following prolonged treatment can lead to acute adrenal insufficiency, hypotension and death. (See Warnings Section).

A 'withdrawal syndrome' may also occur including fever, myalgia, arthralgia, rhinitis, conjunctivitis, painful itchy skin nodules and loss of weight.

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 via the National Center of Pharmacovigilance (NCPV).

4.9 Overdose

Treat anaphylaxis with adrenaline and positive pressure ventilation. Other supportive measures aimed to maintain the patient unstressed.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacology of the corticosteroids is complex and the drugs affect almost all body systems. Maximum pharmacological activity lags behind peak blood concentrations, suggesting that most effects of the drugs result from modification of enzyme activity rather than from direct actions by the drugs.

5.2 Pharmacokinetic properties

Intramuscular injections of dexamethasone phosphate gives maximum plasma concentrations of dexamethasone at 1 hour. Dexamethasone is readily absorbed from the gastro-intestinal tract. Its biological half-life in plasma is about 190 minutes. Binding of dexamethasone to plasma proteins is less than for most other corticosteroids. Dexamethasone

penetrates into tissue fluids and cerebrospinal fluids. Metabolism of the drug takes place in the kidneys and liver and excretion is via the urine.

5.3 Preclinical safety data

In animal studies, cleft palate was observed in rats, mice, hamsters, rabbits, dogs and primates; not in horses and sheep. In some cases these divergences were combined with defects of the central nervous system and of the heart. In primates, effects in the brain were seen after exposure. Moreover, intra-uterine growth can be delayed. All these effects were seen at high dosages.

6. Pharmaceutical particulars

6.1 List of excipients

EDTA sodium, Tribasic Sodium Citrate dihydrate, Methyl parahydroxybenzoate, propyl parahydroxybenzoate, Creatinine, Water for Injections.

6.2 Incompatibilities

Dexamethasone sodium phosphate is physically incompatible with daunorubicin, doxorubicin and vancomycin and should not be admixed with solutions containing these drugs. Also incompatible with doxapram HCl and glycopyrrolate in syringe.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Keep away from light, heat and cold.

6.5 Nature and contents of container

Ampoule DEXAMETHASONE MEDIS 1 ml form D White (OPC), Box of 50 ampoules of 1ml.

6.6 Special precautions for disposal and other handling

When dexamethasone sodium phosphate is given by intravenous infusion, only Sodium Chloride Injection BP or Glucose Injection BP should be used as diluents. The exact concentration of dexamethasone per infusion container should be determined by the desired dose, patient fluid intake and drip rate required.

For single use only. The product should only be used when the solution is clear and particle free. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing authorisation holder

Les laboratoires MédiS , Route de Tunis – Km 7 – BP 206 – 8000 Nabeul – Tunisie.

8. Marketing authorisation number(s) 9233132H

9. Date of first authorisation/renewal of the autorisation

Date of first Marketing Authorisation: 31/10/2000
Date of first renewal: 31/10/2005
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10. Date of revision of the text

03/2022