1.3 Product Information

1.3.1 Summary of Product Characteristics (SmPC)

1. Name of the medicinal product

Dexamethasone sodium phosphate injection 4mg/1ml

2. Qualitative and quantitative composition700

Each 1ml of solution contains Dexamethasone sodium phosphate equivalent to dexamethasone phosphate 4mg.

3. Pharmaceutical form

Solution for injection

A clear, colourless liquid

4. Clinical particulars

4.1 Therapeutic indications

Coriticosteroids are used where their anti-inflammatory and immunosuppressive effects are desirable, including intensive treatment during shorter periods.

4.2 Posology and method of administration

All dosage recommendations are given in units of dexamethasone ***base.***

General considerations

Dosage must be individualized on the basis of the disease and the response of the patient. In order to minimize side effects, the lowest possible dosage adequate to control the disease process should be used.

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 16.6 mg (0.12 to 5 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 1.7 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 stabilized and usually for no longer than 48-72 hours.

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 6hours 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.

Life-Threatening Cerebral Oedema**:** (**all doses are expressed as mg dexamethasone base**):

High Dose Schedule	Adults	Children ≥ 35 kg	Children < 35 kg
Initial dose	41.5 mg (12.5 ml) IV	20.8 mg (6.25 ml) IV	16.6 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 of1.7 mg (0.5 ml)	Decrease by daily reduction of 0.83 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.

Dual therapy:

In acute self-limiting allergic disorders or acute exacerbations of chronic allergic disorders, the following schedule combining oral and parenteral therapy is suggested:	
First day:	Dexamethasone 4 mg/ml solution for injection, 3.3 mg – 6.6 mg (1.0 ml -2.0ml) intramuscularly
Second day:	
Third day:	Two 500µg dexamethasone tablets twice a day
Fourth day:	Two 500µg dexamethasone tablets twice a day
Fifth day:	One 500µg dexamethasone tablets twice a day
Sixth day:	One 500µg dexamethasone tablets twice a day
Seventh day:	One 500µg dexamethasone tablets once daily
Eighth day:	Reassessment day

Subcutaneous administration

In palliative care, subcutaneous Dexamethasone sodium phosphate injection 4 mg/1ml may be administered by injection or Continuous Subcutaneous Infusion (CSCI). Doses usually range between 4 mg to 16 mg over 24 hours, taking into consideration local clinical guidelines, and should be titrated according to the response.

Intraarticular, intrabursal or intralesional injection

In general, these injections are employed when only one or two joints or areas are affected.

Injections may be repeated from once every 3-5 days (e.g. for bursae) to once every 2-3 weeks (for joints).

Some of the usual single doses are:

SITE OF INJECTION	**DEXAMETHASONE DOSE**	
Large joint (e.g. knee)	1.7 mg – 3.3 mg	(0.5 ml – 1.0 ml)
Small joints (e.g. interphalangeal, temporomandibular)	0.66 mg – 0 .8 mg	(0.2 ml – 0.25 ml)

Bursae	1.7 mg – 2 .5 mg	(0.5 ml – 0.75 ml)
Tendon sheaths*	0.33 mg – 0.8 mg	(0.1 ml – 0.25 ml)
Soft-tissue infiltration	1.7 mg – 5.0 mg	(0.5 ml – 1.5 ml)
Ganglia	0.8 mg – 1.7 mg	(0.25 ml – 0.5 ml)

*Injection should be made into the tendon sheath and not directly into the tendon.

Pediatric 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. In order to minimize 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

Systemic fungal infection; systemic infection unless specific anti-infective therapy is employed; hypersensitivity to the active ingredient or any other component of this medication. Administration of live virus vaccines (see 'Special warnings and precautions for use').

4.4 Special warnings and precautions for use

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. Patient 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 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.

Frequent intraarticular injections over a prolonged period may lead to joint destruction with bone necrosis. Intraarticular injection of corticosteroid may produce systemic adverse reactions including adrenal suppression.

Undesirable effects may be minimised by using the lowest effective dose for minimum period. Frequent patient review is required to appropriately titrate the dose against disease activity. When reduction in dosage is possible, the reduction should be gradual (see 'Posology and method of administration').

Corticosteroids may exacerbate systemic fungal infections and, therefore, should not be used in the presence of such infections, unless they are needed to control drug reactions due to amphotericin. Moreover, there have been cases reported in which, concomitant use of amphotericin and hydrocortisone, was followed by cardiac enlargement and congestive failure.

Average and large doses of hydrocortisone or cortisone can cause elevation of blood pressure, retention of salt and water and increased excretion of potassium, but these effects are less likely to occur with synthetic derivates, except when used in large doses. Dietary salt restrictions and potassium supplementation may be necessary. All corticosteroids increase calcium excretion.

The slower rate of absorption by intramuscular administration should be recognised.

In patients on corticosteroid therapy subjected to unusual stress (e.g. intercurrent illness, trauma or surgical procedures), dosage should be increased before, during and after the stressful situation. Drug-induced secondary adrenocortical insufficiency may result from too rapid withdrawal of corticosteroids and may be minimised by gradual dosage reduction, being tapered off over weeks and months, depending on the dose and duration of treatment, but may persist for up to a year after discontinuation of therapy. In any stressful situation during that period, therefore, corticosteroid therapy should be reinstated. If the patient is already receiving corticosteroids, the current dosage may have to be temporarily increased. Salt and/or a mineralocorticoid should be given concurrently, since mineralocorticoid secretion may be impaired.

Stopping corticosteroids after prolonged therapy may cause withdrawal symptoms, including fever, myalgia, arthralgia and malaise. This may occur in patients even without evidence of adrenal insufficiency.

In patients who have received more than physiological doses of systemic corticosteroids (approximately 1 mg dexamethasone) for greater than three 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 hypothalamic-pituitary adrenal (HPA) suppression, the dose of systemic corticosteroids *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 three weeks is appropriate if it is considered that the disease is unlikely to relapse. Abrupt withdrawal of doses of up to 6 mg daily of dexamethasone for three 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 three weeks or less:

• patients who have had repeated courses of systemic corticosteroids, particularly if taken for greater than three 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.

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.

Because anaphylactoid reactions have occurred, rarely, in patients receiving parenteral corticosteroid therapy, appropriate precautions should be taken prior to administration, especially when the patient has a history of allergy to any drug.

Administration of live virus vaccines is contraindicated in individuals receiving immunosuppressive doses of corticosteroids. If inactivated viral or bacterial vaccines are administered to individuals receiving immunosuppressive doses of corticosteroids, the expected serum antibody response may not be obtained. However, immunisation procedures may be undertaken in patients who are receiving corticosteroids as replacement therapy, e.g. for Addison's disease.

Literature reports suggest an apparent association between use of corticosteroids and left ventricular free wall rupture after a recent myocardial infarction; therefore, therapy with corticosteroids should be used with great caution in these patients.

The use of Dexamethasone 4 mg/ml solution 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 an appropriate antituberculosis regimen. If the corticosteroids are indicated in patients with latent tuberculosis or tuberculin reactivity, close observation is necessary as reactivation may occur. During prolonged corticosteroid therapy, these patients should receive prophylactic chemotherapy.

Corticosteroids may mask some signs of infection and new infections may appear during their use. Suppression of the inflammatory response and immune function increasing the susceptibility to infections and their severity. The clinical presentation may often be atypical and serious

infections such as septicaemia and tuberculosis may be masked and reach an advanced stage before being recognised. There may be decreased resistance and inability to localise infection.

A report shows that the use of corticosteroids in cerebral malaria is associated with a prolonged coma and an increased incidence of pneumonia and gastro-intestinal bleeding.

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 corticosteroids or who have used them within the previous three month; this should be given within ten 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.

Measles can have a more serious or even fatal course in immunosuppressed patients. In such children or adults particular care should be taken to avoid exposure to measles. If exposed, prophylaxis with intramuscular pooled immunoglobulin (IG) may be indicated. Exposed patients should be advised to seek medical advice without delay.

Corticosteroids may activate latent amoebiasis or strongyloidiasis or exacerbate active disease. Therefore, it is recommended that latent or active amoebiasis and strongyloidiasis be ruled out, before initiating corticosteroid therapy in any patient at risk of or with symptoms of either condition.

Prolonged use of corticosteroids may produce posterior subcapsular cataracts, glaucoma with possible damage to the optic nerves and may enhance the establishment of secondary ocular infections due to fungi or viruses.

Corticosteroids may increase or decrease motility and number of spermatozoa.

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 side-effects.

This medicinal product contains up to 1.9 mmol (or 43 mg) sodium per maximum single dose of the medicinal product (350 mg for a person with 70 kg bodyweight). To be taken into consideration by patients on a controlled sodium diet.

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: renal insufficiency, hypertension, diabetes or in those with a family history of diabetes, congestive heart failure, osteoporosis, previous steroid myopathy, glaucoma (or family history of glaucoma), myasthenia gravis, non-specific ulcerative colitis, diverticulitis, fresh intestinal anastomoses, active or latent peptic ulcer, existing or previous history of severe affective disorders (especially previous steroid psychosis), liver failure and epilepsy. Signs of peritoneal irritation, following gastrointestinal perforation in patients receiving large doses of corticosteroids, may be minimal or absent. Fat embolism has been reported as a possible complication of hypercortisonism.

There is an enhanced effect of corticosteroids in patients with hypothyroidism and in those with cirrhosis.

Corticosteroids should be used cautiously in patients with ocular herpes simplex because of possible corneal perforation.

Local steroid injection should be undertaken in an aseptic environment to reduce the particular risk of bacterial infection, injection of a steroid into an infected site should be avoided.

Appropriate examination of joint fluids is necessary 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 the diagnosis of sepsis is confirmed, appropriate antimicrobial therapy should be instituted.

Patients should understand the great importance of not over-using joints that are still diseased, despite symptomatic improvement.

Corticosteroids should not be injected into unstable joints.

Frequent intraarticular injections have been reported to cause development of Charcot-like arthropathies.

<u>Paediatric population</u>

Preterm neonates:

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/kg twice daily.

Children:

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 hypothalamo-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.

Dexamethasone has been used to treat and prevent chronic lung disease in preterm infants (unlicensed use). Clinical trials have shown no long term benefit in reducing time to discharge, the incidence of chronic lung disease or mortality. 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.

4.5 Interaction with other medicinal products and other forms of interaction

Aspirin should be used cautiously in conjunction with corticosteroids in hypoprothrombinaemia.

The renal clearance of salicylates is increased by corticosteroids and therefore salicylate dosage should be reduced along with steroid withdrawal.

As phenytoin, barbiturates, ephedrine, rifabutin, carbamazepine, rifampicin and aminoglutethimide may enhance the metabolic clearance of corticosteroids, resulting in decreased blood levels and reduced physiological activity, the dosage may have to be adjusted. These interactions interfere with dexamethasone suppression tests which should be interpreted with caution during administration of these drugs.

False-negative results in the dexamethasone suppression test in patients being treated with indometacin have been reported.

The efficacy of coumarin anticoagulants may be changed by concurrent corticosteroid treatment. The prothrombin time should be checked frequently in patients who are receiving corticosteroids and coumarin anticoagulants at the same time, in order to avoid spontaneous bleeding.

The desired effects of hypoglycaemic agents (including insulin) are antagonised by corticosteroids.

When corticosteroids are administered concomitantly with potassium-depleting diuretics, patients should be observed closely for development of hypokalaemia.

Corticosteroids may affect the nitroblue tetrazolium test for bacterial infection and produce false-negative results.

Antiretroviral protease inhibitors (ritonavir, darunavir, indinavir, lopinavir, saquinavir and efavirenz) are metabolised by CYP3A. Medicinal products that induce CYP3A activity, such as dexamethasone, may increase the clearance of medicines metabolised by CYP3A, resulting in lowered plasma concentrations.

Certain antiretroviral protease inhibitors (ritonavir, indinavir) may also be inhibitors of CYP3A themselves and as a result may increase the plasma concentration of dexamethasone.

4.6 Pregnancy and lactation

Pregnancy

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

Administration of corticosteroids to pregnant animals can cause abnormalities of foetal development including cleft palate, intrauterine growth retardation and effects 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 intrauterine 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 non-gravid state.

Lactation

Corticosteroids appear in breast milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other unwanted effects. Mothers taking pharmacologic doses

of corticosteroids should be advised not to nurse.

4.7 Undesirable effects

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 'Special warnings and precautions for use').

Fluid and electrolyte disturbances:

Sodium retention, fluid retention, congestive heart failure in susceptible patients, potassium loss, hypokalaemic alkalosis, hypertension, increased calcium excretion (see 'Special warnings and precautions for use')

Musculoskeletal:

Muscle weakness, steroid myopathy, loss of muscle mass, osteoporosis (especially in post-menopausal females), vertebral compression fractures, aseptic necrosis of femoral and humeral heads, pathological fracture of long bones, tendon rupture and post-injection flare (following intraarticular use')

Gastrointestinal:

Peptic ulcer with possible perforation and haemorrhage, perforation of the small and large bowel, particularly in patients with inflammatory bowel disease, pancreatitis, abdominal distension, ulcerative oesophagitis, dyspepsia, oesophageal candidiasis

Dermatological:

Impaired wound healing, thin fragile skin, petechiae and ecchymoses, erythema, striae, telangiectasia, acne, increased sweating, possible suppression of skin tests, burning or tingling especially in the perineal area (after intravenous injection), other cutaneous reactions such as allergic dermatitis, urticaria, angioneurotic oedema and hypo- or hyper-pigmentation

Neurological:

Convulsions, increased intracranial pressure with papilloedema (pseudotumour cerebri) usually after treatment, vertigo, headache, cerebral palsy in pre-term infants

Psychiatric:

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.

Endocrine:

Menstrual irregularities, amenorrhoea, development of Cushingoid state, suppression of growth in children and adolescents, secondary adrenocortical and pituitary unresponsiveness (particularly in times of stress as in trauma, surgery or illness), decreased carbohydrate tolerance, manifestation of latent diabetes mellitus, increased requirements for insulin or oral hypoglycaemic agents in diabetes, hirsutism

Anti-inflammatory and immunosuppressive effects:

Increased susceptibility and severity of infections with suppression of clinical symptoms and signs; opportunistic infections, recurrence of dormant tuberculosis (see 'Special warnings and precautions for use')

Ophthalmic:

Posterior subcapsular cataracts, increased intraocular pressure, papilloedema, corneal or scleral thinning, exacerbation of ophthalmic viral disease, glaucoma exophthalmos, rare instances of blindness associated with intralesional therapy around the face and head, retinopathy of prematurity, chorioretinopathy.

Metabolic:

Negative nitrogen balance due to protein catabolism, negative calcium balance

Cardiovascular:

Myocardial rupture following recent myocardial infarction (see 'Special warnings and precautions for use'), hypertrophic cardio-myopathy in low birth weight infants

Other:

Hypersensitivity, including anaphylaxis has been reported, leucocytosis, thrombo-embolism, weight gain, increased appetite, nausea, malaise, hiccups and sterile abscess.

Multiple myeloma patients treated with lenalidomide or thalidomide in combination with dexamethasone have an increased risk of thromboembolic events including deep vein thrombosis and pulmonary embolism.

Withdrawal symptoms and signs

Too rapid a reduction of corticosteroid dosage following prolonged treatment can lead to acute adrenal insufficiency, hypotension and death (see 'Special warnings and precautions for use')

In some instances, withdrawal symptoms may simulate a clinical relapse of the disease for which the patient has been undergoing treatment.

4.8 Overdose

Reports of acute toxicity and/or deaths following overdosage with glucocorticoids are rare. No antidote is available. Treatment is probably not indicated for reactions due to chronic poisoning, unless the patient has a condition that would render a patient unusually susceptible to ill effects from corticosteroids. In this case, symptomatic treatment should be instituted as necessary.

Anaphylactic and hypersensitivity reactions may be treated with adrenaline, positive-pressure artificial respiration and aminophylline. The patient should be kept warm and quiet.

The biological half-life of dexamethasone in plasma is about 190 minutes.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Glucocorticoids

ATC code: H02AB02

Dexamethasone possesses the actions and effects of other basic glucocorticoids and is among the most active members of its class.

Glucocorticoids are adrenocortical steroids, both naturally occurring and synthetic, which are readily absorbed from the gastrointestinal tract. They cause profound and varied metabolic effects and in addition, they modify the body's immune responses to diverse stimuli.

Naturally-occurring glucocorticoids (hydrocortisone and cortisone), which also have salt-retaining properties, are used primarily for their potent anti-inflammatory effects in disorders of many organ systems.

Dexamethasone has predominant glucocorticoid activity with little propensity to promote renal retention of sodium and water. Therefore it does not offer complete replacement therapy and must be supplemented with salt or desoxycorticosterone.

5.2 Pharmacokinetic properties

The biological half-life of dexamethasone in plasma is about 190 minutes.

Binding of dexamethasone to plasma proteins is less than for most other corticosteroids and is estimated to be about 77%.

Up to 65% of a dose is excreted in the urine in 24 hours, the rate of excretion being increased following concomitant administration of phenytoin.

The more potent halogenated corticosteroids such as dexamethasone, appear to cross the placental barrier with minimal inactivation.

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

Nicotinamide

Sodium bisulfite

Anhydrous sodium sulphite

Disodium edetate

Water for injection

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Three years.

6.4 Special precautions for storage

Store below 30 ℃.

6.5 Nature and contents of container

Glass ampoule

7. Marketing authorisation holder

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