Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Dexamethasone Phosphate 4 mg/ml Solution for Injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each millilitre (ml) of solution contains 3.32 milligrams (mg) dexamethasone (as sodium phosphate) which is equivalent to 4.00 mg of dexamethasone phosphate or 4.37 mg dexamethasone sodium phosphate.

Each 2 ml of solution contains 6.64 mg dexamethasone (as sodium phosphate) which is equivalent to 8.00 mg of dexamethasone phosphate or 8.74 mg dexamethasone sodium phosphate.

Excipients with known effect:

Each ml of solution contains 0.07 mg of sodium sulfite (E 221). Each vial of 2 ml of solution contains 0.14 mg of sodium sulfite (E 221).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection.

Clear, colourless solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

In the management of acute adrenocortical insufficiency, pre and post operative support, shock and in the active management of corticosteroid responsive conditions.

In the management of inflammatory diseases of joints and soft tissue such as rheumatoid arthritis.

In the 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.

4.2 Posology and method of administration

Route of Administration:

Intravenous
Intramuscular
Intra-articular and intralesional

Recommended Dosage:

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

The usual dosage is 0.5-24 mg daily depending on the individual patient's condition and response.

In Shock:
Usually a dose of 2 to 6 mg/kg bodyweight is given intravenously as a single dose. This may be repeated if required, in 2 to 6 hours, or followed by the same dose as an intravenous infusion**.**

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 3 mg/kg bodyweight per 24 hours.

Dexamethasone Injection can be diluted with Sodium Chloride Injection B.P. or Glucose Injection B.P.

In Cerebral Oedema:
Initially 10 mg is given intravenously followed by 4 mg intramuscularly every 6 hours. When response occurs dosage may be gradually reduced and stopped over 5-7 days. If required, maintenance therapy may be effective at doses of 2 mg IM or IV 2-3 times daily.

Life-Threatening Cerebral Oedema**:**

High Dose Schedule**:**

	Adults	Children > 35 kg	Children < 35 kg
Initial dose	50 mg IV	25 mg IV	20 mg IV
1st day	8 mg IV every 2 hrs	4 mg IV every 2 hrs	4 mg IV every 3 hrs
2nd day	8 mg IV every 2 hrs	4 mg IV every 2 hrs	4 mg IV every 3 hrs
3rd day	8 mg IV every 2 hrs	4 mg IV every 2 hrs	4 mg IV every 3 hrs
4th day	4 mg IV every 2 hrs	4 mg IV every 4 hrs	4 mg IV every 6 hrs
5th – 8th day	4 mg IV every 4 hrs	4 mg IV every 6 hrs	2 mg IV every 6 hrs
After 8 days	Decrease by daily reduction of 4 mg	Decrease by daily reduction of 2 mg	Decrease by daily reduction of 1 mg

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

Intra-Articular 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 2 mg to 4 mg

2. Small Joints 800 microgram to 1 mg

3. Bursae 2 mg to 3 mg

4. Tendon Sheaths 400 microgram to 1 mg

5. Soft Tissue Infiltration 2 mg to 6 mg

6. Ganglia 1 mg to 2 mg

Paediatric population:
Dosage requirements are variable and may have to be changed according to individual need. Usually 200 micrograms/kg to 400 micrograms/kg of body weight daily.

Corticosteroids cause growth retardation in infancy, childhood and adolescence**.** 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.

4.3 Contraindications

Hypersensitivity to the active substance, sulfites or to any of the excipients listed in section 6.1.

Use in patients with peptic ulcer, active tuberculosis, acute psychosis, acute bacterial or viral infection. Systemic infection unless specific anti-infective therapy is employed.

Local injection in:

- bacteraemia
- systemic fungal infections
- unstable joints
- infection at the injection site e.g. septic arthritis resulting from gonorrhoea or tuberculosis

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 therapeutic 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.

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.

Patients currently on corticosteroid therapy or those who have been on such treatment within the previous year may require special control measures if involved in anaesthesia, surgical procedures and other stress.

Withdrawal of corticosteroids should always be gradual and related to the duration of use. Too rapid a reduction of dexamethasone dosage following prolonged treatment can lead to acute adrenal insufficiency, hypotension and death.

A withdrawal syndrome may occur. Withdrawal may result in acute rebound exacerbation of disease, acute adrenocortical insufficiency, polyarteritis. Symptoms of this may include fever, myalgia, arthralgia, rhinitis, conjunctivitis, painful itchy skin nodules and loss of weight.

In patients who have received more than physiological doses of systemic corticosteroids (approximately 1 mg dexamethasone (equivalent to 1.2 mg dexamethasone phosphate)) 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 (equivalent to 7.3 mg dexamethasone phosphate) 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. 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 treatment 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, such as glottis oedema, urticaria and bronchospasm, particularly in patients with a history of allergy. Appropriate precautions should be taken prior to administration. If such an anaphylactoid reaction occurs, the following measures are recommended: immediate slow intravenous injection of adrenaline, intravenous administration of aminophylline, and artificial respiration if necessary. The slower rate of absorption after intramuscular injection should be noted. Intra-articular 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 intra-articular corticosteroid injections should be undertaken in an aseptic environment. Charcot-like arthropathies have been reported particularly after repeated injections. Prior to intra-articular 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. Corticosteroids may mask some signs of infection, decrease resistance and inhibit localisation of infection. 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. Live vaccines should not be given to individuals with impaired immune responsiveness. The antibody response to other vaccines may be diminished. 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 chicken pox 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 immunoglobin (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. 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 pooled immunoglobin may be indicated. Exposed patients should be advised to seek medical advice without delay.Prolonged use of corticosteroids may produce posterior subcapsular cataracts, glaucoma with possible damage to the optic nerve and may enhance the establishment of secondary ocular infections due to fungi or viruses. 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, renal insufficiency, gastro-intestinal ulceration, congestive heart failure, hypertension, epilepsy, migraine and patients with Cushing's syndrome
- 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.
- Certain parasitic infestations, in particular amoebiasis. 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.
- Incomplete statural growth since glucocorticoids on prolonged administration may accelerate epiphyseal closure.
- In the treatment of conditions such as tendinitis or tenosynovitis care should be taken to inject into the space between the tendon sheath and the tendon as cases of ruptured tendon have been reported. Corticosteroids should also be used with caution in patients with diabetes mellitus (or a family history of diabetes), affective disorders, glaucoma (or a family history of glaucoma), 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.

The use of corticosteroids in the presence of other disorders or of drugs with specific actions (e.g hypoglycaemics), impinging on the effects of corticosteroids will result in imbalance of control.

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. 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.

In view of multiple adverse effects noted in premature infants who received dexamethasone, the risks in many cases outweigh the benefits. Very serious consideration should therefore be given before dexamethasone is administered to such patients.

Available evidence suggests long-term neurodevelopmental adverse events after early treatment (< 96 hours) of premature infants with chronic lung disease at starting doses of 0.25 mg/hg twice daily.

Prolonged use in children may lead to growth retardation. Some recovery may occur on discontinuing therapy.

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 reaction.
Corticosteroids should not be used for the management of head injury or stroke because it is unlikely to be of any benefit and may even be harmful.

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.

Patient/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.

The results of a randomised, placebo-controlled study suggest an increase in mortality if methylprednisolone therapy starts more than two weeks after the onset of Acute Respiratory Distress Syndrome (ARDS). Therefore, treatment of ARDS with corticosteroids should be initiated within the first two weeks of onset of ARDS.
Pheochromocytoma crisis
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.
Excipient Information:
This medicinal product contains less than 1 mmol sodium (23 mg) per 2ml, that is to say essentially 'sodium-free'.

The excipient, sodium sulfite may rarely cause severe hypersensitivity reactions and bronchospasm.

The vial stopper contains dry natural rubber (a derivative of latex), which may cause allergic reactions.

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

Concurrent administration of barbiturates, phenylbutazone, phenytoin may increase the metabolism of corticosteroids, while if anticoagulants are given with the corticosteroid, adjustment of dosage of the former is usually necessary.

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

The prothrombin time of patients undergoing concomitant treatment with corticosteroids and coumarin anti-coagulants should be checked frequently.

Corticosteroids may affect glucose tolerance and increase theneed for anti-diabetic drugs.

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

Salicylate intoxication has been reported to occur when adjustment is made to corticosteroid dosage, in patients concomitantly receiving aspirin. The renal clearance of salicylates is increased by corticosteroids and steroid withdrawal may result in salicylate intoxication. There may be interaction with salicylates in patients with hypoprothrombinaemia.

The desired effects of hypoglycaemic agents (including insulin), anti-hypertensives, cardiac glycosides and 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.
Live virus vaccines should not be administered to patients on immunosuppressant doses of corticosteroids. If inactivated vaccines are administered to such individuals, the expected serum antibody response may not be obtained.

The effects of anticholinesterases are antagonised by corticosteroids in myasthenia gravis.
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:

Corticosteroids should only be used during pregnancy or lactation if considered essential by the physician. Corticosteroids have been shown to be teratogenic in animals. To date there is no confirmed report of a similar effect in human beings.

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 fetal 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 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.

Breastfeeding:

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.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

Corticosteroid administration will result in certain effects, the severity, significance and extent of which vary with the dosage and duration of treatment and the particular corticosteroid used.
High doses of Dexamethasone 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:
Weight gain; suppression of growth in infants, children and adolescents; secondary adrenocortical unresponsiveness, particularly in times of stress, as in surgery or trauma; 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.

Reproductive system and breast disorders:
Menstrual irregularities and amenorrhoea; a transient burning or tingling sensation mainly in the perineal area following intravenous injection of large doses of corticosteroid phosphates.

Infections and Infestations:
Increased susceptibility to and severity of infection with suppression of clinical symptoms and signs; opportunistic infections; recurrence of dormant tuberculosis, exacerbation of ophthalmic viral or fungal diseases, candidiasis.

Musculoskeletal and joint disorders:
Charcot-like arthropathy, muscular atrophy, proximal myopathy, premature epiphyseal closure, osteoporosis, avascular osteonecrosis, muscle weakness.

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; allergic dermatitis; urticaria, candidiasis, acne, hyperpigmentation; hypopigmentation; subcutaneous and cutaneous atrophy; sterile abscess, hirsuitism, panniculitis (frequency not known)*.
*Few cases of panniculitis have been reported following dose reduction or discontinuation of therapy, especially after long-term, high-dose treatment. Panniculitis is more common in paediatric patients than in adults, and most cases resolve spontaneously.

Psychiatric disorders:
Mental disturbances, psychological dependence, affective disorders (such as euphoria, depression, irritable labile mood and suicidal thoughts), psychotic reactions (including mania, delusions, hallucinations, and aggravation of schizophrenia)**,** behavioral disturbances, irritability, anxiety, insomnia, confusion.

Nervous System disorders:
Aggravation of epilepsy. Increased intra-cranial pressure with papilloedema in children (pseudotumour cerebri), usually after treatment withdrawal, headache, convulsions, vertigo, cognitive dysfunction and amnesia.

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, blindness

associated with intralesional therapy around the face and neck. Chorioretinopathy, blurred vision though the frequency is unknown (see also section 4.4).

Immune system disorders:
Diminished immune response, decreased responsiveness to vaccination and skin tests,hypersensitivity including anaphylaxis has been reported.

General disorders and administration site conditions:
Post injection flare (following intra-articular injection), impaired healing.

Blood and lymphatic disorders:
Diminished lymphoid tissue,leucocytosis.

Vascular disorders:
Hypertension, thromboembolism.

Respiratory, thoracic and mediastinal disorders:
Hiccups (frequency not known).

Injury, poisoning, and procedural complications:
Vertebral and long bone fractures, tendon rupture, bruising.
Cardiac disorders:
Hypertrophic cardiomyopathy in prematurely born infants (see section 4.4).

Withdrawal

Withdrawal symptoms and signs: Too rapid a reduction of corticosteroid dosage following prolonged treatment can lead to acute adrenal insufficiency, hypotension and death (*see section 4.4, Special warnings and precautions for use*).

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

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 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.

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 HPRA Pharmacovigilance.
Website: www.hpra.ie.

4.9 Overdose

It is difficult to define an excessive dose of a corticosteroid as the therapeutic dose will vary according to the indication and patient requirements. High-dose corticosteroids given as recommended for pulse therapy are relatively free from hazardous effects.

Exaggeration of corticosteroid related adverse effects may occur. Treatment should be asymptomatic and supportive as necessary.

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

Sodium Citrate
Disodium edetate
Sodium sulfite, anyhydrous (E221)
Sodium Hydroxide (for pH adjustment)
Hydrochloric Acid (for pH adjustment)
Water for Injection

6.2 Incompatibilities

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

6.3 Shelf life

As packaged for sale – 24 months.

In use: Following dilution in sodium chloride 0.9% w/v injection BP or glucose 5% w/v injection BP, chemical and physical in-use stability has been demonstrated for 24 hours at a temperature not exceeding 25ºC.

From a microbiological point of view, use the product immediately. If you do not use the product immediately, store in the fridge at 2-8ºC for no longer than 24 hours from the time of preparation. The in-use storage times and conditions prior to use are the responsibility of the user. Dilute in controlled and validated aseptic conditions.

6.4 Special precautions for storage

As packaged for sale: Do not store above 25ºC. Do not freeze. Keep vial in the outer carton in order to protect from light.

In use: *see section 6.3, Shelf life and section 6.6, Special precautions for disposal and other handling.*

6.5 Nature and contents of container

Amber Type I glass vial containing 2 ml of solution, with a chlorobutyl-based stopper in cartons of 5 vials.

6.6 Special precautions for disposal and other handling

For single use only.

When dexamethasone phosphate is given by intravenous infusion, only Sodium Chloride 0.9% w/v Injection BP or Glucose 5% w/v Injection BP should be used as diluents. The exact concentration of dexamethasone (as phosphate) per infusion container should be determined by the desired dose, patient fluid intake and drip rate required.

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

Pfizer Healthcare Ireland Unlimited Company
The Watermarque Building
Ringsend Road
Dublin 4
D04 K7N3
Ireland

8 MARKETING AUTHORISATION NUMBER

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10 DATE OF REVISION OF THE TEXT

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