1.3.1.1 PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

DECASONE INJECTION 4 mg/ml

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 ml ampoule contains 4,0 mg dexamethasone phosphate as the disodium salt.

Antioxidant: Sodium metabisulfite 0,1 % *m/v* .

Sugar free.

Each 1 ml injection contains 0,150 mmol Sodium

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for Injection.

DECASONE INJECTION 4 mg/ml is a clear, colourless to slight yellowish solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

DECASONE INJECTION 4 mg/ml is indicated in:

- Conditions where the anti-inflammatory and immunosuppressive effects of a corticosteroid are desirable, including intensive treatment during shorter periods.
- Decasone injections does not replace other forms of therapy for the treatment of shock and status asthmaticus.
- The treatment of coronavirus disease 2019 (COVID-19) in adult and adolescent patients (aged 12 years and older with body weight at least 40 kg) who require supplemental oxygen therapy.

4.2 Posology and method of administration

Posology

Adults

DECASONE INJECTION 4 mg/ml should not be administered intrathecally or subconjunctivally.

Usual adult dosage ranges from 0,5 mg to 20 mg daily depending on the severity of the disorder. DECASONE INJECTION 4 mg/ml may be administered intravenously or intramuscularly.

The parenteral administration must be reserved for administration in emergencies and intensive therapy (see Method of Administration below).

Intra-articular, intra-lesional, intra-muscular or soft-tissue injection:

0,8 mg to 4 mg (depending on the size of the joint).

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 section 4.4).

For the treatment of COVID-19

6 mg IV once a day for up to 10 days.

Duration of treatment should be guided by clinical response and individual patient requirements.

Special populations

Elderly, renal impairment, hepatic impairment

No dose adjustment is needed.

Elderly population

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.

Paediatric population

Corticosteroids cause growth retardation in infancy, childhood and adolescence, which may be irreversible. Treatment should be limited to the minimum dosage for the shortest

possible time. In order to minimise suppression of the HPA axis and growth retardation, consideration should be given to administration of single dose on alternate days.

For treatment of COVID-19

Paediatric patients (adolescents aged 12 years and older) are recommended to take 6 mg dose IV once a day for up to 10 days.

Duration of treatment should be guided by clinical response and individual patient requirements.

Method of administration

DECASONE INJECTION 4 mg/ml may be administered intravenously or intramuscularly.

For COVID-19 treatment: IV dose recommended

The parenteral administration must be reserved for administration in emergencies and intensive therapy.

Not for intrathecal use – contains sulphites (see section 4.4).

4.3 CONTRAINDICATIONS

DECASONE INJECTION 4 mg/ml is contraindicated in:

- Patients with hypersensitivity to dexamethasone, corticosteroids or to any excipients in DECASONE INJECTION 4 mg/ml (see section 6.1).
- Patients with a known hypersensitivity to sulphites.
- Active or latent tuberculosis.
- Ocular herpes simplex.

- Primary glaucoma.
- Acute psychosis and psychoneurosis.
- Systemic infection, unless specific anti-infective therapy is employed.
- Active peptic ulcer.
- Osteoporosis.
- Administration of live virus vaccines (see section 4.4).
- Local injection in bacteraemia and systemic fungal infections, unstable joints, infection at the injection site e.g. septic arthritis resulting from gonorrhoea or tubercolosis.

4.4 Special warnings and precautions for use

Hypersensitivity/ serious anaphylactoid reactions

After parenteral administration of glucocorticoids serious anaphylactoid reactions, such as glottis oedema, have been reported. Urticarial and bronchospasm, have occurred, particularly in patients with history of allergy. If such an anaphylactoid reaction occurs, the following measures are recommended: immediate slow intravenous injection of 0,1 to 0,5 ml of adrenaline (solution 1:1 000:0,1 to 0,5 mg adrenaline dependent on body weight), intravenous administration of aminophylline and artificial respiration, if necessary.

Patients receiving long courses of DECASONE INJECTION 4 mg/ml should be regularly checked for hypertension, glycosuria, hypokalaemia, gastric discomfort, and mental changes. Sodium intake may need to be reduced and potassium supplements may be necessary. Monitoring of the fluid intake and output and daily weight records may give early warning of fluid retention.Back pain may signify osteoporosis.

Appropriate precautions should be taken prior to DECASONE INJECTION 4 mg/ml administration.

Anaphylactoid/ anaphylactic reactions with a possibility of shock have occurred in patients receiving parenteral corticosteroid therapy, such as DECASONE INJECTION 4 mg/ml. Appropriate precautionary measures should be taken with patients who have a history of allergic reactions to corticosteroids (see section 4.3).

Psychiatric adverse reactions

Patients/and or caregivers should be warned that psychiatric adverse reactions may occur with systemic steroids such as DECASONE INJECTION 4 mg/ml (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, 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 supportive treatment may be necessary.

Patients/ caregivers should be encouraged to seek medical advice if worrying psychological symptoms develop, especially if depressed mood or suicidal ideation is suspected. Patients/ caregivers should also be alert to possible psychiatric disturbances that may occur either during or immediately after dose tapering/withdrawal of DECASONE INJECTION 4 mg/ml. Patients with existing or previous history of severe affective disorders (including depressive or bipolar illness and previous steroid psychosis) or their first-degree relatives, are at high risk for developing psychiatric adverse events. These would include depressive and/ or manic-depressive illness and previous steroid psychosis.

Tumour lysis syndrome (TLS)

Tumour lysis syndrome (TLS) has been reported in patients with haematological malignancies following the use of DECASONE INJECTION 4 mg/ml alone or in combination with other chemotherapeutic medicines. Patients at high risk of TLS, such as patients with high proliferative rate, high tumour burden, and high sensitivity to cytotoxic medicines, should be monitored closely and appropriate precautions taken.

Dexamethasone formulations-containing sulphites

Dexamethasone formulations such as DECASONE INJECTION 4 mg/ml, containing sulphites should not be used for intrathecal therapy. This sulphite-containing formulation has an altered risk profile compared to other sulphite-free formulations; there is a potential risk of neurotoxicity when administered intrathecally.

The excipient sodium sulphite may cause severe hypersensitivity reactions and bronchospasm.

Undesirable effects may be minimised by using the lowest effective dose for the minimum period, and by administering the daily requirements as a single morning dose or, whenever possible as a single morning dose on alternative days.

The lowest effective dose of corticosteroid should be used to control the condition under treatment for the minimum period. When dose reduction is possible, it should occur gradually. Too rapid a reduction of dexamethasone, as in DECASONE INJECTION 4

mg/ml,dosage following prolonged treatment can lead to acute adrenal insufficiency, hypotension and death.

Frequent patient review is required to appropriately titrate the dose against disease activity.

Pheochromocytoma crisis, which can be fatal, has been reported after administration of systemic corticosteroids. DECASONE INJECTION 4 mg/ml should only be administered to patients with suspected or identified pheochromocytoma after an appropriate risk/benefit evaluation.

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

Toxic effects may result from withdrawal or from continued use of large doses.

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.

Steroid treatment cards

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, medicine, dosage and the duration of treatment.

Head injury or stroke

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.

Septic shock

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.

Visual disturbance

Visual disturbance have been 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 corticosteroids, as in DECASONE INJECTION 4 mg/ml.

False negatives

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

General

The slower rate of absorption after an 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.

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.

Extreme caution is required when considering the use of DECASONE INJECTION 4 mg/ml in patients with the following conditions and frequent patient monitoring is necessary:

- Uncontrolled hypertension or congestive heart failure.
- Diabetes mellitus (or a family history of diabetes).
- History of tuberculosis, since glucocorticoids may induce reactivation.
- Peptic ulceration.
- Previous corticosteroid-induced myopathy.
- Hepatic failure (liver failure, chronic renal failure)
- Renal insufficiency.
- Epilepsy.
- Gastrointestinal ulceration.
- Migraine.
- Certain parasitic infestations in particular amoebiasis.
- Incomplete stature growth since glucocorticoids on prolonged administration may accelerate epiphyseal closure.
- Patients with Cushing's syndrome.
- Osteoporosis, since corticosteroids increase calcium excretion (post-menopausal females are particularly at risk).
- Existing or previous history of severe affective disorders (especially previous steroid psychosis).
- Glaucoma(or a family history of glaucoma)

- 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.
- Diverticulitis
- Thrombembolism
- Recent myocardial infarction
- Myasthenia gravis

Use in elderly patients

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

High doses administered during pregnancy may cause foetal or neonatal adrenal suppression.

Quiescent tuberculosis

Patients with active or doubtfully quiescent tuberculosis should not be given DECASONE INJECTION 4 mg/ml except, very rarely as adjuncts to treatment with

antituberculosis medicines. Patients with quiescent tuberculosis should be observed closely and should receive chemoprophylaxis if DECASONE INJECTION 4 mg/ml therapy is prolonged, for 1 month or longer (see section 4.3).

Anti-inflammatory/immunosuppressive effects and infection

Patients already receiving DECASONE INJECTION 4 mg/ml are more susceptible to infection, the symptoms of which may be masked until an advanced stage has been reached.The clinical presentation may often be atypical, and serious infections such as septicaemia and tuberculosis may be masked and may reach an advanced stage before being recognised. Appropriate antimicrobial therapy should accompany glucocorticoids therapy when necessary e.g. in tuberculosis and rival and fungal infections of the eye.

Use of vaccines

Because of the risk of precipitating a serious infection, live vaccines should not be given to patients receiving high-dose DECASONE INJECTION 4 mg/ml therapy; killed vaccines or toxoids may be given although the response may be attenuated.
If inactivated viral or bacterial vaccines are administered to individuals receiving immunosuppressive doses of DECASONE INJECTION 4 mg/ml, the expected serum antibody response may not be attained.

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 DECASONE INJECTION 4 mg/ml or who have used

systemic corticosteroids within the previous three months; 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. DECASONE INJECTION 4 mg/ml 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.

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.

Infections should be treated as an emergency.
Patients should carry cards - and preferably also wear bracelets - giving full details of their therapy; they and their relatives should be fully conversant with the implications of their therapy and the precautions to be taken.

Large doses of DECASONE INJECTION 4 mg/ml should be given slowly or by infusion to prevent cardiovascular collapse.
High doses of DECASONE INJECTION 4 mg/ml should not be used for prolonged treatment.

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.

Withdrawal

In patients on DECASONE INJECTION 4 mg/ml therapy subjected to unusual stress (e.g., intercurrent illness, trauma or surgical procedures), dosage should be increased before, during and after the stressful situation. Medicine-induced secondary adrenocortical insufficiency may result from too rapid withdrawal of DECASONE INJECTION 4 mg/ml 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. DECASONE INJECTION 4 mg/ml therapy should be reinstated in any stressful situation during this period. If the patient is already receiving corticosteroids, the current dosage may have to be temporarily increased. Salt and/or mineralocorticoid steroid cover should be given concurrently, if mineralocorticoid secretion is impaired.

Stopping DECASONE INJECTION 4 mg/ml after prolonged therapy may cause withdrawal symptoms, including fever, myalgia, arthralgia, rhinitis, conjunctivitis, painful itchy skin nodules, loss of weight and malaise. This may occur in patients even without evidence of adrenal insufficiency.

In patients who have received more than (1 mg DECASONE INJECTION 4 mg/ml) 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

DECASONE INJECTION 4 mg/ml is reduced. Clinical assessment of disease activity may be needed during withdrawal. If the disease is unlikely to relapse on withdrawal of DECASONE INJECTION 4 mg/ml but there is uncertainty about hypothalamic-pituitary adrenal (HPA) suppression, the dose of DECASONE INJECTION 4 mg/ml may be reduced rapidly to 1 mg DECASONE INJECTION 4 mg/ml per day. Thereafter dose reduction should be slower to allow the HPA-axis to recover.

Abrupt withdrawal of DECASONE INJECTION 4 mg/ml 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 DECASONE INJECTION 4 mg/ml 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 DECASONE INJECTION 4 mg/ml 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 DECASONE INJECTION 4 mg/ml,

• patients repeatedly taking doses in the evening.

Too rapid a reduction of DECASONE INJECTION 4 mg/ml following prolonged treatment can lead to acute adrenal insufficiency, hypotension and death.

Withdrawal symptoms may include a clinical relapse of the disease for which the patient has been undergoing treatment.

Porphyria

DECASONE INJECTION 4 mg/ml can be porphyrinogenic and it should be used only when no safer alternative is available. Precautions should be considered in vulnerable patients.

Paediatric population

Corticosteroids cause dose-related growth retardation in infancy, childhood and adolescence, which may be irreversible.

Preterm neonates

Long-term neurodevelopment adverse events after early treatment (<96 hours) of premature infants with chronic lung disease at starting dose of 0,25 mg/kg twice daily have been reported.

Hypertrophic cardiomyopathy

Hypertrophic cardiomyopathy was reported after systemic administration of corticosteroids including dexamethasone to prematurely born infants. 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).

This medicine contains less than 1 mmol sodium (23 mg) per ml that is to say essentially 'sodium free.'

4.5 Interaction with other medicines and other forms of interaction

Liver enzyme inducing medicines 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.

Corticosteroids may affect glucose tolerance and increase the dosage requirement for hypoglycaemic medicines (including insulin).

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

Concurrent administration with the potassium depleting diuretics such as the thiazides or furosemide, may cause excessive potassium loss.

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 medicines. The effects of anti-hypertensive medicines are also antagonised by corticosteroids.

There may be an increased incidence of gastrointestinal bleeding and ulceration when DECASONE INJECTION 4 mg/ml is given with non-steroidal anti-inflammatory agents.

DECASONE INJECTION 4 mg/ml may interfere with or alter the results of assays for some endogenous substances or other medicines.

Rifampicin, rifabutin, ephedrine, carbamazepine, phenylbutazone; phenobarbital, phenytoin, primidone, aminoglutethimide and ephedrine enhance the metabolism of DECASONE INJECTION 4 mg/ml and its therapeutic effects may be reduced.

The effects of anticholinesterases are antagonised by DECASONE INJECTION 4 mg/ml in myasthenia gravis.

The desired effects of hypoglycaemic agents (including insulin), anti-hypertensives, cardiac glycosides (e.g. digoxin) and diuretics are antagonised by DECASONE INJECTION 4 mg/ml, and the hypokalaemic effects of acetazolamide, loop diuretics, thiazide diuretics and carbenoxolone are enhanced.

The efficacy of coumarin anticoagulants may be enhanced by concurrent corticosteroid therapy and close monitoring of the INR or prothrombin time is required to avoid spontaneous bleeding.

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.

There is also an increased risk of hypokalaemia with concurrent amphotericin B or bronchodilator therapy with xanthines or beta$_2$ agonists.

Concomitant administration of dexamethasone with known strong inhibitors of CYP 3A4 (e.g.,ketoconazole, intraconazole, macrolide antibiotics such as erythromycin, clarithromycin, ritonavir cobicistat-containing medicines) has the potential to result in increased plasma concentrations of dexamethasone. This may lead to increased plasma concentrations of corticosteroids and potentially increase the risk for systemic corticosteroid side effects.

Concomitant administration of dexamethasone with erythromycin has the potential to result in increased plasma concentrations of dexamethasone.

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.

4.6. Fertility, pregnancy and lactation

Safety and efficacy in pregnancy and lactation have not been established.

Pregnancy

The ability of corticosteroids to cross the placenta varies between the individual medicines, however DECASONE INJECTION 4 mg/ml readily crosses the placenta.

Administration of corticosteroids to pregnant animals can cause abnormalities of foetal development including cleft palate, intra-uterine 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.

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. 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.

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.

Breastfeeding

Mothers on DECASONE INJECTION 4 mg/ml should not breastfeed their infants. Corticosteroids may pass into breast milk, although no data are available for DECASONE INJECTION 4 mg/ml. 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.

Fertility

There is no fertility data.

4.7 Effects on ability to drive and use machines

DECASONE INJECTION 4 mg/ml has moderate influence on the ability to drive and use machines.

Since adverse reactions such as visual disturbances, hallucinations and confusion have been reported in patients receiving DECASONE INJECTION 4 mg/ml , patients should not drive, use machinery or perform any tasks that require concentration, until they are certain that DECASONE INJECTION 4 mg/ml does not adversely affect their ability to do so (see section 4.8).

4.8 Undesirable effects

a) Summary of the safety profile

A wide range of psychiatric reactions including affective disorders (such as irritability, euphoria, depressed and labile mood, and suicidal thoughts) have been reported. 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 to 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 medicine, dosage, timing of administration and the duration of treatment (see section 4.4).

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.

b) Tabulated list of adverse reactions

System organ class	**Frequent**	**Less frequent**	**Frequency unknown** (cannot be estimated from the available data)
Infections and infestations		Tuberculosis, fungal and viral infections	
Blood and the lymphatic system disorders		thromboembolic complications, leucocytosis	
Immune system disorders			Hypersensitivity including anaphylaxis,increased susceptibility and severity of infections with suppression of clinical symptoms and signs, diminished lymphoid tissue and immune response, opportunistic infections, recurrence of dormant tuberculosis and decreased responsiveness to vaccination and skin tests.
Endocrine disorders		Adreno-cortical atrophy, leading to tertiary adrenocortical insufficiency	Suppression of the hypothalamic-pituitary-adrenal axis, premature epiphyseal closure, menstrual irregularities and amenorrhoea.
Metabolism and nutrition disorders		Excessive metabolic effects may lead to	Hypercalcaemia, weight gain, impaired carbohydrate tolerance

		mobilisation of calcium and phosphorous, with osteoporosis and spontaneous fractures, nitrogen depletion and hyperglycaemia with accentuation or precipitation of diabetes mellitus,Cushingoid symptoms	with increased requirement for anti-diabetic therapy, negative protein balance and calcium balance, increased appetite, sodium and water retention, hypertension, potassium loss, hypokalaemic alkalosis, suppression of growth in infants, children and adolescents; secondary adrenocortical unresponsiveness, particularly in times of stress, as in surgery or trauma,electrolyte imbalance (retention of sodium and water with oedema and hypertension); hypokalaemic alkalosis; increased calcium and potassium excretion and hypertension.
Psychiatric disorders	Affective disorders, irritable, euphoric, depressed, labile mood, suicidal thoughts, behavioural disturbances	Mental and neurological disturbances, including mania, delusions, hallucinations, aggravation of schizophrenia, irritability, anxiety, sleep disturbances, cognitive dysfunction, confusion, amnesia, psychological dependence	Psychological effects (on withdrawal), 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.
Nervous system disorders		Benign intracranial hypertension, aggravation of epilepsy	
Eye disorders		Posterior sub capsular cataract, increased intraocular pressure, glaucoma, papilloedema, corneal or scleral thinning	Exacerbation of ophthalmic viral or fungal disease, chorioretinopathy, blurred vision, blindness
Cardiac disorders		Cardiac failure	Hypertrophic cardiomyopathy in prematurely born infants; Myocardial rupture following recent myocardial infarction
Vascular disorders		Hypertension	Thromboembolism
Gastrointestinal disorders	Increased appetite	Acute pancreatitis, peptic ulceration with haemorrhage and perforation, dyspepsia,	Candidiasis, nausea, abdominal distention

Skin and subcutaneous tissue disorders		Hyperhidrosis, skin thinning	Impaired healing, skin atrophy, bruising, telangiectasia, striae, increased sweating, acne, petechiae, ecchymoses; possible suppression of skin tests; burning or tingling; bruising; allergic dermatitis; urticaria,hyperpigmentation; hypopigmentation,subcutaneous and cutaneous atrophy, Stevens-Johnson Syndrome
Musculoskeletal and connective tissue disorders		Avascular necrosis of bone, muscular weakness and wasting,growth retardation in infants, children and adolescents, osteoporosis, vertebral and long bone fractures, avascular osteonecrosis, tendon rupture, proximal myopathy.	
Reproductive system and breast disorders		Menstrual irregularities, Amenorrhoea	
Congenital and familial and genetic disorders		Transient burning or tingling sensation (perineal area)	
General disorders and administrative site conditions		Oedema	Sterile abscess; post injection flare (following intraarticular injection): Charcot-like arthropathy, Leucocytosis, malaise, hiccups.
Investigations		An increased excretion, hypokalaemic alkalosis	
Injury, poisoning and procedural complications			Arachnoiditis

c) Description of selected adverse reactions

Infections and infestations

Infections may also be masked. Impaired tissue repair and immune function can lead to delayed wound healing.

Blood and the lymphatic system disorders

Increase in the coagulability of blood may lead to thromboembolic complications.

Endocrine disorders

Acute adrenal insufficiency may occur during prolonged treatment on cessation of treatment and may be precipitated by stressful situations, for example an infection or trauma.

DECASONE INJECTION 4 mg/ml has little or no effect on sodium and water retention.

Metabolism and nutrition disorders

The insulin requirements of diabetic patients are increased.

Large doses of DECASONE INJECTION 4 mg/ml may produce Cushingoid symptoms (typical of hyperactivity of the adrenal cortex, with moon-face, sometimes with hirsutism, buffalo hump, flushing, increased bruising, ecchymoses, striae and acne).

Psychiatric disorders

Psychological effects have been reported on withdrawal of corticosteroids.

Cardiac disorders

Rapid intravenous administration of large doses may cause cardiovascular collapse.

Musculoskeletal, connective tissue and bone disorders

Muscular weakness and wasting (occur occasionally, particularly when taken in large doses).

Reproductive system and breast disorders

Transient burning or tingling sensation mainly in the perineal are following injection of large doses of corticosteroid phosphates.

Eye disorders

Blindness associated with intralesional therapy around the face and neck.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to:

SAHPRA: https://www.sahpra.org.za/Publications/Index/8

and

Aspen Pharmacare:

E-mail: Drugsafety@aspenpharma.com

Tel: 0800 118 088

4.9. Overdose

Symptoms

In overdose, side effects will be exacerbated and exaggerated.

(see section 4.8).

Treatment

No antidote is available.

Treatment is symptomatic and supportive.

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

Should overdosage occur, the possibility of adrenal suppresion should be minimised by gradual reduction of dosage over a period of time.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and Class: A 21.5.1 Corticosteroids and analogues

Pharmacotherapeutic group: Corticosteroids for systemic use, Glucocorticoids

ATC code:H02A

Mechanism of action

Dexamethasone phosphate acts by controlling the rate of protein synthesis.It forms a steroid-receptor complex with receptor proteins, moves into the nucleus where it binds the chromatin and thus directs the genetic apparatus to transcribe RNA.It has a biological half-life in plasma of about 190 minutes and has relatively very weak sodium retaining properties.

5.2 Pharmacokinetic properties

Absorption

After administration dexamethasone sodium phosphate is hydrolysed to dexamethasone.

Distribution

After an intravenous dose of 20 mg dexamethasone plasma levels peak within 5 minutes.

Dexamethasone is bound (up to 77 %) by plasma proteins, mainly albumin. There is uptake of dexamethasone by the liver, kidney and adrenal glands.

Biotransformation

Metabolism in the liver is slow.

Elimination

Excretion is mainly in the urine, largely as unconjugated steroids.

The plasma half-life is 3,5 to 4,5 hours but plasma half-life is of little relevance and the use of biological half-life is more applicable.

The biological half-life of dexamethasone is 36 to 54 hours.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Creatinine, sodium citrate dihydrate, sodium hydroxide (for pH-adjustment), sodium metabisulfite, water for injection.

6.2 Incompatibilities

In the absence of compatibility studies, this medicine must not be mixed with other medicines.

6.3 Shelf life

48 months

6.4 Special precautions for storage

Store at or below 25 °C.

Protect from light.

Keep in original packaging until required for use.

6.5 Nature and contents of container

1 ml is packed into a clear type 1 glass ampoule. 10 ampoules are packed into a polystyrene container together with a leaflet.

6.6 Special precautions for disposal

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead 2191

8. REGISTRATION NUMBER

Z/21.5.1/0285

9. DATE OF FIRST AUTHORISATION

10 March 1993

10.DATE OF REVISION OF TEXT

29 January 2024

Botswana: BOT0901580 S2

Namibia: NS2 04/21.5.1/102

ZA_DECASINJ_2401_00