1 NAME OF THE MEDICINE
Dexamethasone sodium phosphate

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each mL of DEXAMETHASONE VIATRIS injection contains dexamethasone sodium phosphate 4.4 mg (equivalent to 4 mg dexamethasone phosphate) as the active ingredient.

For the full list of excipients, see Section 6.1 LIST OF EXCIPIENTS.

3 PHARMACEUTICAL FORM
Solution for injection.

DEXAMETHASONE VIATRIS is a clear, colourless solution, free from visible particulate matter and packaged in a 2 mL amber vial with rubber stopper and aluminium seal.

4 CLINICAL PARTICULARS
4.1 THERAPEUTIC INDICATIONS
Replacement Therapy
Adrenocortical insufficiency
Dexamethasone has predominantly glucocorticoid activity and, therefore is not a complete replacement therapy in cases of adrenocortical insufficiency. Dexamethasone should be supplemented with salt and/or a mineralocorticoid, such as deoxycorticosterone. When so supplemented, dexamethasone is indicated in the following:

- Acute adrenocortical insufficiency - Addison's disease; bilateral adrenalectomy
- Relative adrenocortical insufficiency - Prolonged administration of adrenocortical steroids can produce dormancy of the adrenal cortex. The reduced secretory capacity gives rise to a state of relative adrenocortical insufficiency which persists for a varying length of time after therapy is discontinued. Should a patient be subjected to sudden stress during this period of reduced secretion (for up to two years after therapy has ceased) the steroid output may not be adequate. Steroid therapy should, therefore be reinstituted to help cope with stress such as that associated with surgery, trauma, burns or severe infections where specific antibiotic therapy is available.
- Primary and secondary adrenocortical insufficiency

Disease Therapy
Dexamethasone is indicated for therapy of the following diseases:

1. **Collagen diseases.** Systemic lupus erythematosus, polyarteritis nodosa, dermatomyositis, giant cell arteritis, adjunctive therapy for short-term administration during an acute episode or exacerbation, acute rheumatic carditis - during an exacerbation or as maintenance therapy.
2. **Pulmonary disorders.** Status asthmaticus, chronic asthma, sarcoidosis, respiratory insufficiency.
3. **Blood disorders.** Leukaemia, idiopathic thrombocytopenic purpura in adults, acquired (autoimmune) haemolytic anaemia.
4. **Rheumatic diseases.** Rheumatoid arthritis, osteoarthritis, adjunctive therapy for short-term administration during an acute episode or exacerbation of rheumatoid arthritis or osteoarthritis.
5. **Skin diseases.** Psoriasis, erythema multiforme, pemphigus, neutrophilic dermatitis, localised neurodermatitis, exfoliative dermatitis, sarcoidosis of skin, severe seborrhoeic dermatitis, contact dermatitis.

6. **Gastrointestinal disorders.** Ulcerative colitis, regional enteritis.

7. **Oedema.** Cerebral oedema associated with primary or metastatic brain tumours, neurosurgery or stroke, oedema associated with acute non-infectious laryngospasm (or laryngitis).

8. **Eye disorders.** Allergic conjunctivitis, keratitis, allergic corneal marginal ulcers, chorioretinitis, optic neuritis, anterior ischaemic optic neuropathy.

9. **Neoplastic states.** Cerebral neoplasms, hypercalcaemia associated with cancer, leukaemias and lymphomas in adults, acute leukaemia in children.

10. **Endocrine disorders.** Adrenal insufficiency.

**Preoperative and postoperative support**

Dexamethasone may be used in any surgical procedure when the adrenocortical reserve is doubtful. This includes the treatment of shock due to excessive blood loss during surgery.

**Shock**

Dexamethasone may be used as an adjunct in the treatment of shock. Refer to section 4.2 DOSE AND METHOD OF ADMINISTRATION. Dexamethasone should not be used as a substitute for normal shock therapy.

**4.2 DOSE AND METHOD OF ADMINISTRATION**

DEXAMETHASONE VIATRIS may be administered intravenously or intramuscularly for systemic effect, or as an intrasynovial or soft tissue injection for local effect.

Dosage of dexamethasone sodium phosphate is usually expressed in terms of dexamethasone phosphate.

For single patient use. Use once only and discard any residue.

Dosage requirements are variable and must be individualised on the basis of the disease being treated and patient response.

**Intravenous and Intramuscular Administration**

Intravenous or intramuscular dosage usually ranges from 0.5 to 24 mg of dexamethasone phosphate 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.

Parenteral dexamethasone is generally reserved for patients who are unable to take the drug orally or for use in an emergency situation.

**Shock (of haemorrhagic, traumatic or surgical origin)**

The usual dose for the treatment of shock is 2 to 6 mg/kg bodyweight as a single intravenous injection.

This may be repeated in two to six hours if shock persists.

An alternative regimen of 20 mg by intravenous injection initially, followed by continuous intravenous infusion of 3 mg/kg bodyweight per 24 hours, has been suggested. If required for intravenous infusion, DEXAMETHASONE VIATRIS may be diluted with glucose or sodium chloride injection. High dose therapy should be continued only until the patient's condition has stabilised and usually for no longer than 48 to 72 hours.

To avoid microbial contamination hazards, infusion should be commenced as soon as practicable after preparation of the mixture and, if storage is necessary, store solution at 2°C to 8°C. Infusion should be completed within 24 hours of preparation of the solution and any residue discarded.
**WARNING:** Further diluted solutions which are not clear, or which show evidence of particulate matter contamination, should be discarded.

**Cerebral Oedema**
The treatment schedule and route of administration should reflect the severity and aetiology of the cerebral oedema. Treatment needs to be tailored to the individual response. An initial dose of 10 mg intravenously followed by 4 mg intramuscularly every six hours until the symptoms of oedema subside (usually after 12 to 24 hours). After two to four days the dosage should be reduced and gradually stopped over a period of five to seven days. Patients with cerebral malignancy may require maintenance therapy with doses of 2 mg intramuscularly or intravenously two to three times daily.

High doses of dexamethasone may be used to initiate short-term intensive therapy for acute cerebral oedema. Following an initial high loading dose, the dose is scaled down over the seven to ten-day period of intensive therapy and subsequently reduced to zero over the next seven to ten days (see Table 1 for high dose schedule).

### Table 1: High Dose Schedule

<table>
<thead>
<tr>
<th>Initial Dose</th>
<th>Adults</th>
<th>Children &gt; 35 kg</th>
<th>Children &lt; 35 kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st day</td>
<td>8 mg IV every 2 hrs</td>
<td>4 mg IV every 2 hrs</td>
<td>4 mg IV every 3 hrs</td>
</tr>
<tr>
<td>2nd day</td>
<td>8 mg IV every 2 hrs</td>
<td>4 mg IV every 2 hrs</td>
<td>4 mg IV every 3 hrs</td>
</tr>
<tr>
<td>3rd day</td>
<td>4 mg IV every 2 hrs</td>
<td>4 mg IV every 2 hrs</td>
<td>4 mg IV every 3 hrs</td>
</tr>
<tr>
<td>4th day</td>
<td>4 mg IV every 3 hrs</td>
<td>4 mg IV every 6 hrs</td>
<td>4 mg IV every 6 hrs</td>
</tr>
<tr>
<td>5th – 8th day</td>
<td>Decrease by daily reduction of 4 mg</td>
<td>Decrease by daily reduction of 2 mg</td>
<td>Decrease by daily reduction of 1 mg</td>
</tr>
</tbody>
</table>

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

**Intra-synovial 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 three to five days (e.g. for bursae) to once every two to three weeks (for joints). Frequent intra-articular injection may result in damage to joint tissues (see Table 2 for dosages).

### Table 2: Intra-synovial and Soft Tissue Injection

<table>
<thead>
<tr>
<th>Site of Injection</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Large joints</td>
<td>2 mg to 4 mg</td>
</tr>
<tr>
<td>Small joints</td>
<td>800 micrograms to 1 mg</td>
</tr>
<tr>
<td>Bursae</td>
<td>2 mg to 3 mg</td>
</tr>
<tr>
<td>Tendon sheaths</td>
<td>400 micrograms to 1 mg</td>
</tr>
<tr>
<td>Soft tissue infiltration</td>
<td>2 mg to 6 mg</td>
</tr>
<tr>
<td>Ganglia</td>
<td>1 mg to 2 mg</td>
</tr>
</tbody>
</table>

### 4.3 CONTRAINDICATIONS
Administration of DEXAMETHASONE VIATRIS is contraindicated in the following cases:

- Systemic fungal infections or other systemic infections unless specific anti-infective therapy is given (see section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE)
- Hypersensitivity to dexamethasone or other corticosteroids or to any component of the injection
- Administration of live virus vaccines (see section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE)
- In patients with myasthenia gravis, peptic ulcer, osteoporosis or psychoses
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. 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.

Corticosteroids may increase susceptibility to or mask the symptoms of infection, and therefore should be used with caution in patients with systemic infections. Chicken pox, measles and other infections can have a more serious or even fatal effect in non-immune children or adults on corticosteroids. Immunosuppression is most likely to occur in patients receiving longer term; high dose systemic corticosteroid treatment, however, patients receiving moderate doses for short periods, or low doses over a prolonged period, may also be at risk.

Corticosteroids should be administered with caution to patients with latent tuberculosis or tuberculin reactivity, as reactivation of the disease may occur. These patients should, therefore, undergo chemoprophylaxis during prolonged corticosteroid therapy.

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

Administration of live virus vaccines is contraindicated in individuals receiving immunosuppressive doses of corticosteroids (see section 4.3 CONTRAINDICATIONS). The antibody response to other vaccines may be diminished. If inactivated viral or bacterial vaccines are administered to patients 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.

Long-term treatment should not be abruptly discontinued, as too rapid withdrawal may lead to drug induced secondary adrenocortical insufficiency. This may be minimised by gradual dosage reduction. This type of relative insufficiency may persist for months after therapy is discontinued. Therefore, in any situation of stress occurring in that period (such as anaesthesia, surgery or trauma) corticosteroid doses may need to be increased or the therapy reinstituted. Following prolonged therapy, withdrawal of corticosteroids may result in symptoms of the corticosteroid withdrawal syndrome including fever, myalgia, arthralgia, rhinitis, conjunctivitis, painful itchy skin nodules, loss of weight and malaise.

Dexamethasone should be used only with extreme caution and frequent monitoring necessary in patients with diabetes mellitus or in those with:

- Diabetes mellitus or a family history of diabetes
- Infectious diseases
- Congestive heart failure or recent myocardial infarction
- Chronic renal failure
- Diverticulitis
- Hypertension
- Keratitis
- Epilepsy and/or seizure disorder, migraine
- Non-specific ulcerative colitis (if there is a probability of impending perforation, abscess or other pyogenic infection), fresh intestinal anastomoses, active or latent peptic ulcer
• osteoporosis, myasthenia gravis or in elderly persons.

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

Corticosteroids should be used with caution in patients who have had a recent cardiac infarction, as there have been reports of an apparent association between the use of corticosteroids and left ventricular free wall rupture in these patients; in patients with a history of severe affective disorders particularly of steroid induced psychoses; patients with previous steroid myopathy, liver failure, renal insufficiency, glaucoma (or family history of glaucoma); patients with thromboembolic disorders; patients with Duchenne’s muscular dystrophy since transient rhabdomyolysis and myoglobinuria have been reported following strenuous physical activity; Cushing’s disease. Corticosteroids show an enhanced effect in patients with hypothyroidism or cirrhosis.

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.

Intra-articular injection of corticosteroids may produce systemic as well as local effects. Appropriate examination of any joint fluid present 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 sepsis is confirmed, appropriate antimicrobial therapy should be commenced.

Local injection of a steroid into an infected site is to be avoided. Corticosteroids should not be injected into unstable joints.

Frequent intra-articular injection may result in damage to joint tissues. Patients should be advised strongly of the importance of not overusing joints in which symptomatic benefit has been obtained as long as the inflammatory process remains active.

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

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

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

**Adrenocortical Insufficiency**

Pharmacologic doses of corticosteroids administered for prolonged periods may result in hypothalamic-pituitary-adrenal (HPA) suppression (secondary adrenocortical insufficiency). The degree and duration of adrenocortical insufficiency produced is variable among patients and depends on the dose, frequency, time of administration and duration of therapy.

Symptoms of adrenal insufficiency include: malaise, muscle weakness, mental changes, muscle and joint pain, desquamation of the skin, dyspnoea, anorexia, nausea and vomiting, fever, hypoglycaemia, hypotension and dehydration.

During prolonged courses of corticosteroid therapy, sodium intake may need to be reduced and calcium and potassium supplements may be necessary. Monitoring of fluid intake and output and daily weight records may give an early warning of fluid retention.

Acute adrenal insufficiency leading to a fatal outcome may occur if glucocorticoids are withdrawn abruptly, therefore withdrawal of corticosteroids should always be gradual. A degree of adrenal insufficiency may persist for 6 to 12 months; therefore, in any situation of stress occurring during that period, steroid therapy may need to
be reinstated. Since mineralocorticoid secretion may be impaired, treatment with salt and/or a mineralocorticoid may also be needed.

**Anti-inflammatory/Immunosuppressive Effects and Infection**

Suppression of the inflammatory response and immune function increases susceptibility to infections, and their severity. The clinical presentation may often be atypical and serious infections such as sepsis and tuberculosis may be masked and may reach an advanced stage before being recognised when corticosteroids are used. The immunosuppressive effects of glucocorticoids may result in activation of latent infection or exacerbation of intercurrent infections.

Chicken pox is of particular concern, since this may be fatal in immunosuppressed patients. Patients 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. If a diagnosis of chickenpox is confirmed the illness warrants specialist care and urgent treatment.

Live vaccines are contraindicated in individuals on high doses of corticosteroids and should be postponed until at least 3 months after stopping corticosteroid therapy.

**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.

Prolonged use of corticosteroids may produce subcapsular cataracts and nuclear cataracts (particularly in children), exophthalmos or increased intraocular pressure, which may result in glaucoma with possible damage to the optic nerves.

Corticosteroids should only be initiated in patients with ocular herpes simplex with appropriate viral cover by ophthalmologists because of the risk of corneal scaring, loss of vision and corneal perforation.

**Psychiatric Effects**

Patients and/or carers should be warned that potentially severe psychiatric reactions may occur. Symptoms typically emerge within a few days or weeks of starting treatment. Most reactions resolve after either dose reduction or withdrawal, although specific treatment may be necessary. Patients and/or carers should be encouraged to seek medical advice if worrying psychological symptoms develop, especially if depressed mood or suicidal ideation is suspected.

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

Psychic derangements range from euphoria, insomnia, mood swings, personality changes and severe depression to frank psychotic manifestations.

Patients/carers should also be alert to possible psychiatric disturbances that may occur either during or immediately after dose tapering/withdrawal of systemic steroids, although such interactions have been reported infrequently.

**Use in the Elderly**

Geriatric patients may be more likely to develop hypertension and osteoporosis as a result of corticosteroid therapy.

Long-term use in the elderly should be planned bearing in mind the more serious consequences of the common side-effects of corticosteroids in old age, especially osteoporosis, diabetes, hypertension, hypokalaemia,
susceptibility to infection and thinning of the skin. Close medical supervision is required to avoid life-threatening reactions.

**Paediatric Use**

Corticosteroids cause growth retardation in infancy, childhood and adolescence, which may be irreversible and therefore long-term administration of pharmacological doses should be avoided. If prolonged therapy is necessary, treatment should be limited to the minimum suppression of the hypothalamic-pituitary adrenal axis and growth retardation, the growth and development of infants and children should be closely monitored. Treatment should be limited, where possible, to a single dose on alternate days.

Children are at special risk from raised intracranial pressure.

Hypertrophic cardiomyopathy has been reported after administration of 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 to date, the effect is temporary and can reverse on withdrawal of treatment.

**Effects on Laboratory Tests**

Dexamethasone suppression tests may be affected by drugs which enhance the metabolic clearance of corticosteroids (see section 4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS).

False negative results in the dexamethasone suppression test have been reported in patients being treated with indomethacin or high doses of benzodiazepines or cyproheptadine.

Corticosteroids have been reported to alter the response to anticoagulant agents (see section 4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS). The prothrombin time should be checked frequently in patients receiving these combinations.

Corticosteroids may affect a wide range of diagnostic tests. They may affect brain and skeletal imaging using $^{99}$Tc, by decreasing uptake of $^{99}$Tc into cerebral tumours or bone, respectively, and may decrease $^{123}$I and $^{131}$I uptake into the thyroid. Corticosteroids may alter the results of the gonadorelin test for hypothalamic-pituitary-gonadal axis function, affect thyroid function test results, and suppress skin test reactions including tuberculin and histoplasmin skin tests and patch tests for allergy. Corticosteroids may also affect the nitroblue tetrazolium test for bacterial infection and produce false negative results.

**4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS**

Medicines that induce hepatic enzyme cytochrome P450 isoenzyme 3A4 such as barbiturates, phenylbutazone, phenytoin or rifampicin, rifabutin, carbamazepine, primidone and aminogluthethimide may increase the metabolism and thus reduce the effects of corticosteroids.

Ephedrine and aminogluthethimide may also increase dexamethasone metabolism.

Medicines that inhibit hepatic enzyme cytochrome P450 isoenzyme 3A4 such as ketoconazole, ciclosporin or ritonavir may decrease glucocorticoid clearance. A reduction in corticosteroid dose may be needed to reduce the risk of adverse effects.

Antithyroid agents, estrogens and other oral contraceptives may decrease hepatic metabolism and thus increase the effects of corticosteroids. The dose of corticosteroid may need to be adjusted if estrogen therapy is commenced or stopped.

The effects of anticoagulant agents are usually decreased (but may be increased in some patients) if corticosteroids are administered concurrently. Close monitoring of the INR or prothrombin time is required to avoid spontaneous bleeding.
Seizures have reportedly occurred in adult and paediatric patients receiving high dose corticosteroid therapy concurrently with ciclosporin.

Concurrent administration of dexamethasone with anticoagulants, heparin, streptokinase, urokinase, alcohol or non-steroidal anti-inflammatory drugs (NSAIDs) including aspirin may increase the risk of gastrointestinal ulceration or haemorrhage. Aspirin should be used cautiously in conjunction with corticosteroid in patients with hypothyrombinaemia. The renal clearance of salicylates is increased by corticosteroids and steroid withdrawal may result in salicylate intoxication. Patients should be observed closely for adverse effects of either medicine. 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.

Potassium loss may occur as a result of dexamethasone administration (see section 4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)). Concurrent administration of corticosteroids with potassium depleting diuretics (such as thiazides, furosemide (frusemide) or etacrynic acid), carbonic anhydrase inhibitors (such as acetazolamide) or amphotericin B (amphotericin) may result in severe hypokalaemia. The activity of digitalis glycosides and nondepolarising neuromuscular blocking agents may be potentiated as a result of glucocorticoid induced hypokalaemia. The efficacy of potassium supplements and potassium sparing diuretics on serum potassium concentrations may be reduced by concurrent corticosteroid administration. Monitoring of serum potassium concentration is therefore recommended.

Glucocorticoids may increase blood glucose concentrations. Dosage adjustment of asparaginase (colaspase) and of antidiabetic agents such as sulphonylureas and insulins may be necessary.

The growth promoting effect of somatropin may be inhibited.

There is an increased risk of hypokalaemia if high doses of corticosteroids are given with high doses of salbutamol, salmeterol, terbutaline or formoterol (formoterol).

Concurrent use of antacids may decrease absorption of corticosteroids – efficacy may be decreased sufficiently to require dosage adjustments in patients receiving small doses of corticosteroids.

### 4.6 FERTILITY, PREGNANCY AND LACTATION

#### Effects on Fertility
Corticosteroids may increase or decrease the motility and number of spermatozoa in some patients.

#### Use in Pregnancy
Pregnancy Category: C

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

In animal experiments, corticosteroids have been found to cause malformations of various kinds (cleft palate, skeletal malformations). These findings do not seem to be relevant to humans. Reduced placental and birthweight have been recorded in animals and humans after long-term treatment. Since the possibility of suppression of the adrenal cortex in the newborn baby after long-term treatment must be considered, the needs of the mother must be carefully weighed against the risk to the fetus when prescribing corticosteroids. However, the short-term use of antepartum corticosteroids for the prevention of respiratory distress syndrome, when warranted, does not seem to pose a risk.

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.

**Use in Lactation**
Corticosteroids appear in breast milk and could suppress growth, interfere with endogenous corticosteroid production or cause other unwanted effects in breastfed infants. Women taking corticosteroids should be advised not to breastfeed.

Infants of mothers taking high doses of systemic corticosteroids for prolonged periods may have a degree of adrenal suppression. Suppression of growth or other adverse effects may occur.

### 4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The effects of this medicine on a person’s ability to drive and use machines were not assessed as part of its registration. However, adverse effects of DEXAMETHASONE VIATRIS include dizziness, drowsiness, insomnia, convulsions, vertigo and blurred vision which could affect the ability to drive or use machines (see section 4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)).

### 4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

The following adverse reactions have been reported with dexamethasone therapy. Except for allergic reactions, the adverse effects listed have been associated with prolonged therapy and/or high doses.

**Endocrine Effects**
Adrenal suppression, menstrual irregularities, amenorrhoea, development of Cushingoid state, weight gain secondary adrenocortical and pituitary unresponsiveness particularly in times of stress (e.g. trauma, surgery or illness), decreased carbohydrate tolerance, increased requirements for insulin or oral hypoglycaemic agents in diabetes, development of diabetes mellitus, hyperglycaemia, hirsutism, growth suppression in infancy, childhood and adolescence, increased appetite.

**Cardiovascular Effects**
Thromboembolism, hypertension, polymorphonuclear leucocytosis, neuropathy, vasculitis, impaired myocardial contractility (prolonged treatment), congestive heart failure in susceptible patients, myocardial rupture following recent cardiac infarction, hypertrophic cardiomyopathy in low birthweight and prematurely born infants.

**Musculoskeletal Effects**
Proximal myopathy, osteoporosis, arthropathy, muscular atrophy, premature epiphyseal closure, muscleatrophy, steroid myopathy, vertebral compression fractures, aseptic necrosis of femoral and humeral heads, pathological fracture of long bones, avascular osteonecrosis, tendon rupture, myalgia. These may occur as a result of protein catabolism associated with prolonged glucocorticoid therapy.

**Ocular Effects**
Increased intraocular pressure, glaucoma, papilloedema, posterior subcapsular cataracts, or increased intraocular pressure may lead to glaucoma or occasionally damage to the optic nerve, cataracts, vision blurred, exophthalmos, corneal or scleral thinning, retinopathy of prematurity, enhanced establishment of secondary fungal and viral eye infections, chorioretinopathy, blurred vision.

**Dermatological Effects**
Impaired wound healing, hirsutism, skin atrophy, allergic dermatitis, urticaria, erythema, thin fragile skin, telangiectasia, petechiae and ecchymoses, increased sweating, may suppress skin test reactions, burning or tingling especially in the perineal area (after intravenous injection), angioneurotic oedema, acne, striae, easy bruising, candidiasis.
**Anti-Inflammatory and Immunosuppressive Effects**

Increased susceptibility to and severity of infections with suppression of clinical symptoms and signs. Opportunistic infections, recurrence of dormant tuberculosis.

**Gastrointestinal Effects**

Dyspepsia, nausea, peptic ulcer with possible perforation and haemorrhage, abdominal distension, abdominal pain, increased appetite which may result in weight gain, diarrhoea, acute pancreatitis, perforation of the small or large bowel particularly in patients with inflammatory bowel disease, abdominal distension, ulcerative oesophagitis, oesophageal candidiasis, nausea.

**Neurological Effects**

Euphoric side effects, mental disturbances, psychological dependence, depression, insomnia, dizziness, headache, convulsions, increased intracranial pressure with papilloedema, vertigo, labile mood. Aggravation of schizophrenia, aggravation of epilepsy, suicidal ideation, behavioural disturbances, sleep disturbances, mania, delusions, hallucinations, irritability, anxiety, insomnia and cognitive dysfunction.

**Fluid and Electrolyte Disturbances**

Electrolyte imbalance (retention of sodium and water with oedema and hypertension), potassium loss, hypokalaemic alkalosis, hypocalcaemia, increased calcium and potassium excretion.

**Metabolic Effects**

Nitrogen depletion, negative nitrogen and calcium balance due to protein catabolism.

**Other Effects**

Allergic reactions, leucocytosis, anaphylactic or hypersensitivity reactions, weight gain, increased appetite, fatigue, malaise, hiccups, blindness associated with intralesional therapy around the face and neck.

Glucocorticoids, especially in large doses, increase susceptibility to infection, and may mask the symptoms of infection (see section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE).

Too rapid a reduction of corticosteroids following prolonged treatment can lead to acute adrenal insufficiency, hypotension and death.

A steroid withdrawal syndrome, seemingly unrelated to adrenocortical insufficiency, and consisting of anorexia, nausea and vomiting, lethargy, headache, fever, joint pain, desquamation, myalgia, weight loss and/or hypotension, has been reported following abrupt withdrawal of glucocorticoids.

Hyperpigmentation or hypopigmentation, subcutaneous and cutaneous atrophy, sterile abscess, post-injection flare (following intra-articular use) and Charcot-like arthropathy have also been associated with parenteral corticosteroid therapy.

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.

**Reporting Suspected Adverse Effects**

4.9 OVERDOSE

**Symptoms**
Reports of acute toxicity and/or deaths following overdosage with glucocorticoids are rare. Exaggeration of corticosteroid related adverse effects may occur including hypertension, oedema, peptic ulceration, hyperglycaemia and altered mental state. Anaphylactic or hypersensitivity reactions may occur.

**Treatment**
No antidote is available. Treatment of overdosage is symptomatic. The dosage should be reduced, or the drug withdrawn. Anaphylactic and hypersensitivity reactions may be treated with adrenaline (epinephrine), positive pressure artificial respiration and aminophylline. The patient should be kept warm and quiet.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

**Mechanism of Action**
Dexamethasone is a synthetic adrenocorticosteroid with glucocorticoid activity. It is one of the most active glucocorticoids, being about 25 to 30 times as potent as hydrocortisone. Unlike hydrocortisone, dexamethasone has little if any mineralocorticoid activity.

Dexamethasone has anti-inflammatory and immunosuppressant activity. Glucocorticoids prevent the development of the inflammatory response, i.e. redness, swelling, tenderness. They also inhibit capillary dilation and phagocytosis and appear to prevent the hypersensitivity responses which occur after antigen-antibody reactions.

The principal metabolic actions of dexamethasone are on gluconeogenesis, glycogen deposition and protein and calcium metabolism. Dexamethasone also influences the mobilisation, oxidation, synthesis and storage of fats.

Dexamethasone suppresses the release of adrenocorticotropic hormone (ACTH) from the pituitary, resulting in inhibition of endogenous corticotrophin secretion.

Except for its use in the treatment of adrenal insufficiency, dexamethasone does not cure disease. Rather, the anti-inflammatory and immunosuppressant actions of dexamethasone suppress the symptoms associated with the disease.

**Clinical Trials**
No data available.

5.2 PHARMACOKINETIC PROPERTIES

**Absorption**
Dexamethasone sodium phosphate is absorbed rapidly following intramuscular or intravenous injection.

Intramuscular injections of dexamethasone phosphate give maximum plasma concentrations of dexamethasone at one hour.

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

**Distribution**
In the circulation, small amounts of dexamethasone are bound to plasma proteins.
**Metabolism**
Synthetic corticosteroids such as dexamethasone are less extensively protein bound and more slowly metabolised than hydrocortisone. Dexamethasone penetrates into tissue fluids and cerebrospinal fluids. Metabolism occurs in most tissues, but primarily in the liver.

**Excretion**
The inactive metabolites are excreted in the urine, mainly as glucuronides and sulfates but also as unconjugated metabolites. Small amounts of unchanged drug are also excreted in the urine. Up to 65% of a dose of dexamethasone is excreted in the urine within 24 hours.

### 5.3 PRECLINICAL SAFETY DATA

**Genotoxicity**
No data available.

**Carcinogenicity**
No data available.

### 6 PHARMACEUTICAL PARTICULARS

#### 6.1 LIST OF EXCIPIENTS
Sodium citrate, creatinine and water for injections.

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

#### 6.3 SHELF LIFE
In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

#### 6.4 SPECIAL PRECAUTIONS FOR STORAGE
Store below 25°C. Protect from light.

#### 6.5 NATURE AND CONTENTS OF CONTAINER
DEXAMETHASONE VIATRIS is supplied in a Type 1 amber glass vial with a chlorobutyl rubber stopper and aluminium flip-off seal.

Pack sizes: 5 vials, 10 vials.

Some strengths, pack sizes and/or pack types may not be marketed.

**Australian Register of Therapeutic Goods (ARTG)**
AUST R 163199 – DEXAMETHASONE VIATRIS dexamethasone phosphate (as dexamethasone sodium phosphate) 8mg/2mL solution for injection

AUST R 163200 – DEXAMETHASONE VIATRIS dexamethasone phosphate (as dexamethasone sodium phosphate) 4mg/1mL solution for injection
6.6 SPECIAL PRECAUTIONS FOR DISPOSAL
In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical Structure

Chemical name: 9-fluoro-11β,17-dihydroxy-16α-methyl-3,20-dioxopregna-1,4-dien-21-y1 disodium phosphate
Molecular formula: C$_{22}$H$_{28}$FN$_{2}$O$_8$P
Molecular weight: 516.4

Dexamethasone sodium phosphate is a white or slightly yellow, very hygroscopic, crystalline powder. It is odourless or has a slight odour of alcohol. Dexamethasone sodium phosphate is freely soluble in water, slightly soluble in alcohol, practically insoluble in chloroform and ether and very slightly soluble in 1,4-dioxane.

The pH of a 1% solution in water is between 7.5 and 9.5.

CAS Number
2392-39-4

7 MEDICINE SCHEDULE (POISONS STANDARD)
S4 (Prescription Only Medicine)

8 SPONSOR
Alphapharm Pty Ltd trading as Viatris
Level 1, 30 The Bond
30 – 34 Hickson Road
Millers Point NSW 2000
www.viatris.com.au
Phone: 1800 274 276

9 DATE OF FIRST APPROVAL
02/03/2011

10 DATE OF REVISION
15/03/2023

Summary Table of Changes

<table>
<thead>
<tr>
<th>Section Changed</th>
<th>Summary of New Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>Minor editorial changes</td>
</tr>
<tr>
<td>4.4</td>
<td>Addition of the following information for: tumour lysis syndrome; use in intrathecal therapy and hypersensitivity reactions due to formulation containing sulphites; withdrawal symptoms such as rhinitis, conjunctivitis, painful skin nodules; advice for extreme caution and frequent monitoring in patients with liver failure and migraine; reactivation of latent amoebiasis; caution for patients with family history of glaucoma; septic shock; risks associated with intraarticular corticosteroids; severe anaphylactoid reactions; slower rate absorption after intramuscular injection; psychiatric disturbances may occur during or after dose tapering/withdrawal if systemic steroids; consideration of the needed in patients with existing conditions such as depressive or manic-depressive illnesses; treatment in paediatrics; visual disturbances</td>
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<tr>
<td>4.5</td>
<td>Addition of the following information: Closing monitor of INR or prothrombin time is required to avoid spontaneous bleeding; co-treatment with CYP4A3 inhibitors</td>
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<tr>
<td>4.6</td>
<td>Addition of the following information: Dexamethasone readily crosses the placenta; mothers on substantial high doses should be carefully observed for adrenal insufficiency; close monitoring required in pre-eclampsia or fluid retention; lactating mothers on high doses may have a degree of adrenal suppression and suppression of growth; evidence of harmful effects on pregnancy in animals.</td>
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<tr>
<td>4.8</td>
<td>The following adverse effects are added: Premature epiphyseal closure; increased intraocular pressure leading to glaucoma or optic nerve damage; chorioretinopathy; blurred vision; candidiasis; labile mood; behavioural disturbances and sleep disturbances; increase calcium and potassium excretion; negative protein/nitrogen and calcium balance; blindness associated with intralesional therapy around the face and neck; incidence of predictable undesirable effects, including hypothalamic-pituitary-adrenal suppression.</td>
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<tr>
<td>6.2</td>
<td>Physical incompatibility with daunorubicin, doxorubicin, vancomycin, doxapram HCL and glycopyrrolate.</td>
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