PROFESSIONAL INFORMATION

SCHEDULING STATUS: S4

1. NAME OF THE MEDICINE

HIDROTEF 100 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial contains hydrocortisone sodium succinate equivalent to 100 mg of hydrocortisone.

Contains phosphate buffer as excipient.

Excipients:

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

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

A white powder.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

HIDROTEF 100 mgis indicated for any condition in which a rapid and intense corticosteroid effect is required, such as:

Severe shock (adjunctive therapy)

In severe shock adjunctive use of intravenous **HIDROTEF 100 mg** may aid in achieving haemodynamic restoration. **HIDROTEF 100 mg** therapy should not replace standard methods of combating shock, but present evidence indicates that concurrent use of large doses of corticoids with

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other measures may improve survival rates.

Acute hypersensitivity reactions

In status asthmaticus, **HIDROTEF 100 mg** is used as adjunctive therapy to epinephrine (adrenaline) in anaphylactic reactions.

4.2 Posology and method of administration

Posology

HIDROTEF 100 mg may be administered by intravenous injection, by intravenous infusion, or by intramuscular injection. The preferred method for initial emergency use being intravenous injection. Following the initial period, consideration should be given to employing a longer acting Injectable preparation or an oral preparation.

Therapy is initiated by administering **HIDROTEF 100 mg** intravenously over a period of 30 seconds (100 mg) to 10 minutes (500 mg). This dose may be repeated at intervals of 4 to 6 hours, as indicated by the patient's response and clinical condition. While the dose may be reduced for infants and children, it is governed more by the severity of the condition and response of the patient, than by age or body mass, but should not be less than 25 mg daily.

In general, high dose **HIDROTEF 100 mg**therapy should be continued only until the patient's condition has stabilised, usually not beyond 48 to 72 hours. When high doses of **HIDROTEF 100 mg** must be continued beyond 48 to 72 hours, hyponatraemia may occur. Under such circumstances it may be desirable to replace **HIDROTEF 100 mg** with a corticoid which causes little or no sodium retention.

Used the lowest effective dose for the shortest duration of treatment. For prolonged treatment, consider other dosage forms.

Patients subjected to severe stress following **HIDROTEF 100 mg** therapy should be observed closely for signs and symptoms of adrenocortical insufficiency.

Preparation of solutions:

For intravenous or intramuscular injection, prepare the solution by aseptically adding not more than 2 ml of Water for Injection to the contents of one vial.

For intravenous infusion:

First, prepare the solution by adding not more than 2 ml of sterile water for injection to the vial. This

solution may then be added to 100 ml to 1000 ml of the following 5 % dextrose in water or 0.9 % sodium chloride or 5 % dextrose in 0.9 % sodium chloride if patient is not on sodium restriction).

The reconstituted solution must be inspected visually for particulate matter and discoloration.

Method of administration

For intravenous or intramuscular use.

4.3 Contraindications

- Patients with known hypersensitivity to hydrocortisone or to any constituents of the product.
- Systemic fungal infection, unless specific anti-infective therapy is employed.
- Herpes simplex keratitis
- Acute psychoses
- Latent, healed or active tuberculosis
- Administration of live or live, attenuated vaccines is contra-indicated in patients receiving immunosuppressive doses of **HIDROTEF 100 mg**.

4.4 Special warnings and precautions for use

A Patient Information Leaflet is provided in the pack by the manufacturer.

Undesirable effects may be minimised by using the lowest effective dose for the minimum period. Frequent patient review is required to appropriately titrate the dose against disease activity (see Section 4.2).

Rapid intravenous administration of high doses of **HIDROTEF 100 mg** may cause anaphylactic reactions. Equipment, medication and trained personnel necessary for treating these complications should be immediately available.

Tuberculosis (active positive skin test, latent or history of) may be exacerbated or reactivated by **HIDROTEF 100 mg**; appropriate antitubercular chemotherapy or prophylaxis should be administered concurrently. Concurrent use of **HIDROTEF 100 mg** and ciclosporin may cause convulsions (see section

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4.5). Infants born of mothers who have received prolonged therapy with high doses of **HIDROTEF 100 mg** should be carefully monitored for signs of adrenal insufficiency (see section 4.6).

Patients on **HIDROTEF 100 mg**, especially in high doses, should not be immunized because of the possible risk of lack of antibody response (see section 4.5).

HIDROTEF 100 mg should be used with caution in:

- Diverticulitis
- Non-specific ulcerative colitis, if there is a risk of impending perforation, abscess or other infection
- Recent intestinal anastomoses
- Active or latent peptic ulcer
- Myasthenia gravis. As muscle weakness may initially be increased, leading to possible respiratory distress
- Osteoporosis (post-menopausal females are particularly at risk)
- Renal function impairment
- Hypertension or congestive heart failure
- Ocular herpes simplex as this may result in corneal perforation
- Glaucoma (or a family history of glaucoma).
- Acute psychosis, which may be aggravated
- Glucose intolerance
- Previous corticosteroid-induced myopathy
- Liver failure or cirrhosis
- Epilepsy
- Predisposition to thrombophlebitis
- Hypothyroidism
- Existing or previous history of severe affective disorders (especially previous steroid psychosis)
- Diabetes mellitus (or a family history of diabetes).
- History of tuberculosis
- Recent myocardial infarction (myocardial rupture has been reported).
- Kaposi's sarcoma has been reported to occur in patients receiving corticosteroid therapy. Discontinuation of corticosteroids may result in clinical remission

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- 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.
- Hydrocortisone can cause elevation of blood pressure, salt and water retention and increased excretion of potassium. Dietary salt restriction and potassium supplementation may be necessary. All corticosteroids increase calcium excretion.
- 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 treatment. Risks may be higher with high doses/systemic exposure (see also section 4.5 Interaction with Other Medicaments and Other Forms of Interaction that can increase the risk of side effects), although dose levels do not allow prediction of the onset, type, severity or duration of reactions. Most reactions recover after either dose reduction or withdrawal, although specific treatment may be necessary. Patients/carers should be encouraged to seek medical advice if worrying psychological symptoms develop, especially if depressed mood or suicidal ideation is suspected. Patients/carers should 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.

Decrease or discontinue the dosage gradually if **HIDROTEF 100 mg**has been administered for more than a few days.

Withdrawal syndrome may occur with a too rapid reduction in dosage, which can lead to acute adrenal insufficiency, hypotension and death.

Adrenal cortical atrophy develops during prolonged therapy and may persist for months after stopping treatment. In patients who have received more than physiological doses of systemic corticosteroids (approximately 30 mg hydrocortisone) 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

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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 30 mg hydrocortisone 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 considered that the disease is unlikely to relapse. Abrupt withdrawal of doses up to 160 mg hydrocortisone 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 160 mg hydrocortisone.
- Patients repeatedly taking doses in the evening.

Immunosuppressant Effects/Increased Susceptibility to Infections:

Corticosteroids may increase susceptibility to infection, may mask some signs of infection, and new infections may appear during their use. Suppression of the inflammatory response and immune function increases the susceptibility to fungal, viral and bacterial infections and their severity. The clinical presentation may often be atypical and may reach an advanced stage before being recognised.

In patients on **HIDROTEF 100 mg** therapy subjected to unusual stress, increased dosage of rapidly acting corticosteroids before, during and after stressful situations, is indicated.

Pharmacologic doses of corticosteroids administered for prolonged periods may result in hypothalamic-pituitary-adrenal (HPA) suppression (secondary adrenocortical insufficiency). The degree and duration

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of adrenocortical insufficiency produced is variable among patients and depends on the dose, frequency, time of administration, and duration of glucocorticoid therapy. In addition, acute adrenal insufficiency leading to a fatal outcome may occur if glucocorticoids are withdrawn abruptly. Drug-induced secondary adrenocortical insufficiency may therefore be minimized by gradual reduction of dosage. This type of relative insufficiency may persist for months after discontinuation of therapy; therefore, in any situation of stress occurring during that period, hormone therapy should be reinstituted. A steroid “withdrawal syndrome,” seemingly unrelated to adrenocortical insufficiency, may also occur following abrupt discontinuance of glucocorticoids. This syndrome includes symptoms such as: anorexia, nausea, vomiting, lethargy, headache, fever, joint pain, desquamation, myalgia, weight loss, and/or hypotension. These effects are thought to be due to the sudden change in glucocorticoid concentration rather than to low corticosteroid levels. Because glucocorticoids can produce or aggravate Cushing's syndrome, glucocorticoids should be avoided in patients with Cushing's disease. There is an enhanced effect of corticosteroids on patients with hypothyroidism.

Because of the inhibitory effect of **HIDROTEF 100 mg** on fibroplasia, hydrocortisone may mask the signs of infection and enhance dissemination of the infecting organism. Hence, all patients receiving **HIDROTEF 100 mg** should be observed for evidence of intercurrent infection. Should infection occur, it must be brought under control by use of appropriate antibacterial measures.

Prolonged use of **HIDROTEF 100 mg** may produce posterior subcapsular cataracts, glaucoma with possible damage to the optic nerves and may enhance establishment of secondary ocular infections due to fungi or viruses.

Chicken pox and measles can have a more serious or even fatal course in patients on **HIDROTEF 100 mg**. **HIDROTEF 100 mg**must be used with great care in patients with known or suspected Strong gyloides (threadworm) infestation.

Chickenpox is of serious concern since this normally minor illness may be fatal in immune suppressed 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 immunization with varicella/zoster immunoglobin (VZIG) is needed by exposed non-immune patients who are receiving systemic corticosteroids or who have used them within the previous 3 months; this should be given within 10 days of exposure to chickenpox. If a diagnosis of

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chickenpox is confirmed, the illness warrants specialist care and urgent treatment. Corticosteroids should not be stopped and the dose may need to be increased.

Exposure to measles should be avoided. Medical advice should be sought immediately if exposure occurs. Prophylaxis with normal intramuscular immunoglobulin may be needed.

Systemic corticosteroids are not indicated for, and therefore should not be used to treat traumatic brain injury or stroke because it is unlikely to be of benefit and may even be harmful. For traumatic brain injury a multicenter study revealed an increased mortality at 2 weeks and 6 months after injury in patients administered methylprednisolone sodium succinate compared to placebo. A casual association with methylprednisolone sodium succinate treatment has not been established.

Since mineralocorticoid secretion may be impaired, administration of a mineral corticosteroid may be considered.

HIDROTEF 100 mg can cause elevation of blood pressure, salt and water retention and increased potassium and calcium excretion. Dietary salt restriction and potassium supplementation may be necessary.

HIDROTEF 100 mg may aggravate diabetes mellitus so that higher insulin dosage may become necessary or manifestation of latent diabetes mellitus may be precipitated.

The use of **HIDROTEF 100 mg** in myasthenia gravis may aggravate myasthenic symptoms and should therefore be given with proper precautions.

Weakness and atrophy of voluntary musculature may occur following administration of **HIDROTEF 100 mg**. In some instances hypokalaemia may be a contributing factor. This effect should be kept in mind and periodic determinations of serum potassium performed in patients receiving **HIDROTEF 100 mg** for prolonged periods.

Retardation of linear growth has been noted in children receiving corticoids for 6 months or longer, the

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retardation being roughly proportional to the dose. The growth of children receiving prolonged **HIDROTEF 100 mg** therapy should be observed carefully. If growth is retarded, the dose should be reduced sufficiently to permit recovery before epiphyseal closure.

Continued supervision of the patient after cessation of **HIDROTEF 100 mg** therapy is essential since there may be a sudden re-appearance of severe manifestations of the disease for which the patient was treated.

Administration of live or live, attenuated vaccines is contraindicated in patients receiving immunosuppressive doses of corticosteroids. Killed or inactivated vaccines may be administered to patients receiving immunosuppressive doses of corticosteroids; however, the response to such vaccines may be diminished. Indicated immunization procedures may be under taken in patients receiving non-immunosuppressive doses of corticosteroids.

The use of Hydrocortisone in active tuberculosis should be restricted to those cases of fulminating or disseminated tuberculosis in which the corticosteroid is used for the management of the disease in conjunction with appropriate anti tuberculosis regimen. If corticosteroids are indicated in patients with latent tuberculosis or tuberculin reactivity, close observation is necessary as reactivation of the disease may occur. During prolonged corticosteroid therapy, these patients should receive chemoprophylaxis.

Allergic reactions may occur. Rarely skin reactions and anaphylactic/anaphylactoid reactions have been reported following parenteral hydrocortisone therapy. Physicians using the drug should be prepared to deal with such a possibility. Appropriate precautionary measures should be taken prior to administration, especially when the patient has a history of drug allergy.

Care should be taken for patients receiving cardioactive drugs such as digoxin because of steroid induced electrolyte disturbance/potassium loss (see Section 4.8).

Hepatobiliary disorders have been reported which may be reversible after discontinuation of therapy monitoring is required. Hydrocortisone may have an increased effect in patients with liver diseases since

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the metabolism and elimination of hydrocortisone is significantly decreased in these patients.

Ocular Effects:

Corticosteroids should be used cautiously in patients with ocular herpes simplex for fear of corneal perforation.

Prolonged use of corticosteroids may produce posterior 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. Establishment of secondary fungal and viral infections of the eye may also be enhanced in patients receiving glucocorticoids.

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. Central serous chorioretinopathy, may lead to retinal detachment.

Severe medical events have been reported in association with the intrathecal/epidural routes of administration. There have been reports of epidural lipomatosis in patients taking corticosteroids, typically with long-term use at high doses.

Thrombosis including venous thromboembolism has been reported to occur with corticosteroids. As a result corticosteroids should be used with caution in patients who have or may be predisposed to thromboembolic disorders.

Cardiac effects:

Adverse effects of glucocorticoids on the cardiovascular system, such as dyslipidemia and hypertension, may predispose treated patients with existing cardiovascular risk factors to additional cardiovascular effects, if high doses and prolonged courses are used. Accordingly, corticosteroids should be employed judiciously in such patients and attention should be paid to risk modification and additional cardiac

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monitoring if needed. Low dose therapy may reduce the incidence of complications in corticosteroid therapy. Systemic corticosteroids should be used with caution, and only if strictly necessary, in cases ofcongestive heart failure.

Gastrointestinal effect:

High doses of corticosteroids may produce acute pancreatitis. There is no universal agreement on whether corticosteroids per se are responsible for peptic ulcers encountered during therapy; however, glucocorticoid therapy may mask the symptoms of peptic ulcer so that perforation or hemorrhage may occur without significant pain. Glucocorticoid therapy may mask peritonitis or other signs or symptoms associated with gastrointestinal disorders such as perforation, obstruction or pancreatitis. In combination with non-steroidal anti-inflammatory drugs (NSAIDs), the risk of developing gastrointestinal ulcers is increased.

Other:

Since complications of treatment with glucocorticoids are dependent on the size of the dose and the duration of treatment, a risk/benefit decision must be made in each individual case as to dose and duration of treatment as to whether daily or intermittent therapy should be used.

The lowest possible dose of corticosteroid should be used to control the condition under treatment and when reduction in dosage is possible, the reduction should be gradual.

Co-treatment with CYP3A inhibitors, including cobicistat-containing products, is expected to increase the risk of systemic side-effects. The combination should be avoided unless the benefit outweighs the increased risk of systemic corticosteroid side-effects, in which case patients should be monitored for systemic corticosteroid side-effects (see section 4.5).

Aspirin and nonsteroidal anti-inflammatory agents should be used cautiously in conjunction with corticosteroids (see section 4.5 Interaction with other medicinal products and other forms of interaction).

Corticosteroids should be used with caution in patients with seizure disorders.

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. The use

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of steroids should be restricted to the most serious indications. Growth and development of infants and children on prolonged corticosteroid therapy should be carefully observed. Growth may be suppressed in children receiving long-term, daily-divided dose glucocorticoid therapy. The use of such a regimen should be restricted to the most serious indications. Infants and children on prolonged corticosteroid therapy are at special risk from raised intracranial pressure. High doses of corticosteroids may produce pancreatitis in children.

Hypertrophic cardiomyopathy was reported after administration of hydrocortisone to prematurely born infants, therefore appropriate diagnostic evaluation and monitoring of cardiac function and structure should be performed.

Use in the elderly:

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 react

4.5 Interaction with other medicines and other forms of interaction

Concomitant use of **HIDROTEF 100 mg** with:

- Ciclosporin may result in seizures, especially with high doses in combination with **HIDROTEF 100 mg** as the metabolism of both is inhibited. Adverse effects are therefore more likely to occur (see Section 4.4).
- Medicines that induce hepatic enzymes, such as rifampicin, carbamazepine, phenobarbitone, phenytoin, and aminoglutethimide may result in reduced efficacy of **HIDROTEF 100 mg**.
- Medicines that induce hepatic enzymes such as Phenobarbital, phenytoin and rifampicin may increase the clearance of corticosteroids and may require increases in **HIDROTEF 100 mg** dose to achieve the desired response.
- Medicines such as erythromycin, clarithromycin, troleandomycin, ketoconazole, itraconazole, diltiazem,isoniazid and grapefruit juice that inhibit metabolism, may result in an increase in **HIDROTEF 100 mg**'s adverse effects.
- Attenuated live vaccines may potentiate the replication of the vaccine virus; also, immunization with oral poliovirus vaccines should be postponed in persons in close contact with the patient, especially

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family members. Caution should also be exercised with other vaccines (see section 4.4).

- Corticosteroids may increase the clearance of high-dose aspirin, which can lead to decreased salicylate serum levels. Caution is recommended when salicylate are used concurrently with **HIDROTEF 100 mg** in patients with hypoprothrombinaemia.
- Nondepolarising neuromuscular blocking agents, such as pancuronium may enhance the blockage of nondepolarizing neuromuscular blocking agents, possibly leading to increased or prolonged respiratory depression or paralysis.
- Other immunosuppressant agents such as cyclophosphamide and tacrolimus may increase the risk of infection.
- Diuretics may result in severe hypokalaemia. Monitoring of serum potassium concentration and cardiac function is recommended. There is also an increased risk of hypokalaemia with concurrent use of corticosteroids with amphotericin B, xanthines, or beta2 agonists. There have been cases reported in which concomitant use of amphotericin B and hydrocortisone was followed by cardiac enlargement and congestive heart failure.
- Digoxin may increase the risk of cardiac dysrhythmias associated with hypokalaemia. Concurrent use of corticosteroids with cardiac glycosides may enhance the possibility of arrhythmias or digitalis toxicity associated with hypokalaemia. In all patients taking any of these drug therapy combinations, serum electrolyte determinations, particularly potassium levels, should be monitored closely.
- Antidiabetic agents, oral and insulin, may require dosage adjustment of both agents as **HIDROTEF 100 mg** may increase blood glucose concentration. Dosage readjustment of the hypoglycaemic agent also may be required when **HIDROTEF 100 mg** is discontinued.
- Coumarin anticoagulants may result in an enhanced anticoagulant effect. Monitoring of INR is recommended.
- Anticholinesterase agents may produce severe weakness in patients with myasthenia gravis Anitcholinesterase agents should be withdrawn at 24 hours before initiating therapy with **HIDROTEF 100 mg**.
- Carbonic anhydrase inhibitors or amphotericin B may result in severe hypokalaemia. Serum potassium concentrations and cardiac function should be monitored.
- Antihypertensives may result in reduced hypotension.
- Killed or inactivated vaccines may be administered to patients receiving immunosuppressive doses

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of **HIDROTEF 100 mg** however the response to such vaccines may be diminished.

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 individual drugs; however, hydrocortisone 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 in man, however, when administered for long periods or repeatedly during pregnancy, corticosteroids may increase the risk of intra- uterine growth retardation.

Some corticosteroids readily cross the placenta. Some retrospective studies have found an increased incidence of low-birth weights in infants born of mothers receiving corticosteroids. In humans, the risk of low birth weight appears to be dose related and may be minimized by administering lower corticosteroid doses.

Cataracts have been observed in infants born to mothers treated with long-term corticosteroids during pregnancy.

Breast-feeding

Corticosteroids are excreted in breast milk, although no data are available for hydrocortisone. Doses up to 160 mg daily of hydrocortisone are unlikely to cause systemic effects in the infant. Infants of mothers taking higher doses than this may have a degree of adrenal suppression.

Fertility

Corticosteroids have been shown to impair fertility in animal studies. The clinical relevance of this information is uncertain.

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4.7 Effects on ability to drive and use machines

The effect of corticosteroids on the ability to drive or use machinery has not been systematically evaluated. Undesirable effects, such as syncope, vertigo, and convulsions are possible after treatment with corticosteroids. If affected, patients should not drive or operate machinery.

4.8 Undesirable effects

Tabulated summary of adverse reactions

System organ class	Frequent	Less frequent	Frequency unknown
Infections and infestations	Aggravation or masking of infection		
Immune system disorders	Generalised anaphylaxis e.g. bronchospasm, laryngeal oedema and urticaria, flushing of face or cheeks, seizures.		
Endocrine disorders	Cushing's syndrome, relative adreno cortical insufficiency particularly in time of stress due to trauma,surgery or severe illness, menstrual irregularities including amenorrhoea, spotting or prolonged bleeding; suppression of growth		

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	in children, weight gain.		
Metabolism and nutrition disorders	Protein catabolism with negative nitrogen balance, electrolyte imbalance, alteration of glucose metabolism with aggravation of diabetes mellitus including hyperglycaemia and glycosuria.		
Psychiatric disorders		Delirium, disorientation, psychic disturbances especially abnormal euphoria, manic-depressive episodes, mental depression or paranoia, anxiety, sleep disturbances.	
Nervous system disorders	Insomnia; nervousness; increased intracranial pressure with papilloedema	Sweating; vertigo; headache; convulsions, vertigo, dizziness, lightheadedness	
Eye disorders	Posterior subcapsular cataracts, increased intra-ocular tension;	Sudden blindness	

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	glaucoma with possible damage to optic nerves, corneal or sclera thinning		
Cardiac disorders		Congestive heart failure	
Vascular disorders		Increased blood pressure	
Hepatobiliary disorders		Reversible increases in ALT and AST.	
Gastrointestinal disorders	Nausea, Vomiting, increased appetite, indigestion; activation and complication of peptic ulcer including perforation and haemorrhage; pancreatitis, oesophageal ulceration	Hiccups	
Skin and subcutaneous disorders	Petechiae and Purpura, thin, fragile skin.	Acne, delayed wound healing.	
Musculoskeletal disorders	Osteoporosis reversible only with difficulty; spontaneous fractures; aseptic necrosis of the femural	Weakness; myopathy, tendon rupture.	

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	head and humerus head.		
General disorders and administrative site conditions	Scarring at injection site	Burning, numbness pain or tingling at or near injection site, local allergic reaction at the injection site.	

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. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications:

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

4.9 Overdose

Treatment should be symptomatic and supportive.

There is no clinical syndrome of acute overdosage with Hydrocortisone. Hydrocortisone is dialysable.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 21.5 Corticosteroids

Pharmacotherapeutic group: Glucocorticoids

ATC code: H02AB09

Mechanism of action

Hydrocortisone sodium succinate has the same metabolic and anti-inflammatory actions as hydrocortisone. It is a glucocorticosteroid. Used in pharmacological doses, it has anti-inflammatory and immunosuppressive effects.

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5.2 Pharmacokinetic properties

Following the intravenous injection of hydrocortisone sodium succinate, demonstrable effects are evident within one hour and persist for a variable period. Excretion of the administered dose is nearly complete within 12 hours. This preparation is also rapidly absorbed when administered intramuscularly and is excreted in a pattern similar to that observed after intravenous injections.

5.3. Preclinical safety data

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6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Powder for injection:

Contains phosphate buffer as excipient.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store at or below 25 °C.

The solution is stable for 2 hours after reconstitution and must therefore be used immediately. Unused solution must be discarded.

KEEP OUT OF REACH OF CHILDREN

6.5 Nature and contents of container

A 7.5 ml clear colourless glass vial sealed with grey bromo butyl rubber stopper and dark blue aluminium flip off seal. Each vial is packed in an outer carton box in packs of 1's or 5's.

Not all pack sizes may be marketed. VR

6.6 Special precautions for disposal

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

MACLEODS PHARMACEUTICALS SA (PTY) LTD

GROUND FLOOR, BLOCK 1,

BASSONIA ESTATE OFFICE PARK (EAST),

1 CUSSONIA DRIVE,

BASSONIA ROCK EXT 12

ALBERTON

GAUTENG

8. REGISTRATION NUMBERS

59/21.5/0169

9. DATE OF FIRST AUTHORISATION

13 February 2024

10. DATE OF REVISION OF THE TEXT

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