# SUMMARY OF PRODUCT CHARACTERISTICS

## 1 NAME OF THE MEDICINAL PRODUCT

Hydrocortisone 20 mg Tablets

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 20 mg hydrocortisone

Excipient(s) with known effect
Each tablet contains 284.8 mg of lactose monohydrate.

For the full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Tablet

White, oval shaped tablet, engraved “H20” on one side and bisect breakline on the other. Dimensions: Approx. 9 mm x 14 mm.

The tablet can be divided into equal doses.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

- Replacement therapy in congenital adrenal hyperplasia in children.
- Pre-operatively, and during serious trauma or illness in patients with known adrenal insufficiency in children and adolescents or doubtful adrenocortical reserve.
- Emergency treatment of severe bronchial asthma, drug hypersensitivity reactions, serum sickness, angioneurotic oedema and anaphylaxis in adults and children.

Hydrocortisone Tablets are indicated in adults and children aged from 1 month to 18 years where the doses of 10 mg and 20 mg and tablet formulation are considered appropriate.

## 4.2 Posology and method of administration

Posology
Dose must be individualised according to the response of the individual patient. The lowest possible dose should be used. Doses should be multiples of 10 (i.e 10mg, 20mg, 30mg, etc.).

Undesirable effects may be minimised by using the lowest effective dose for the minimum period and by administering the daily requirement as a single morning dose or whenever possible, as a single morning dose on alternate days. Frequent patient review is required to titrate the dose against disease activity.

To avoid hypoadrenalism and/or a relapse of the underlying disease, it may be necessary to withdraw the drug gradually (see section 4.4).

***Replacement therapy***
In chronic adrenocortical insufficiency, a dosage of 20 to 30mg a day is usually recommended, sometimes together with 4-6 g of sodium chloride or 50-300 micrograms of fludrocortisone daily.
When immediate support is mandatory, one of the soluble adrenocortical hormone preparations (e.g. dexamethasone sodium phosphate), which may be effective within minutes after parenteral administration, can be lifesaving.

*Paediatric population*:
In chronic adrenocortical insufficiency, the dosage should be approximately 0.4 to 0.8mg/kg/day in two or three divided doses, adjusted to the needs of the individual child.

Acute emergencies
60–80 mg every 4–6 hours for 24 hours, then gradually reduce the dose over several days.

*Elderly patients*
Treatment of elderly patients, particularly if long-term, should be planned bearing in mind the more serious consequences of the common side effects of corticosteroids in old age, especially osteoporosis, diabetes, hypertension, susceptibility to infection and thinning of the skin.

In patients requiring replacement therapy, the first dose in the morning should be higher than the other doses, to simulate the normal diurnal rhythm of cortisol secretion.

***Use in serious trauma or illness with known adrenal insufficiency or doubtful adrenocortical reserve***

*Paediatric population:*
Doses are generally higher than that used for chronic adrenocortical

insufficiency and should be selected as appropriate for the clinical situation.

Patients should be observed closely for signs that might require dose adjustment, including changes in clinical status resulting from remissions or exacerbations of the disease, individual drug responsiveness, and the effect of stress (e.g. surgery, infection, and trauma). During stress it may be necessary to increase the dose temporarily.

***Pre-operative use***

Anaesthetists must be informed if the patient is taking corticosteroids or has previously taken corticosteroids.

When long term treatment is to be discontinued, the dose should be gradually reduced over a period of weeks or months, depending on dosage and duration of therapy (see section 4.4).

**Method of administration**

Oral use.

## 4.3 Contraindications

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

High-dose corticosteroid therapy potentially inducing immune deficiency is contraindicated in tuberculosis and other systemic acute and chronic bacterial, fungal, viral and parasitic infections without appropriate antimicrobial drug therapy.

Vaccines containing live, attenuated viruses or bacteria should not be given to patients receiving high-dose corticosteroid therapy during treatment-induced immune deficiency.

## 4.4 Special warnings and precautions for use

Patients should carry 'steroid treatment' cards, which give clear guidance on the precautions to be taken to minimise risk and which provide details of the prescriber, drug, dosage and the duration of treatment.

The lowest possible dosage of corticosteroids should be used and when reduction in dosage is possible, the reduction should be gradual. Stopping corticosteroid, after prolonged therapy may cause withdrawal symptoms (see section 4.8).

Patients/and or carers should be warned that potentially severe psychiatric adverse reactions may occur with systemic steroids (see section 4.8). Symptoms typically emerge within a few days or weeks of starting the treatment. Risks may be higher with high doses/systemic exposure (see also section 4.5), although dose levels do not allow prediction of the onset, type, severity or duration of reactions. Most reactions recover after either dose reduction or withdrawal, although specific treatment may be necessary.

Patients/carers should be encouraged to seek medical advice if worrying psychological symptoms develop, especially if depressed mood or suicidal ideation is suspected. Patients/carers should also be alert to possible psychiatric disturbances that may occur either during or immediately after dose tapering/withdrawal of systemic steroids, although such reactions have been reported infrequently.

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

Caution should be exercised in immunocompromised patients.

Chickenpox is of particular concern since this normally minor illness may be fatal in immunosuppressed patients. Patients (or parents of children receiving hydrocortisone tablets) without a definite history of chickenpox should be advised to avoid close personal contact with chickenpox or herpes zoster. If exposed, they should seek urgent medical attention. Passive immunisation with *Varicella zoster* immunoglobulin (VZIG) is needed by exposed non- immune patients who are receiving systemic corticosteroids or who have used them within the previous 3 months; this should be given within 10 days of exposure to chickenpox. If a diagnosis of chickenpox is confirmed, the illness warrants specialist care and urgent treatment.

Patients should be advised to take particular care to avoid exposure to measles and to seek immediate medical advice if exposure occurs.. Prophylaxis with intramuscular normal immunoglobulin may be needed.

Live vaccines should not be given to individuals with impaired immune responsiveness caused by high doses of corticosteroids. Killed vaccines or toxoids may be given though their effects may be attenuated. Corticosteroids should not be stopped and the dose may need to be increased. Corticosteroids may exacerbate systemic fungal infections and therefore should not be used in the presence of such infections unless they are needed to control life-threatening drug reactions due to amphotericin. Moreover, there have been cases reported in which concomitant use of amphotericin and hydrocortisone was followed by cardiac enlargement and congestive failure.

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

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

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

If corticosteroids are indicated in patients with latent tuberculosis or tuberculin reactivity, close observation is necessary as reactivation may occur. During prolonged corticosteroid therapy, these patients should receive prophylactic chemotherapy.

The use of hydrocortisone tablets in active tuberculosis should be restricted to those cases of fulminating or disseminated tuberculosis.

Corticosteroids should be used with caution in renal insufficiency, hypertension, diabetes mellitus or in those with a family history of diabetes, congestive heart failure, thrombophlebitis, exanthematous disease, chronic nephritis, acute glomerulonephritis, metastatic carcinoma, osteoporosis (postmenopausal patients are at special risk), severe affective disorders (particularly if there is a history of steroid-induced psychosis), epilepsy, previous steroid myopathy, liver failure, glaucoma (or family history of glaucoma), myasthenia gravis, non-specific ulcerative colitis if there is a probability of impending perforation, diverticulitis, fresh intestinal anastomoses, active or latent peptic ulcer. Signs of peritoneal irritation following gastro-intestinal perforation in patients receiving large doses of corticosteroids may be minimal or absent.

During treatment, the patient should be observed for psychotic reactions, weakness, electrocardiographic changes, hypertension and untoward hormonal effects.

Fat embolism has been reported as a possible complication of hypercortisonism.

There is an enhanced effect of corticosteroids in patients with hypothyroidism and in those with cirrhosis. Corticosteroid clearance may be decreased in patients with hypothyroidism and increased in patients with hyperthyroidism.

Prolonged courses of corticosteroids increase susceptibility to infections and their severity. The clinical presentation of infections may also be atypical.

Corticosteroids may mask some signs of infection and some serious infection such as septicaemia and tuberculosis may reach an advanced stage before being recognised. There may be an inability to localise infection in patients on corticosteroids. Corticosteroids may affect the nitrobluetetrazolium test for bacterial infection and produce false negative results.

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

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

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

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.

Corticosteroids may increase or decrease motility and number of spermatozoa. Diabetes may be aggravated, necessitating a higher insulin dosage. Latent diabetes mellitus may be precipitated.

Menstrual irregularities may occur, and this possibility should be mentioned to female patients.

Rare instances of anaphylactoid reactions have occurred in patients receiving corticosteroids, especially when a patient has a history of drug allergies.

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

Corticosteroid therapy may affect blood coagulation. Caution should be observed in the concomitant use of medicines affecting blood coagulation (such as warfarin or ASA).

Thyrotoxic Periodic Paralysis (TPP) can occur in patients with hyperthyroidism and with hydrocortisone-induced hypokalaemia. TPP must be suspected in patients treated with hydrocortisone presenting signs or symptoms of muscle weakness, especially in patients with hyperthyroidism.

If TPP is suspected, levels of blood potassium must be immediately monitored and adequately managed to ensure the restoration of normal levels of blood potassium.

Withdrawal

Drug-induced secondary adrenocortical insufficiency may result from too rapid a withdrawal of corticosteroids and may be minimised 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, corticosteroid therapy should be reinstated. If the patient is receiving steroids already, the dosage may have to be increased. Since mineralocorticoid secretion may be impaired, salt and/or a mineralocorticoid should be administered concurrently (see section 4.5).

Stopping corticosteroid after prolonged therapy may cause withdrawal symptoms, including fever, myalgia, arthralgia and malaise. In patients who have received more than physiological doses of systemic corticosteroids (approximately 30mg hydrocortisone) for greater than three weeks, withdrawal should not be abrupt. How dose reduction should be carried out depends largely on whether the disease is likely to relapse as the dose of systemic corticosteroids is reduced. Clinical assessment of disease activity may be needed during withdrawal. If the disease is unlikely to relapse on withdrawal of systemic corticosteroids but there is uncertainty about hypothalamic-pituitary adrenal (HPA) suppression, the dose of systemic 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 three weeks, is appropriate if it is considered that the disease is unlikely to relapse. Abrupt withdrawal of doses of up to 160mg hydrocortisone for three weeks is unlikely to lead to clinically relevant HPA-axis suppression, in the majority of patients. In the following patient groups, gradual withdrawal of systemic

corticosteroid therapy should be considered even after courses lasting three weeks or less:

- Patients who have had repeated courses of systemic corticosteroids, particularly if taken for greater than three weeks
- When a short course has been prescribed within one year of cessation of long-term therapy (months or years)
- Patients who may have reasons for adrenocortical insufficiency other than exogenous corticosteroid therapy
- Patients receiving doses of systemic corticosteroid greater than 160 mg hydrocortisone
- Patients repeatedly taking doses in the evening.

Paediatric population

The adverse effects of systemic corticosteroid therapy may be stronger in elderly patients and in children.

Pharmacological corticosteroid therapy may cause growth retardation in infancy, childhood and adolescence. Treatment should be limited to the minimum dosage in order to minimise suppression of the hypothalamo-pituitary-adrenal axis and growth retardation. Growth and development of infants and children on prolonged corticosteroid therapy should be carefully monitored.

Hypertrophic cardiomyopathy
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.

Excipients

**This medicine contains lactose**

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

## 4.5 Interaction with other medicinal products and other forms of interaction

Drug interactions listed below have been reported in pharmacological doses of corticosteroids and may not occur at replacement therapy doses of corticosteroids.

Aspirin should be used cautiously in conjunction with corticosteroids in hypoprothrombinaemia. There is an increased risk gastro-intestinal bleeding and ulceration when corticosteroids are given with aspirin and NSAIDs, although topical NSAIDs do not generally interact with corticosteroids. The renal clearance of salicylates is increased by corticosteroids and steroid withdrawal may result in salicylate intoxication.

Corticosteroids reduce plasma concentrations of salicylate and such an interaction may occur with pharmacological doses of glucocorticoids.

Phenytoin, ephedrine, rifabutin, carbamazepine, barbiturates, rifampicin, primidone, sympathomimetics and aminoglutethimide may enhance the metabolic clearance of corticosteroids, resulting in decreased blood levels and lessened physiological activity, thus requiring adjustment in corticosteroid dosage.

The INR or prothrombin time should be checked frequently in patients who are receiving corticosteroids and coumarin anticoagulants at the same time to avoid spontaneous bleeding because of reports of altered response to these anticoagulants. Studies have shown that the usual effect produced by adding corticosteroids is inhibition of response to coumarins, although there have been some conflicting reports of potentiation not substantiated by studies.

Ketoconazole alone can inhibit adrenal corticosteroid synthesis and may cause adrenal insufficiency during corticosteroid withdraw (see section 4.4).

Corticosteroids antagonise the effects of diuretics. Glucocorticosteroids are necessay for free water clearance by the kidneys. When corticosteroids are administered concomitantly with potassium-depleting diuretics (e.g. acetazolamide, loop diuretics, thiazides, carbenoxolone), patients should be observed closely for development of hypokalaemia.

Moreover, corticosteroids may affect the nitroblue tetrazolium test for bacterial infaction and produce false negative results.

Corticosteroids antagonise the hypotensive effects of beta-blockers, alpha- blockers, calcium channel blockers, clonidine, diazoxide, methyldopa, moxonidine, nitrates, nitroprusside, hydralazine, minoxidil, adrenergic neurone blockers, ACE inhibitors and angiotensin II receptor antagonists.

Corticosteroids increase risk of hypokalaemia when given with cardiac glycosides, e.g. digoxin, theophylline and beta2 sympathomimetics, e.g. bambuterol, fenoterol, formoterol, ritodrine, salbutamol, salmeterol and terbutaline.

There is an increased risk of hypokalaemia when corticosteroids are given with amphotericin. Concomitant use of amphotericin with corticosteroids should be avoided unless amphotericin is needed to control reactions

The effect of corticosteroids may be reduced for 3-4 days after interaction with mifepristone.

The plasma concentration of corticosteroids is increased by oral contraceptives containing oestrogens dosage adjustments may be required if oral contraceptives are added to or withdrawn from a stable dosage regimen. Interactions of combined oral contraceptives may also apply to combined contraceptive patches. In the case of hormone replacement therapy, low doses are unlikely to induce interactions. The plasma concentration of corticosteroids may possibly be increased by ritonavir.

Corticosteroids reduce absorption of calcium salts.

The metabolism of corticosteroids can be inhibited by erythromycin, although not when small amounts of erythromycin are used topically.

Corticosteroids antagonise hypoglycaemic effect of antidiabetics.

There is an increased risk of haematological toxicity when corticosteroids are given with methotrexate.

Corticosteroids may inhibit the growth-promoting effect of somatropin.

Corticosteroids may decrease the efficacy of vaccines and increase the risk of neurological complications in connection with vaccinations. Live virus vaccines may cause an infection in patients receiving hydrocortisone. Vaccines containing live, attenuated viruses or bacteria should not be given to patients receiving high-dose corticosteroid therapy during treatment-induced immune deficiency.

Corticosteroids possibly reduce the effects of sodium benzoate and sodium phenyl butyrate.

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.

Hydrocortisone may increase blood pressure. This should be taken into account in concomitant administration of antihypertensive medication.

Hydrocortisone may decrease, or in some cases increase, the effect of anticoagulants. Caution should be observed in the concomitant use of warfarin and systemic corticosteroids.

The effect of antidiabetics (including insulin) may be weakened in concomitant use with corticosteroids, and a dose increase may be necessary.

When used with anticholinesterases, corticosteroids may cause muscle weakness in patients with *myasthenia gravis*.

The effect of corticosteroids may be reduced for 3–4 days after treatment with mifepristone.

The concomitant use of fluoroquinolones and corticosteroid may increase the risk of tendon rupture.

## 4.6 Fertility, pregnancy and lactation

Pregnancy

The ability of corticosteroids to cross the placenta varies between individual drugs, however, hydrocortisone readily crosses the placenta. Besides replacement therapy, other systemic corticosteroid therapy during pregnancy should be regarded with caution. However, treatment should not be avoided if clearly indicated. If the mother has received hydrocortisone in pharmacological doses during pregnancy, the neonate should be monitored for adrenal insufficiency.

Corticosteroid therapy during pregnancy has been associated with foetal growth reduction, particularly in long-term use, and with insignificant contraction of the

*ductus arteriosus* in isolated cases. During late pregnancy, hydrocortisone may cause adverse effects to the foetus that are similar to those of long-term therapy in general.

In animal tests, corticosteroids have caused cheiloschisis and palatoschisis. An increase in palatoschisis has not been shown in humans. 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. Pregnant patients should be monitored closely if they develop fluid retention or pre-eclampsia. Hypoadrenalism may, in theory, occur in the neonate following prenatal exposure to corticosteroids but usually resolves spontaneously following birth and is rarely clinically important. As with all drugs, corticosteroids should only be prescribed when the benefits to the mother and child outweigh the risks. When corticosteroids are essential however, patients with normal pregnancies may be treated as though they were in the non-gravid state.

Breastfeeding

Corticosteroids are excreted in breast milk, although no data are available for hydrocortisone. Infants of mothers taking high doses of systemic corticosteroids for prolonged periods may have a degree of adrenal suppression. Mothers taking pharmacological doses of corticosteroids should be advised not to breast-feed. Maternal treatment should be carefully documented in the infant's medical records to assist in follow up.

Fertility

Corticosteroids may impair semen quality and cause amenorrhoea.

Patients with adrenal insufficiency have been shown to have reduced parity, which is most likely due to the underlying disease, but there is no indication that hydrocortisone in doses for replacement therapy will affect fertility.

## 4.7 Effects on ability to drive and use machines

Hydrocortisone has minor influence on the ability to drive and use machines.

Hydrocortisone may cause fatigue, vertigo, visual field loss and muscle wasting and weakness. If affected, patients should not drive or operate machinery (see section 4.8).

## 4.8 Undesirable effects

The incidence of predictable undesirable effects, including hypothalamicpituitary-adrenal suppression correlates with the relative potency of the drug, dosage, timing of administration and the duration of treatment (see section 4.4).

The following side effects may be associated with the long-term systemic use of corticosteroids with the following frequency:

Not known (cannot be estimated from available data)

| System organ class | Frequency | Undesirable effects |
|---|---|---|
| Infections and infestations | Not known | Infection[a], candidiasis. |
| Blood and lymphatic system disorders | Not known | Leukocytosis, erythrocytosis and granulocytosis, lymphoma and eosinopenia. |
| Immune system disorders | Not known | Hypersensitivity including anaphylaxis. |
| Endocrine disorders | Not known | Suppression of the hypothalamo-pituitary-adrenal axis, cushingoid facies. |
| Metabolism and nutrition disorders | Not known | Hypokalaemia, potassium decrease with hypokalaemic alkalosis, sodium and water retention, impaired carbohydrate tolerance with increased requirement for antidiabetic therapy, negative protein and calcium balance and increased appetite, centripetal obesity (face,trunk). |
| Psychiatric disorders | Not known | Affective disorders, behavioural disturbances, irritability, anxiety, sleep disturbances, cognitive dysfunction including confusion and amnesia[b], euphoria, psychological dependence, depression, insomnia and aggravation of schizophrenia. Aggravation of epilepsy, depressed and labile mood and suicidal thoughts, mania, delusions, hallucinations. |
| Nervous system disorders | Not known | Increased intracranial pressure with papilledema (*pseudotumor cerebri*), insomnia |
| Eye disorders | Not known | Increased intra-ocular pressure, glaucoma, papilledema, posterior subcapsular cataracts, corneal or scleral thinning, exacerbation of ophthalmic viral or fungal diseases, exophthalmos, vision blurred (see also section 4.4) |
| Cardiac disorders | Not known | Myocardial rupture following recent myocardial infarction, hypertrophic cardiomyopathy in prematurely born infants |
| Vascular disorders | Not known | Hypertension, thromboembolism. |
| Gastrointestinal disorders | Not known | Dyspepsia, peptic ulceration with possible perforation and haemorrhage, ulcerative oesophagitis, abdominal distension, acute pancreatitis, nausea |
| Skin and subcutaneous tissue disorders | Not known | Skin atrophy (thin, fragile skin), striae, acne, erythema, telangiectasia, urticaria, hirsutism |
| Musculoskeletal and connective tissue disorders | Not known | Proximal myopathy or steroid myopathy, osteoporosis, vertebral and long bone fractures, avascular osteonecrosis, tendon rupture |
| Reproductive system and breast disorders | Not known | Menstrual irregularities, amenorrhoea |
| General disorders and administration site conditions | Not known | Impaired healing, malaise |
| Injury, poisoning and procedural complications | Not known | Tendon rupture, bruising |
| Investigations | Not known | Weight increased |

a. Increased susceptibility and severity of infections with suppression of clinical symptoms and signs, opportunistic infections and recurrence of dormant tuberculosis (see section 4.4). An unfavourable course of infection (sepsis and reactivation of latent tuberculosis and parasitic infections such as amoebiasis and strongyloidiasis)

b. Reactions are common and may occur in both adults and children. In adults, the frequency of severe reactions has been estimated to be 5-6%. Psychological effects have been reported on withdrawal of corticosteroids.

Corticosteroid therapy may also cause increased coagulation tendency, hyperlipidaemia and nephroliths. It may decrease semen quality and cause amenorrhoea.

Paediatric population and elderly

The adverse effects of systemic corticosteroid therapy may be stronger in elderly patients and in children. Growth suppression in infancy, childhood and adolescence, increased intracranial pressure with papilloedema in children (pseudotumour cerebri), usually after treatment withdrawal.

Withdrawal symptoms

Too rapid a reduction of corticosteroid dosage following prolonged treatment can lead to acute renal insufficiency, hypotension and death (see section 4.4). A withdrawal syndrome may also occur including fever, myalgia, arthralgia, rhinitis, conjunctivitis, painful itchy skin nodules and weight loss.

**Reporting of suspected adverse reactions**

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme, Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

## 4.9 Overdose

Acute, massive hydrocortisone overdose is unlikely. Considerably high single doses are tolerated without severe adverse effects. The treatment for oral overdose is supportive; if necessary, activated charcoal may be administered and gastric lavage performed.

Symptoms

Overdosage may cause nausea and vomiting, sodium and water retention, hyperglycemia and occasional gastrointestinal bleeding.

Management

Treatment is probably not indicated for reactions due to chronic poisoning unless the patient has a condition that would render him unusually susceptible to ill effects from corticosteroids. In this case, symptomatic treatment should be instituted as necessary although cimetidine (200-400 mg by slow intravenous injection every 6 hours) or ranitidine (50 mg by slow intravenous injection every 6 hours) may be administered to prevent gastrointestinal bleeding.

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

The biological half-life of hydrocortisone is about 100 minutes.

# 5 PHARMACOLOGICAL PROPERTIES

## 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Corticosteroids for systemic use, Glucocorticoids, ATC code: H02AB09

Hydrocortisone is a glucocorticoid. Glucocorticoids are adrenocortical steroids, both naturally-occurring and synthetic, which are readily absorbed from the gastro-intestinal tract. Like all glucocorticoids, its effects are mediated by binding to steroid receptors in the cytoplasm. This leads to the formation of a steroid-receptor complex that passes into the nucleus, where it binds to the DNA and thus regulates the transcription of many genes as well as protein synthesis. Its effects are mediated by factors such as increased lipocortin synthesis.

Hydrocortisone is believed to be the principal corticosteroid secreted by the adrenal cortex. Naturally-occurring glucocorticosteroids (hydrocortisone and cortisone), which also have salt-retaining properties, are used as replacement therapy in adrenocortical deficiency states. They are also used for their potent anti-inflammatory effects in disorders of many organ systems. Glucocorticoids cause profound and varied metabolic effects. In addition they modify the body's immune responses to diverse stimuli.

The effect of glucocorticoids is catabolic, especially in muscle tissue. They decrease the production of lymphokines and eicosanoids and the amount of lymphatic tissue, and they weaken the immune response and exert an anti-inflammatory effect regardless of the cause of inflammation. They also reduce fibroblast activity and scarring. Glucocorticoids reduce ACTH secretion and suppress the hypothalamic-pituitary-adrenal axis. Hydrocortisone exerts some mineralocorticoid effect. After a 250 mg single dose of hydrocortisone, ACTH secretion is suppressed for approximately 1 to 1.5 days.

## 5.2 Pharmacokinetic properties

Hydrocortisone is rapidly and completely absorbed from the gastrointestinal tract . Due to first-pass metabolism, its availability varies between 25 and 90%. The peak plasma concentration of hydrocortisone is reached 1–2 hours after dosing. It binds to transcortin and albumin in plasma. In low concentrations, 10% of the hydrocortisone is in the free form, while in higher concentrations, transcortin binding capacity is saturated, and the proportion of free hydrocortisone may increase to 40–50%. The

volume of distribution is 0.4–0.7 L/kg. The mean pharmacological half-life of hydrocortisone is 1.5 h, but the biological effect half-life is considerably longer, approximately 10 hours. Hydrocortisone crosses the placental barrier and is excreted in milk in low quantities.

Hydrocortisone is metabolised in the liver and most body tissues to hydrogenated and degraded forms such as tetrahydrocortisone and tetrahydrocortisol which are excreted in the urine, mainly conjugated as glucuronides, together with a very small proportion of unchanged hydrocortisone.

Hydrocortisone elimination may be slower in hepatic diseases and shorter in thyrotoxicosis.

### 5.3 Preclinical safety data

Administration of corticosteroids to pregnant animals can cause abnormalities of foetal development including cleft palate, intra-uterine growth retardation, cheiloschisis, effects on brain growth and development.

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Lactose monohydrate

Maize starch

Povidone K30

Silica, colloidal anhydrous

Magnesium stearate

### 6.2 Incompatibilities

Not applicable.

### 6.3 Shelf life

23 months

### 6.4 Special precautions for storage

Do not store above 25°C. Store in the original package in order to protect from light.

### 6.5 Nature and contents of container

OPA/Alu/PVC-Aluminium blisters containing 30 and 100 tablets.

Not all pack sizes may be marketed.

### 6.6 Special precautions for disposal

No special requirements for disposal.

## 7 MARKETING AUTHORISATION HOLDER

Teva UK Limited, Ridings Point, Whistler Drive, Castleford, WF10 5HX, United Kingdom

## 8 MARKETING AUTHORISATION NUMBER(S)

PL 00289/2036

## 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

29/11/2016

## 10 DATE OF REVISION OF THE TEXT

16/07/2025