Hydrocortisone 10mg Tablets

Summary of Product Characteristics Updated 05-Sep-2018 | Auden Mckenzie (Pharma Division) Ltd (a subsidiary of Actavis PLC)

1. Name of the medicinal product

Hydrocortisone 10mg Tablets

Hydrocortone 10mg Tablets

Hydrocortisone Accord 10mg Tablets

Hitoden 10mg Tablets

2. Qualitative and quantitative composition

10mg tablet: 10mg hydrocortisone

3. Pharmaceutical form

Tablets

10mg tablets: white, quarter-scored tablets, marked 'HYD 10'. The tablet can be divided into equal halves or quarters

4. Clinical particulars

4.1 Therapeutic indications

Corticosteroid

For use as replacement therapy in primary, secondary, or acute adrenocortical insufficiency.

Pre-operatively, and during serious trauma or illness in patients with known adrenal insufficiency or doubtful adrenocortical reserve.

4.2 Posology and method of administration

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

Patients should be observed closely for signs that might require dosage 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, trauma). During stress it may be necessary to increase the dosage temporarily.

To avoid hypoadrenalism and/or a relapse of the underlying disease, it may be necessary to withdraw the drug gradually (see 4.4 'Special warnings and precautions for use').

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 (eg dexamethasone sodium phosphate), which may be effective within minutes after parenteral administration, can be life-saving.

Use in children: 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.

Use in the elderly: 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.

Pre-operative use:

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

4.3 Contraindications

Systemic fungal infections. Hypersensitivity to any component of this product.

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 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.

Patients/and or carers should be warned that potentially severe psychiatric adverse reactions may occur with systemic steroids (see section 4.8). Symptoms typically emerge within a few days or weeks of starting the treatment. Risks may be higher with high doses/systemic exposure (see also section 4.5 pharmacokinetic interactions that can

increase the risk of side effects), although dose levels do not allow prediction of the onset, type, severity or duration of reactions. Most reactions recover after either dose reduction or withdrawal, although specific treatment may be necessary. 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 disorders in themselves or in their first degree relatives. These would include depressive or manic-depressive illness and previous steroid psychosis.

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.

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 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, glaucoma (or family history of glaucoma), myasthenia gravis, non-specific ulcerative colitis, 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.

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.

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 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.

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 4.5 'Interaction with other medicinal products and other forms of interactions').

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 30 mg 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 160 mg 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.

Children: Corticosteroids 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.

Patients with rare hereditary problems of galactose intolerance, the Lapp 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 of 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 prothrombin time should be checked frequently in patients who are receiving corticosteroids and coumarin anticoagulants at the same time 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 4.4 'Special warnings and precautions for use').

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), 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, theophylline and $beta_2$ sympathomimetics.

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. 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.

High doses of corticosteroids impair immune response to vaccines, avoid concomitant use with live vaccines.

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.

4.6 Fertility, pregnancy and lactation

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/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.

Use in breast-feeding mothers: 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. Maternal treatment should be carefully documented in the infant's medical records to assist in follow up.

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

Blood and Lymphatic System Disorders: Leucocytosis

Immune System Disorders: Hypersensitivity.

Endocrine Disorders: *:* Increased or decreased motility and number of spermatozoa, menstrual irregularities, amenorrhoea, development of Cushingoid state, suppression of growth in children, secondary adrenocortical and pituitary unresponsiveness (particularly in times of stress, as in trauma, surgery, or illness), decreased carbohydrate tolerance, manifestations of latent diabetes mellitus, hyperglycemia, increased requirements for insulin or oral hypoglycaemic agents in diabetes, hirsutism.

Metabolism & Nutrition Disorders: Sodium retention, fluid retention, potassium loss, hypokalaemic alkalosis, increased calcium excretion, negative nitrogen balance due to protein catabolism, weight gain, increased appetite.

Psychiatric Disorders: psychic disturbances, psychological dependence, insomnia. A wide range of psychiatric reactions including affective disorders (such as irritable, euphoric, depressed and labile mood, and suicidal thoughts), psychotic reactions (including mania, delusions, hallucinations and aggravation of schizophrenia), behavioural disturbances, irritability, anxiety, sleep disturbances, and cognitive dysfunction including confusion and amnesia have been reported. Reactions are common and may occur in both adults and children. In adults, the frequency of severe reactions have been estimated to be 5-6%. Psychological effects have been reported on withdrawal of corticosteroids; the frequency is unknown.

Nervous System Disorders: Convulsions, increased intracranial pressure with papilloedema (pseudotumour cerebri) usually after treatment, vertigo, headache, malaise.

Eye disorders: Posterior subcapsular cataracts, increased intra-ocular pressure, papilloedema, corneal or scleral thinning, exacerbation of ophthalmic viral disease, glaucoma, exophthalmos, vision, blurred (see also section 4.4) (frequency not known).

Gastro-intestinal Disorders: Peptic ulcer with possible perforation and haemorrhage, perforation of the small and large bowel particularly in patients with inflammatory bowel disease, pancreatitis, abdominal distension, ulcerative oesophagitis, dyspepsia, oesophageal candidiasis, nausea.

Skin and Subcutaneous Tissue Disorders:: Impaired wound healing, thin fragile skin, petechiae, and ecchymoses, erythema, striae, telangiectasia, acne, increased sweating, may suppress reactions to skin tests, other cutaneous reactions such as allergic dermatitis, urticaria, angioneurotic oedema

Musculoskeletal, Connective Tissue & Bone Disorders: Muscle weakness, steroid myopathy, loss of muscle mass, osteoporosis (especially in post- menopausal females), vertebral compression fractures, aseptic necrosis of femoral and humeral heads, pathological fracture of long bones, tendon rupture.

Cardiac Disorders: Myocardial rupture following recent myocardial infarction (see 4.4 'Special warnings and precautions for use'), congestive heart failure in susceptible patients,

Vascular Disorders: thrombo-embolism, hypertension,

Respiratory, Thoracic & Mediastinal Disorders: Hiccups.

Other: Hypersensitivity, leucocytosis, weight gain, increased appetite, nausea, malaise.

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 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

Reports of acute toxicity and/or deaths following overdosage with glucocorticoids are rare. No antidote is available. 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.

Anaphylactic and hypersensitivity reactions may be treated with adrenaline, positive-pressure artificial respiration and arninophylline. 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

ATC Code: H02AB02 Systemic Hormonal Preparations (excluding sex hormones and insulins); Corticosteroids for Systemic Use; Plain; Hydrocortisone.

Hydrocortisone is a glucocorticoid. Glucocorticoids are adrenocortical steroids, both naturally-occurring and synthetic, which are readily absorbed from the gastro-intestinal tract.

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.

5.2 Pharmacokinetic properties

Hydrocortisone is readily absorbed from the gastro-intestinal tract and 90% or more of the drug is reversibly bound to protein.

The binding is accounted for by two protein fractions. One, corticosteroid- binding globulin is a glycoprotein; the other is albumin.

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.

5.3 Preclinical safety data

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.

6. Pharmaceutical particulars

6.1 List of excipients

Lactose

Magnesium stearate

Maize starch

6.2 Incompatibilities

None known

6.3 Shelf life

3 years

6.4 Special precautions for storage

Do not store above 25°C

Store in original package

6.5 Nature and contents of container

PVC/aluminium blister containing 30 tablets

6.6 Special precautions for disposal and other handling

None

7. Marketing authorisation holder

Accord Healthcare Limited

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8. Marketing authorisation number(s)

PL 20075/1249

9. Date of first authorisation/renewal of the authorisation

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10. Date of revision of the text

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