

Hydrocortisone 100mg/ml solution for injection

Summary of Product Characteristics Updated 02-Nov-2018 | ADVANZ Pharma

1. Name of the medicinal product

Efcortisol Injection.

Hydrocortisone 100mg/ml solution for injection

Hydrocortisone 500mg/5ml solution for injection

2. Qualitative and quantitative composition

Hydrocortisone Sodium Phosphate 13.39% w/v.

3. Pharmaceutical form

Solution for injection

4. Clinical particulars

4.1 Therapeutic indications

This presentation permits rapid use in emergency situations involving the following conditions:

Status asthmaticus and acute allergic reactions, including anaphylactic reaction to drugs. This medicine supplements the action of adrenaline.

Severe shock arising from surgical or accidental trauma or overwhelming infection.

Acute adrenal insufficiency caused by abnormal stress in Addison's disease, hypopituitarism, following adrenalectomy, and when adrenocortical function has been suppressed by prolonged corticosteroid therapy.

Soft tissue lesions such as tennis elbow, tenosynovitis, or bursitis.

Note: This medicine does not replace other forms of therapy for the treatment of shock and status asthmaticus

4.2 Posology and method of administration

Undesirable effects may be minimised by using the lowest effective dose for the minimum period. Frequent patient review is required to titrate appropriately the dose against disease activity (see Section 4.4).

Systemic therapy in adults: 100 to 500mg hydrocortisone (1 to 5ml) administered by slow intravenous injection, taking at least half to one minute. This dose can be repeated three or four times in 24 hours, depending upon the condition being treated and the patient's response. Alternatively, This medicine may be given as an intravenous infusion. A clinical effect is seen in two to four hours, and it persists for up to eight hours after intravenous injection. The same dose can be given by intramuscular injection, but the response is likely to be less rapid, especially in shock.

Systemic therapy in children: As a guide, infants up to 1 year may be given 25mg hydrocortisone intravenously; children 1 to 5 years, 50mg; 6 to 12 years, 100mg (1ml). This dose can be repeated three or four times in 24 hours depending upon the condition being treated and the patient's response.

Other uses: Local treatment of soft-tissue lesions - 100 to 200mg. This daily dose may be repeated on two or three occasions depending upon the patient's response.

This medicine is not recommended for intrathecal use.

Route(s) of administration

Intravenous or intramuscular injection, or injection into soft tissues.

4.3 Contraindications

Systemic infections, unless specific anti-infective therapy is employed. Live virus immunisation. Hypersensitivity to any component.

This medicine should not be injected directly into tendons.

4.4 Special warnings and precautions for use

Corticosteroids should **NOT** be used in the treatment of cerebral oedema associated with acute head injury or cerebrovascular accident, as they are unlikely to be of benefit and may even be harmful.

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)-axis suppression, the dose

of systemic corticosteroid may be reduced rapidly to physiological doses. Once a daily dose of 30mg hydrocortisone is reached, dose reduction should be slower to allow the HPA-axis to recover.

Abrupt withdrawal of systemic corticosteroid treatment, which has continued for 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 corticosteroids greater than 160mg hydrocortisone.
- Patients repeatedly taking doses in the evening.

Suppression of the HPA-axis and other undesirable effects may be minimised by using the lowest effective dose for the minimum period (see Section 4.2). The pronounced hormonal effects associated with prolonged corticosteroid therapy will probably not be seen when this injection is used for short-term adjunctive therapy in shock. Frequent patient review is required to titrate appropriately the dose against disease activity.

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

Suppression of the inflammatory response and immune function increases the susceptibility to infections and their severity. The clinical presentation may often be atypical and serious infections such as septicaemia and tuberculosis may be masked and may reach an advanced stage before being recognised.

Chickenpox is of particular concern since this normally minor illness may be fatal in immunosuppressed patients. Patients without a definite history of chickenpox should be advised to avoid close personal contact with chickenpox or herpes zoster and if exposed they should seek urgent medical attention. If the patient is a child, parents must be given the above advice. 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 three 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.

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 immunoglobulins may be needed.

Live vaccines should not be given to individuals with impaired immune responsiveness. The antibody response to other vaccines may be diminished.

Adrenal cortical atrophy develops during prolonged therapy and may persist for years after stopping treatment. Withdrawal of corticosteroids after prolonged therapy must therefore always be gradual to avoid acute adrenal insufficiency, being tapered off over weeks or months according to the dose and duration of treatment. During prolonged therapy any intercurrent illness, trauma or surgical procedure will require a temporary increase in dosage; if corticosteroids have been stopped following prolonged therapy they may need to be temporarily re-introduced.

Because of the possibility of fluid retention, care must be taken when corticosteroids are administered to patients with renal insufficiency or congestive heart failure.

Corticosteroids may worsen diabetes mellitus, osteoporosis, hypertension, glaucoma and epilepsy and therefore patients with these conditions or a family history should be monitored frequently.

Care is required and frequent patient monitoring necessary where there is a history of severe affective disorders (especially a previous history of steroid psychosis), previous steroid myopathy, peptic ulceration or in patients with a history of tuberculosis.

In patients with liver failure, blood levels of corticosteroid may be increased, as with other drugs which are metabolised in the liver and therefore patients should be monitored frequently. Care and monitoring are also required in patients with renal insufficiency.

Patients and/or carers should be warned that potentially severe psychiatric adverse reactions may occur with systemic steroids (see Section 4.8 Undesirable effects). 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 Interaction with other medicinal products and other forms of interaction), although dose levels do not allow prediction of the onset, type, severity or duration of reactions. Most adverse reactions resolve after either dose reduction or withdrawal of the medicine, 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 a 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.

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.

4.5 Interaction with other medicinal products and other forms of interaction

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.

Drug interactions: rifampicin, rifabutin, carbamazepine, phenobarbital, phenytoin, primidone, ephedrine and aminoglutethimide enhance the metabolism of corticosteroids and their therapeutic effects may be reduced.

The desired effects of hypoglycaemic agents (including insulin), anti-hypertensives and diuretics are antagonised by corticosteroids, and the hypokalaemic effects of acetazolamide, loop diuretics, thiazide diuretics and carbenoxolone are enhanced. The efficacy of coumarin anticoagulants may be enhanced by concurrent corticosteroid therapy and close monitoring of the INR or prothrombin time is required to avoid spontaneous bleeding.

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

Steroids may reduce the effects of anticholinesterases in myasthenia gravis and cholecystographic x-ray media.

Oestrogens may potentiate the effects of glucocorticoids.

4.6 Pregnancy and lactation

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/lip in man. However, when administered for prolonged periods or repeatedly during pregnancy, corticosteroids may increase the risk of intra-uterine growth retardation. Hypoadrenalism may, in theory, occur in the neonate following prenatal exposure to 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.

Patients with pre-eclampsia or fluid retention require close monitoring.

Depression of hormone levels has been described in pregnancy but the significance of this finding is not clear.

Lactation:

Corticosteroids are excreted in breast milk, although no data are available for hydrocortisone. Doses of up to 160mg 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 but the benefits of breast feeding are likely to outweigh any theoretical risk.

4.7 Effects on ability to drive and use machines

None stated.

4.8 Undesirable effects

Side effects: Paraesthesia may occur following intravenous administration and is probably related to the rate of injection. It is often localised to the genital area but in some cases may radiate over the entire body. The unpleasant and sometimes painful sensation usually passes off within a few minutes and no sequelae have been reported. The effect seems to be related to the sodium phosphate salt of hydrocortisone.

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

Endocrine/metabolic

Suppression of the hypothalamic-pituitary-adrenal axis, growth suppression in infancy, childhood and adolescence,

menstrual irregularity and amenorrhoea, cushingoid faces, hirsutism, weight gain, impaired carbohydrate tolerance with increased requirement for anti-diabetic therapy. Negative protein and calcium balance. Increased appetite.

Anti-inflammatory and immunosuppressive effects

Increased susceptibility and severity of infections with suppression of clinical symptoms and signs, opportunistic infections, recurrence of dormant tuberculosis (see Section 4.4).

Musculoskeletal

Osteoporosis, vertebral and long bone fractures, avascular osteonecrosis, tendon rupture. Proximal myopathy.

Fluid and electrolyte disturbance

Sodium and water retention, hypertension, potassium loss, hypokalaemic alkalosis.

Neuropsychiatric

Euphoria, psychological dependence, depression, insomnia, aggravation of schizophrenia and increased intra-cranial pressure with papilloedema in children (pseudotumour cerebri), usually after treatment withdrawal. Aggravation of epilepsy.

Ophthalmic

Increased intra-ocular pressure, glaucoma, papilloedema, posterior subcapsular cataracts, corneal or scleral thinning, exacerbation of ophthalmic viral or fungal diseases.

Not known: Vision, blurred (see also section 4.4).

Gastrointestinal

Dyspepsia, peptic ulceration with perforation and haemorrhage, acute pancreatitis, candidiasis.

Dermatological

Impaired healing, skin atrophy, bruising, telangiectasia, striae, acne.

General

Hypersensitivity, including anaphylaxis, has been reported. Leucocytosis. Thrombo-embolism. Flushing and pruritus.

Withdrawal symptoms and signs

Too rapid a reduction of corticosteroid dosage following prolonged treatment can lead to adrenal 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 loss of weight.

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

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 infections and thinning of the skin. Close clinical supervision is required to avoid life-threatening reactions.

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 has been estimated to be 5-6%. Psychological effects have been reported on withdrawal of corticosteroids; the frequency is unknown.

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 at: www.mhra.gov.uk/yellowcard.

4.9 Overdose

None stated.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Hydrocortisone is a glucocorticoid with anti-inflammatory properties.

5.2 Pharmacokinetic properties

Hydrocortisone is readily absorbed from the gastrointestinal tract and peak blood concentrations are attained in about an hour. It is more than 90% bound to plasma proteins.

Hydrocortisone is metabolised in the liver and most body tissues to hydrogenated and degraded forms such as tetrahydrocortisone and tetrahydrocortisol.

These are then excreted in the urine, mainly conjugated as glucuronides, together with a very small proportion of unchanged hydrocortisone.

5.3 Preclinical safety data

There are no preclinical data of relevance to the prescriber which are additional to those in other sections of the SPC.

6. Pharmaceutical particulars

6.1 List of excipients

Disodium Edetate

Disodium Hydrogen Phosphate, Anhydrous

Sodium Acid Phosphate

Sodium Formaldehyde Bisulphite Monohydrate

Phosphoric Acid (10% solution)

Water for injections

6.2 Incompatibilities

None known

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store below 25°C. Keep the ampoules in the outer carton.

6.5 Nature and contents of container

1ml and 5ml neutral glass ampoules.

6.6 Special precautions for disposal and other handling

No special instructions.

7. Marketing authorisation holder

Amdipharm UK Limited

Capital House,

85 King William Street,

London EC4N 7BL, UK

8. Marketing authorisation number(s)

PL 20072/0229

9. Date of first authorisation/renewal of the authorisation

13/01/2009

10. Date of revision of the text

29/10/2018

Company Contact Details

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