SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Hydrocortisone sodium succinate for Injection BP 100mg /Vial

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial contains:
Hydrocortisone sodium succinate BP
Equivalent to Hydrocortisone 100mg

3. PHARMACEUTICAL FORM

Powder for Injection
White or nearly white hygroscopic powder

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Anti-inflammatory agent.
Hydrocortisone is indicated for any condition in which rapid and intense corticosteroid effect is required such as:
1. Collagen diseases
Systemic lupus erythematosus
2. Dermatological diseases
Severe erythema multiforme (Stevens-Johnson syndrome)
3. Allergic states
Bronchial asthma, anaphylactic reactions
4. Gastro-intestinal diseases
Ulcerative colitis, Crohn's disease
5. Respiratory diseases
Aspiration of gastric contents

4.2 Posology and method of administration

Anti-inflammatory agent.
Hydrocortisone Sodium Succinate For Injection BP 100 mg/vial is indicated for any condition in which rapid and intense corticosteroid effect is required such as:
1. Endocrine disorders
Primary or secondary adrenocortical insufficiency
2. Collagen diseases
Systemic lupus erythematosus
3. Dermatological diseases
Severe erythema multiforme (Stevens-Johnson syndrome)
4. Allergic states
Bronchial asthma, anaphylactic reactions
5. Gastro-intestinal diseases
Ulcerative colitis, Crohn's disease
6. Respiratory diseases
Aspiration of gastric contents
7. Medical emergencies
Hydrocortisone Sodium Succinate For Injection BP 100 mg/vial is indicated in the treatment of shock secondary to adrenocortical insufficiency or shock unresponsive to conventional therapy when adrenocortical insufficiency may be present.

4.2 Posology and method of administration

Hydrocortisone Sodium Succinate for Injection BP 100 mg/vial 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 emergency period,

consideration should be given to employing a longer-acting injectable preparation or an oral preparation.
Dosage usually ranges from 100 mg to 500 mg depending on the severity of the condition, administered by intravenous injection over a period of one to ten minutes. This dose may be repeated at intervals of 2, 4 or 6 hours as indicated by the patient's response and clinical condition.
In general high-dose corticosteroid therapy should be continued only until the patient's condition has stabilized - usually not beyond 48 to 72 hours. If hydrocortisone therapy must be continued beyond 48 to 72 hours hypernatraemia may occur, therefore it may be preferable to replace Hydrocortisone Sodium Succinate for Injection BP 100 mg/vial with a corticosteroid such as methylprednisolone sodium Succinate as little or no sodium retention occurs. Although adverse effects associated with high dose, short-term corticoid therapy are uncommon, peptic ulceration may occur. Prophylactic antacid therapy may be indicated.
Patients subjected to severe stress following corticoid therapy should be observed closely for signs and symptoms of adrenocortical insufficiency.
Corticosteroid therapy is an adjunct to, and not a replacement for, conventional therapy.
In patients with liver disease, there may be an increased effect and reduced dosing may be considered.
Elderly patients: Hydrocortisone Sodium Succinate for Injection BP 100 mg/vial is primarily used in acute short-term conditions. There is no information to suggest that a change in dosage is warranted in the elderly. However, treatment of elderly patients should be planned bearing in mind the more serious consequences of the common side-effects of corticosteroids in old age and close clinical supervision is required (see Special warnings and special precautions for use).
Children: 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 weight but should not be less than 25 mg daily.
Preparation of solutions: For intravenous or intramuscular injection prepare the solution aseptically by adding not more than 2 ml of Sterile Water for Injections to the contents of one vial of Hydrocortisone Sodium Succinate for Injection BP 100 mg, shake and withdraw for use.
For intravenous infusion, first prepare the solution by adding not more than 2 ml of Sterile Water for Injections to the vial; this solution may then be added to 100 ml - 1000 ml (but not less than 100 ml) of 5% dextrose in water (or isotonic saline solution or 5% dextrose in isotonic saline solution if patient is not on sodium restriction).
When reconstituted as directed the pH of the solution will range from 7.0 to 8.0.

4.3 Contraindications
Hydrocortisone Sodium Succinate for Injection BP 100 mg/vial is contra-indicated where there is known hypersensitivity to components and in systemic fungal infection unless specific anti-infective therapy is employed.
Administration of live or live, attenuated vaccines is contraindicated inpatients receiving immunosuppressive doses of corticosteroids.

4.4 Special warnings and precautions for use
Warnings and Precautions:
1. A Patient Information Leaflet is provided in the pack by the manufacturer.
2. 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 Posology and method of administration).
3. 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 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.

4. 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.

5. Corticosteroids 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.

6. Chickenpox is of serious concern since this normally minor illness may be fatal in immunosuppressed 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 chickenpox is confirmed, the illness warrants specialist care and urgent treatment. Corticosteroids should not be stopped and the dose may need to be increased.

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

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

9 The use of Hydrocortisone Sodium Succinate For Injection BP 100 mg/vial 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 antituberculosis 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.

10. Rarely anaphylactoid reactions have been reported following parenteral Hydrocortisone Sodium Succinate For Injection BP 100 mg/vial 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.

11. Care should be taken for patients receiving cardioactive drugs such as digoxin because of steroid induced electrolyte disturbance/potassium loss.

12. Hydrocortisone may have an increased effect in patients with liver diseases since the metabolism and elimination of hydrocortisone is significantly decreased in these patients.

Special precautions:

Particular care is required when considering the use of systemic corticosteroids in patients with the following conditions and frequent patient monitoring is necessary.

1. Osteoporosis (post-menopausal females are particularly at risk).
2. Hypertension or congestive heart failure.
3. Existing or previous history of severe affective disorders (especially previous steroid psychosis).
4. Diabetes mellitus (or a family history of diabetes).
5. History of tuberculosis.
6. Glaucoma (or a family history of glaucoma).
7. Previous corticosteroid-induced myopathy.

8. Liver failure or cirrhosis.
9. Renal insufficiency.
10. Epilepsy.
11. Peptic ulceration.
12. Fresh intestinal anastomoses.
13. Predisposition to thrombophlebitis.
14. Abscess or other pyogenic infections.
15. Ulcerative colitis.
16. Diverticulitis.
17. Myasthenia gravis.
18. Ocular herpes simplex, for fear of corneal perforation.
19. Hypothyroidism.
20. Recent myocardial infarction (myocardial rupture has been reported).
21. Kaposi's sarcoma has been reported to occur in patients receiving corticosteroid therapy. Discontinuation of corticosteroids may result in clinical remission.
22. 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.
23. Patients and/or carers should be warned that potentially severe psychiatric adverse reactions may occur with systemic steroids. 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.
Use in children: 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 of steroids should be restricted to the most serious indications.
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 reactions.
"Corticosteroids should not be used for the management of head injury or stroke because it is unlikely to be of benefit and may even be harmful."

4.5 Interaction with other medicinal products and other forms of interaction
1. Convulsions have been reported with concurrent use of corticosteroids and cyclosporin. Since concurrent administration of these agents results in a mutual inhibition of metabolism, it is possible that convulsions and other adverse effects associated with the individual use of either drug may be more apt to occur.
2. Drugs that induce hepatic enzymes, such as rifampicin, rifabutin, carbamazepine, phenobarbitone, phenytoin, primidone, and aminoglutethimide enhance the metabolism of corticosteroids and its therapeutic effects may be reduced.
3. Drugs which inhibit the CYP3A4 enzyme, such as cimetidine, erythromycin, ketoconazole, itraconazole, diltiazem and mibefradil, may decrease the rate of metabolism of corticosteroids and hence increase the serum concentration.
4. Steroids may reduce the effects of anticholinesterases in myasthenia gravis. 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.
5. 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.
6. The renal clearance of salicylates is increased by corticosteroids and steroid withdrawal may result in salicylate intoxication. Salicylates and non-steroidal anti-inflammatory agents should be used cautiously in conjunction with corticosteroids in hypothrombinaemia.
7. Steroids have been reported to interact with neuromuscular blocking agents such as pancuronium with partial reversal of the neuromuscular block.

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 affects 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. 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.

Lactation

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 systemic effects in the infant. Infants of mothers taking higher doses than this may have a degree of adrenal suppression, but the benefits of breastfeeding are likely to outweigh any theoretical risk.

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

Since Hydrocortisone Sodium Succinate for Injection BP 100 mg/vial is normally employed on a short-term basis it is unlikely that side-effects will occur; however, the possibility of side-effects attributable to corticosteroid therapy should be recognised (see Special warnings and special precautions for use). Such side-effects include:

Parenteral Corticosteroid Therapy - Anaphylactoid reaction e.g. bronchospasm, hypopigmentation or hyperpigmentation, subcutaneous and cutaneous atrophy, sterile abscess, laryngeal oedema and urticaria.

Gastro-Intestinal - Dyspepsia, peptic ulceration with perforation and haemorrhage, abdominal distension, oesophageal ulceration, oesophageal candidiasis, acute pancreatitis, perforation of bowel, gastric haemorrhage.

Increases in alanine transaminase (ALT, SGPT) aspartate transaminase (AST, SGOT) and alkaline phosphatase have been observed following corticosteroid treatment. These changes are usually small, not associated with any clinical syndrome and are reversible upon discontinuation.

Anti-Inflammatory And Immunosuppressive Effects - Increased susceptibility and severity of infections with suppression of clinical symptoms and signs, opportunistic infections, may suppress reactions to skin tests, recurrence of dormant tuberculosis (see Special warnings and special precautions for use).

Musculoskeletal - Proximal myopathy, osteoporosis, vertebral and long bone fractures, avascular osteonecrosis, tendon rupture, aseptic necrosis, muscle weakness.

Fluid And Electrolyte Disturbance - Sodium and water retention, potassium loss, hypertension, hypokalaemic alkalosis, congestive heart failure in susceptible patients.

Dermatological - Impaired healing, petechiae and ecchymosis, skin atrophy, bruising, striae, increased sweating, telangiectasia, acne. Kaposi's sarcoma has been reported to occur in patients receiving corticosteroid therapy. Discontinuation of corticosteroids may result in clinical remission.
Endocrine/Metabolic - Suppression of the hypothalamo-pituitary-adrenal axis; growth suppression in infancy, childhood and adolescence; menstrual irregularity and amenorrhoea, Cushingoid facies, hirsutism, weight gain, impaired carbohydrate tolerance with increased requirement for antidiabetic therapy, negative nitrogen and calcium balance. Increased appetite.
NEUROPSYCHIATRIC - A wide range of psychiatric reactions including affective disorders (such as irritable, euphoric, depressed and labile mood psychological dependence and suicidal thoughts), psychotic reactions (including mania, delusions, hallucinations and aggravation of schizophrenia), behavioural disturbances, irritability, anxiety, sleep disturbances, seizures and cognitive dysfunction including confusion and amnesia have been reported for all corticosteroids. Reactions are common and may occur in both adults and children. In adults, the frequency of severe reactions was estimated to be 5-6%. Psychological effects have been reported on withdrawal of corticosteroids; the frequency is unknown. Increased intra-cranial pressure with papilloedema in children (pseudotumour cerebri) has been reported, usually after treatment withdrawal of hydrocortisone.
Ophthalmic - Increased intra-ocular pressure, glaucoma, papilloedema with possible damage to the optic nerve, cataracts, corneal or scleral thinning, exacerbation of ophthalmic viral or fungal disease, exophthalmos.
Cardiovascular – Myocardial rupture following a myocardial infarction.
General - Leucocytosis, hypersensitivity reactions including anaphylaxis, thrombo-embolism, nausea, malaise, persistent hiccups with high doses of corticosteroids.
Withdrawal Symptoms - Too rapid a reduction of corticosteroid dosage following prolonged treatment can lead to acute adrenal insufficiency, hypotension and death. However, this is more applicable to corticosteroids with an indication where continuous therapy is given (see Special warnings and special precautions for use).
A 'withdrawal syndrome' may also occur including, fever, myalgia, arthralgia, rhinitis, conjunctivitis, painful itchy skin nodules and loss of weight.

4.9 Overdose
There is no clinical syndrome of acute overdosage with Hydrocortisone Sodium Succinate for Injection BP 100 mg/vial. Hydrocortisone is dialysable.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties
Hydrocortisone sodium succinate has the same metabolic and anti-inflammatory actions as hydrocortisone. It is a glucocorticosteroid. Used in pharmacological doses, its actions supress the clinical manifestations of disease in a wide range of disorders.

5.2 Pharmacokinetic properties
Absorption
Bioavailability
Readily absorbed after oral administration. Following IM administration, absorption of the water-soluble sodium phosphate and sodium succinate salts is rapid; the rate of absorption of the lipid-soluble acetate is much slower.
Duration
The duration of anti-inflammatory activity of hydrocortisone approximately equals the duration of HPA-axis suppression, about 1.25 1.5 days for a single 100-mg oral dose.
Distribution
Extent
Most glucocorticoids are removed rapidly from the blood and distributed to muscle, liver, skin, intestines, and kidneys.b Glucocorticoids appear in breast milk and cross the placenta.b

Plasma Protein Binding
Extensively bound to corticosteroid-binding globulin (transcortin) and albumin.
Special Populations
Patients with low serum albumin concentrations may be more susceptible to effects of glucocorticoids than those with normal serum albumin concentrations.
Metabolism
Metabolized in most tissues, but primarily in the liver, to inactive compounds.
Elimination Route
Inactive metabolites are excreted by the kidneys, primarily as glucuronides and sulfates, but also as unconjugated products.Small amounts of unmetabolized drugs are also excreted in urine.
Half-life
Following oral or IV administration of hydrocortisone, 1.5 3.5 hours.
Special Populations
Metabolic clearance may be decreased in patients with hypothyroidism and increased in those with hyperthyroidism

5.3 Preclinical safety data

Not known

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
No excipients

6.2 Incompatibilities
Not known

6.3 Shelf life
36 Months

6.4 Special precautions for storage
Store below 30°C. Protect from light.

6.5 Nature and contents of container and special equipment for use, administration or implantation
5.0ml Flint glass vial USP type-III, 20mm grey butyl rubber plugs, & 20mm Aluminium seal

6.6 Special precautions for disposal and other handling
None.

7. MARKETING AUTHORISATION HOLDER

Ciron Drugs & Pharmaceuticals Pvt. Ltd.
C- 1101 /1102, Lotus Corporate Park, Graham Firth Steel Compound,
Jay Coach Junction, Western Express Highway, Goregaon (East)
Mumbai- 400 063, India.

8. MARKETING AUTHORISATION NUMBER(S)

08153/06703/NMR/2018

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 21.11.2022

10. DATE OF REVISION OF THE TEXT
14/07/2023

11. Reference

https://www.medicines.org.uk/emc/product/7812/pil#gref