SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Sontirco10mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 10mg hydrocortisone

Excipients with known effect:

Each tablet contains 37.5 mg lactose monohydrate

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablets

White round (6.0-6.2mm diameter) biconvex with a breakline and embossment “10” on one side. The tablet can be divided into equal doses.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Corticosteroid

- For use as replacement therapy in congenital adrenal hyperplasia in children.
- Treatment of adrenal insufficiency in children and adolescents < 18 years of age
- Emergency treatment of severe bronchial asthma, drug hypersensitivity reactions, serum sickness, angioneurotic oedema and anaphylaxis in adults and children

Sontirco 10 mg tablets are indicated in adults and children aged from 1 month to 18 years where the dose of 10 mg and tablet formulation is considered appropriate.

4.2 Posology and method of administration

Posology

Dosage must be individualised according to the response of the individual patient. The lowest possible dosage should be used.

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.

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, and 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 section 4.4).

Replacement therapy

Paediatric population

In congenital adrenal hyperplasia, 9–15 mg/m^2/day divided in 3 doses, adjusted according to response.

In adrenocortical insufficiency, 8–10 mg/ m^2/day divided in 3 doses, adjusted according to response. Higher doses may be needed.

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.

Dosage in special situations

Hydrocortisone replacement therapy

In patients receiving hydrocortisone replacement therapy, the dosage of Sontirco should be increased 2 to 4-fold in stressful situations, such as in connection with injuries, infections, or surgical procedures. If necessary, the patient should be switched to parenteral treatment.

Hepatic impairment

The elimination of Sontirco may be slower in connection with hepatic diseases, and dose adjustment may be necessary in patients with hepatic impairment.

Method of administration

For oral administration.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients.

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

Adrenal suppression

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.

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.

Anti-inflammatory / immunosuppressive effects and infection

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

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

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. 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 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 be used with caution in: non-specific ulcerative colitis if there is a probability of impending perforation, abscess or other pyogenic infection, diverticulitis; fresh intestinal anastomoses; active or latent peptic ulcer.

Particular care is required when prescribing systemic corticosteroids in patients with the following conditions and frequent patient monitoring is necessary:

a) osteoporosis (postmenopausal females are particularly at risk);
b) hypertension or congestive heart failure;
c) existing or previous history of severe affective disorders (especially
d) previous history of steroid psychosis);
e) diabetes mellitus (or a family history of diabetes);
f) previous history of tuberculosis or characteristic appearance on a chest x-ray. The emergence of active tuberculosis can, however, be prevented by the prophylactic use of anti-tuberculous therapy;
g) glaucoma (or family history or glaucoma);
h) previous corticosteroid-induced myopathy;
i) liver failure;
j) renal insufficiency;
k) epilepsy;
l) peptic ulceration;
m) recent myocardial infarction

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

Corticosteroids should be used with caution in patients with hypothyroidism.

Children: Corticosteroids cause growth retardation in infancy, childhood and adolescence, this may be irreversible. Treatment should be limited to the minimum dosage for the shortest possible time, retardation (see section 4.2, Posology and method of administration)

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.

Withdrawal symptoms:
In patients who have received more than physiological doses of systemic corticosteroids (approximately 40 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.

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 ormanic-depressive illness and previous steroid psychosis.

Excipients:

This medicine contains lactose monohydrate. 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

The metabolism of corticosteroids may be enhanced and the therapeutic effects reduced by ephedrine, certain barbiturates (e.g. phenobarbital) and by phenytoin, rifampicin, rifabutin, primidone, carbamazepine and aminoglutethimide.

Mifepristone may reduce the effect of corticosteroids for 3-4 days.

Erythromycin and ketoconazole may inhibit the metabolism of corticosteroids.

Ketoconazole alone can inhibit adrenal corticosteroid synthesis and may cause adrenal insufficiency during corticosteroid withdrawal (see 4.4 'Special warnings and precautions for use').

Ritonavir may increase the plasma concentration of Sontirco.

Oestrogens and other oral contraceptives increase the plasma concentration of corticosteroids, and dosage adjustments may be required if oral contraceptives are added to or withdrawn from a stable dosage regimen.

The growth promoting effect of somatropin may be inhibited by the concomitant use of corticosteroids.

The desired actions of hypoglycaemic drugs (including insulin), antihypertensives and diuretics are antagonised by corticosteroids.

The effectiveness of coumarin anticoagulants may be affected by concurrent corticosteroid therapy and close monitoring of the INR or prothrombin time is required to avoid spontaneous bleeding.

Serum levels of salicylates, such as aspirin and benorilate, may increase considerably if corticosteroid therapy is withdrawn, possibly causing intoxication. Concomitant use of salicylates or of non-steroidal anti-inflammatory drugs (NSAIDs) with corticosteroids increases the risk of gastrointestinal bleeding and ulceration.

The potassium-depleting effects of acetazolamide, loop diuretics, thiazide diuretics and carbenoxolone are enhanced by corticosteroids and signs of hypokalaemia should be looked for during their concurrent use. The risk of hypokalaemia is increased with theophylline and amphotericin. Corticosteroids should not be given concomitantly with amphotericin, unless required to control reactions.

The risk of hypokalaemia also increases if high doses of corticosteroids are given with high doses of sympathomimetics e.g. bambuterol, fenoterol, formoterol, ritodrine, salbutamol, salmeterol and terbutaline. The toxicity of cardiac glycosides, e.g. digoxin, is increased if hypokalaemia occurs.

Concomitant use with methotrexate may increase the risk of haematological toxicity.

High doses of corticosteroids impair the immune response and so live vaccines should be avoided (see also section 4.4, Special Warnings and Precautions for Use)

4.6 Fertility, pregnancy and lactation

Pregnancy

The ability of corticosteroids to cross the placenta varies between individual drugs; however, cortisone 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 / 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 states

Breast-feeding

Corticosteroids are excreted in breast milk, although no data are available for Sontirco. 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. Any maternal treatment should be carefully documented in the infant's medical records to assist in follow up.

Fertility

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 Sontirco in doses for replacement therapy will affect fertility.

4.7 Effects on ability to drive and use machines

Sontirco has minor influence on the ability to drive and use machines. Fatigue and episodes of short lasting vertigo have been reported.

Untreated and poorly replaced adrenal insufficiency may affect the ability to drive and use machines.

4.8 Undesirable effects

In replacement therapy in physiological doses, adverse effects are unlikely.

The adverse effects of hydrocortisone are similar to those of other glucocorticoids. The medicinal agent also has a mineralocorticoid effect. Treatment duration and the doses used affect the prevalence of adverse effects. In high-dose long-term therapy, adverse effects regularly develop.

In high-dose long-term therapy, hydrocortisone causes adrenocortical insufficiency; therefore, stress such as surgery or infections may lead to hypotension, hypoglycaemia, and even death, unless the steroid dose is increased to accommodate for the stress.

Sudden discontinuation of long-term steroid treatment leads to corticosteroid withdrawal syndrome. 6

The symptoms may include fever, muscle and joint pain, asthenia, nausea, increased intracranial pressure and hypotension.

Glucocorticoids may cause allergy and anaphylactic reactions.

System organ class	**Common** (≥ 1/100 to < 10)	**Uncommon** (≥ 1/1,000 to < 1/100)	**Rare** (≥ 1/10,000 to <1/1,000)	**Not known** (cannot be estimated from the available data)
Blood and lymphatic system disorders				Leukocytosis
Immune system disorders	Increased susceptibility to infections, masked infection symptoms	Allergic reactions		Angioneurotic oedema, aggravation of existing infection, activation of latent infection
Endocrine disorders	Suppression of endogenous ACTH and cortisol secretion (in long-term use), symptoms of Cushing's syndrome, worsening/ development of diabetes			Secondary adrenocortical and pituitary unresponsiveness (particularly in times of stress, as in trauma, surgery, or illness), decreased carbohydrate tolerance
Metabolism and nutrition disorders	Hypokalaemia sodium retention	Increased appetite		Hypokalaemic alkalosis, increased calcium excretion, fluid retention, negative nitrogen balance due to protein catabolism
Psychiatric disorders		Mood changes, depression, mania, psychoses, insomnia		Affective disorders, behavioural disturbances, irritability, anxiety, sleep disturbances, cognitive dysfunction including confusion and amnesia
Nervous system disorders			Increased intracranial pressure (*pseudotumor cerebri*), convulsions	Vertigo, headache

Eye disorders		Increased eye pressure, glaucoma, cataract		Papilledema, corneal or scleral thinning, exophthalmos
Cardiac disorders	Exacerbation of cardiac insufficiency			Myocardial rupture following recent myocardial infarction, hypertrophic cardiomyopathy in prematurely born infants.
Vascular disorders	Hypertension	Thromboses		
Respiratory, thoracic and mediastinal disorders				Hiccups
Gastrointestinal disorders			Pancreatitis	Gastrointestinal ulcer with possible perforation and haemorrhage, ulcerative oesophagitis, perforation of the small and large bowel, abdominal distension, dyspepsia, oesophageal candidiasis
Skin and subcutaneous tissue disorders	Skin atrophy (thin, fragile skin), slow healing and scarring of tissue damage, acne, striae, bruising tendency, ecchymosis			Petechiae, erythema, telangiectasia, increased sweating, allergic dermatitis, urticaria, hirsutism
Musculoskeletal and connective tissue disorders	Muscular atrophy, muscle weakness, osteoporosis		Aseptic bone necrosis, tendon rupture	Steroid myopathy, vertebral compression fractures, pathological fracture of long bones
Reproductive system and				Menstrual irregularities,

breast disorders				amenorrhoea
General disorders and administration site conditions	Growth retardation in children, oedema			Increased appetite, nausea, malaise
Investigations				Weight increased

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.

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 MHRA 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

Overdosage may cause nausea and vomiting, sodium and water retention, hyperglycaemia and occasional gastrointestinal bleeding. Treatment need only be symptomatic 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.

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

Sontirco 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.

Sontirco 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.

Half-life of Sontirco is about 1.5 hours.

5.3 Preclinical safety data

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

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate

Potato starch

Gelatin

Talc (E553b)

Magnesium stearate (E572)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store below 25°C. Store in the original package in order to protect from light

6.5 Nature and contents of container

PVC/PVDC//aluminium blister packs containing 30 or 100 tablets.
Not all pack sizes may be marketed

6.6 Special precautions for disposal and other handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Silicon Pharma Limited
Unit 20, Oliver Business Park, Oliver Road,
Park Royal, London, NW10 7JB, UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 47992/0001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10/02/2025

10 DATE OF REVISION OF THE TEXT

10/02/2025