Sterocort 4 mg

1. NAME OF THE MEDICINAL PRODUCTS

Sterocort 4 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Sterocort 4 mg tablet contains 4 mg triamcinolone.
Excipient with known effect: 90 mg lactose monohydrate

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Sterocort 4 mg: white, round, bi-convex tablets. One side scored.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Rheumatology
- Active phases of systemic vasculitis:
  Polyarteritis nodosa (in patients with concomitant positive hepatitis B serology, the duration of treatment should be restricted to two weeks), polymyalgia rheumatica (PMR), PMR with giant cell arteritis, temporal arteritis with acute vision loss;
- Active phases of systemic rheumatic disease: systemic lupus erythematosus, mixed connective tissue disease;
- Severe progressive forms of active rheumatoid arthritis, e.g. rapidly destructive forms and/or with extra-articular manifestations;
- Other forms of inflammatory rheumatic arthritis, provided that the severity of symptoms requires it and non-steroidal anti-inflammatory drugs (NSAIDs) cannot be used:
  Spondylarthritis (ankylosing spondylitis with involvement of peripheral joints, psoriatic arthritis, enteropathic arthropathy with high inflammatory activity);
- Reactive forms of arthritis;
- Arthritis in sarcoidosis;
- Severe systemic form of juvenile idiopathic arthritis (Still's disease) or with iridocyclitis refractory to topical treatment.

Pulmonary and respiratory tract disorders
- Bronchial asthma:
  For the long-term treatment of severe chronic asthma (category 4) and for treatment of exacerbations in adults and children.
- Chronic obstructive pulmonary disease (COPD):
  For short-term treatment (max. 14 days) of exacerbations;
- Upper respiratory tract disorders:

For short-term treatment of severe forms of allergic rhinitis in adults after failure of all other treatment alternatives, including topical glucocorticoids.

Dermatology
- Oral initial treatment of extensive, severe, acute skin conditions responsive to glucocorticoids, such as:
  Allergic skin disease (e.g. acute urticaria, contact dermatitis, drug eruption), atopic eczema (acute exacerbations or extensive weeping eczema), pemphigus vulgaris.

Nephrology
- Minimal change glomerulonephritis;
- Extracapillary proliferative glomerulonephritis (rapidly progressive glomerulonephritis), generally in combination with cytostatics, tapering and ending treatment in Goodpasture's syndrome; for all other forms, long-term continuation of treatment;
- Idiopathic retroperitoneal fibrosis.

4.2 Posology and method of administration

Posology
The dosage level depends on the nature and severity of the disease and the patient's individual response to treatment. In general, relatively high initial doses are used, which need to be considerably higher in acute, severe forms of disease than in chronic disorders.

Unless otherwise prescribed, the following dosage recommendations apply:

Rheumatology
- Active phases of systemic vasculitis:
  Polyarteritis nodosa: 32 - 80 mg/day (in patients with concomitant positive hepatitis B serology, the duration of treatment should be restricted to 2 weeks), polymyalgia rheumatica (PMR): 8 - 32 mg/day,
  PMR with giant cell arteritis: 32 - 64 mg/day, temporal arteritis with acute vision loss: initially high-dose intravenous pulse therapy, thereafter 64 - 80 mg/day;

- Active phases of systemic rheumatic disease: systemic lupus erythematosus, mixed connective tissue disease: 32 - 80 mg/day;

- Active rheumatoid arthritis: depending on the severity of the disease 1 - 80 mg/day. For severe progressive forms, e.g. rapidly destructive forms, 64 - 80 mg/day and/or for extra-articular manifestations 32 - 64 mg/day;

- Spondylarthritis (ankylosing spondylitis with involvement of peripheral joints): 8 - 64 mg/day, psoriatic arthritis: 1.2 - 32 mg/day, enteropathic arthropathy with high inflammatory activity 64 - 80 mg/day;

- Reactive forms of arthritis: 8 - 32 mg/day;

- Arthritis in sarcoidosis: 32 - 64 mg/day;

- Severe systemic form of juvenile idiopathic arthritis (Still's disease) or with iridocyclitis refractory to topical treatment: 64 - 80 mg/day.

Pulmonary and respiratory tract disorders

- Bronchial asthma:
  Oral long-term treatment of adults: initially 32 - 64 mg/day, lower dosages (approximately 16 mg) in milder cases, maintenance dose generally 2 - 8 mg/day. Daily doses exceeding 12 mg should be avoided in long-term therapy. If oral glucocorticoids are used at doses up to about 16 mg/day, inhaled glucocorticoids should always be additionally used.

  Oral long-term treatment of severe childhood asthma: initial doses of approximately 1.6 mg/kg body weight/day may be necessary. Inhaled glucocorticoid therapy should be maintained. Systemic therapy takes place intermittently or over the longer term, once minimum requirements have been determined.

- Oral treatment of asthma exacerbation:
  Adults: 16 - 32 mg/day until a stable situation (pre-exacerbation level) has been reached for at least 2 days. This is followed by a dose reduction according to the clinical course.
  Children: Approximately 0.8 mg/kg body weight/day, until a significant improvement occurs. This is followed by as rapid a dose reduction as possible, according to the clinical course;

- Chronic obstructive pulmonary disease: for exacerbations, 16 - 32 mg/day for a maximum of 2 weeks. Long-term treatment with oral glucocorticoids is not recommended;

- Allergic rhinitis: 4 mg/day for a maximum of 1 to 3 days.

Dermatology

Adults: initially, 8 - 20 mg/day, for severe pemphigus up to 100 mg/day.
Children: 2 - 12 mg/day; the subsequent dose reduction is guided by the course of the disease.

Nephrology

Adults and children: initially 16 (-48) mg/day until onset of diuresis (generally after 7 - 10 days), maintenance dose 8 - 16 mg/day on 3 days per week.

Method of administration

The tablets may be split if necessary and taken with or after food with sufficient liquid. No information is available about crushing or chewing..
The daily dose should, if possible, be administered as a single dose in the morning (circadian therapy). However, in patients requiring high-dose therapy due to their disease, multiple daily doses are often required to achieve a maximum effect.
The possibility of alternate-day therapy, depending on the clinical picture and the individual response, must be considered. In children and growing adolescents, treatment should preferably be on alternate days or intermittent.

Depending on the underlying disease, clinical symptoms and response to therapy, the dose can be reduced at different rates and terminated or adjusted to the lowest possible maintenance dose, with monitoring of the adrenal axis if necessary. In general, the dose should be kept as high and the duration of treatment as long as necessary, but also as low and as short as possible. Dose reduction should generally be gradual.

In cases of hypothyroidism or liver cirrhosis, relatively low dosages may be sufficient or a dose reduction may be required.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

Depending on the dose and duration of therapy, adrenocortical insufficiency caused by glucocorticoid therapy may still persist for several months and, in isolated cases, for more than one year after discontinuation of therapy. If specific, physically stressful situations (accident, surgery, childbirth, etc.) arise during treatment with Sterocort 4 mg, a temporary dose increase may become necessary. Due to the potential risk in stressful situations, the patient should therefore be issued with a corticosteroid card during prolonged therapy.

Administration of glucocorticoids may also be required in physically stressful situations if adrenocortical insufficiency persists after the end of therapy.

Therapy-induced, acute adrenocortical insufficiency can be minimised by slow dose reduction if discontinuation is envisaged.

Treatment with Sterocort 4 mg may lead to an increased risk of bacterial, viral, parasitic, opportunistic and fungal infections due to immunosuppression. The symptoms of an existing or developing infection can be masked, thus making diagnosis more difficult. Latent infections such as tuberculosis or hepatitis B can be reactivated.

In the following disorders, therapy with Sterocort 4 mg should be administered only when very strictly indicated; with adjuvant targeted anti-infective therapy if necessary:
- acute viral infections (hepatitis B, herpes zoster, herpes simplex, varicella, herpetic keratitis),
- HBsAg-positive chronic active hepatitis,
- approximately 8 weeks before and up to 2 weeks after prophylactic vaccination with live vaccines,
- systemic fungal disease and parasitoses (e.g. nematodes),
- in patients with suspected or confirmed strongyloidiasis (threadworm infection), glucocorticoids can lead to the activation and mass proliferation of these parasites,
- poliomyelitis,
- lymphadenitis after BCG vaccination,
- acute and chronic bacterial infections,
- in patients with a history of tuberculosis use only with tuberculostatic protection.

In addition, therapy with Sterocort 4 mg should be administered only when strictly indicated, with specific adjuvant therapy if necessary, in cases of:
- gastrointestinal ulcers,
- osteoporosis,
- severe heart failure,
- difficult-to-control hypertension,
- difficult-to-control diabetes mellitus,
- psychiatric disorders (including history thereof), including suicidal ideation: neurological or psychiatric monitoring is recommended.
- narrow and open-angle glaucoma: ophthalmic monitoring and adjuvant therapy are recommended.
- corneal ulcerations and corneal lesions: ophthalmic monitoring and adjuvant therapy are recommended.

Due to the risk of intestinal perforation, Sterocort 4 mg may only be used when urgently indicated, alongside appropriate monitoring, in cases of:
- severe ulcerative colitis with the threat of perforation, possibly even without peritoneal irritation,
- diverticulitis,
- intestinal anastomosis (immediately postoperatively).

The signs of peritoneal irritation after gastrointestinal perforation may be absent in patients receiving high glucocorticoid doses.

During the use of Sterocort 4 mg in patients with diabetes, a possibly increased need for insulin or oral antidiabetics should be considered.

During treatment with Sterocort 4 mg, regular blood pressure monitoring is required particularly when using high doses and in patients with difficult-to-control hypertension.

Patients with severe heart failure must be carefully monitored due to the risk of exacerbation.

At high doses, bradycardia may occur.

Severe anaphylactic reactions may occur.

The risk of tendinopathies, tendinitis and tendon rupture is increased when fluoroquinolones and glucocorticosteroids are co-administered.

Concomitant myasthenia gravis may initially deteriorate during treatment with Sterocort 4 mg.

Inoculations with inactivated vaccines are possible in principle. However, it should be noted that the immune response and hence successful vaccination may be compromised at higher corticosteroid dosages.

During long-term therapy with Sterocort 4 mg, regular medical check-ups (including ophthalmological checks at three-monthly intervals) are indicated.

Phaeochromocytoma crisis
After the use of corticosteroids, the occurrence of a phaeochromocytoma crisis has been reported, which may be fatal. In patients with suspected or diagnosed phaeochromocytoma, corticosteroids should only be used after an appropriate benefit-risk assessment.

Visual disturbance
Visual disturbances can occur when corticosteroids are used systemically or topically. If a patient presents with symptoms such as blurred vision or other visual disturbances, referral of the patient to an ophthalmologist for assessment of possible causes should be considered; the latter include, among others, cataract, glaucoma or rare diseases such as central serous retinopathy (CSR), which have been reported after the use of systemic or topical corticosteroids.

At high doses, adequate potassium intake and sodium restriction should be ensured and the serum potassium level monitored.

Depending on the dosage and duration of treatment, a negative effect on calcium metabolism must be anticipated; hence, osteoporosis prophylaxis is recommended. This applies particularly if concomitant risk factors are present, such as familial predisposition, advanced age, post menopause, insufficient protein and calcium intake, heavy smoking, excessive alcohol consumption and lack of physical exercise. Prevention consists of adequate calcium and vitamin D intake, as well as physical exercise. In cases of pre-existing osteoporosis, drug treatment should also be considered.

When ending or, if necessary, interrupting long-term administration, consideration should be given to the following risks:
Exacerbation or relapse of the underlying disease, acute adrenocortical insufficiency, cortisone withdrawal syndrome.

The course of specific viral diseases (chickenpox, measles) may be particularly severe in patients treated with glucocorticoids. At particular risk are immunocompromised (immunosuppressed) patients with no previous chickenpox or measles infection. If these patients come into contact with individuals with measles or chickenpox during treatment with Sterocort 4 mg, prophylactic treatment should be initiated as appropriate.

Paediatric population
In the growth phase of children, the benefit/risk ratio of treatment with Sterocort 4 mg should be carefully assessed. Due to the growth-inhibiting effect of triamcinolone, height gain should be regularly monitored during long-term therapy.

Elderly patients
As elderly patients are at increased risk of osteoporosis, the benefit/risk ratio of treatment with Sterocort 4 mg should be carefully assessed.

Patients with rare hereditary problems of galactose intolerance, complete lactase deficiency or glucose-galactose malabsorption should not take Sterocort 4 mg.

Use of Sterocort 4 mg can lead to positive results in doping tests.

4.5 Interaction with other medicinal products and other forms of interaction

Oestrogens (e.g. ovulation inhibitors): The half-life of glucocorticoids may be prolonged. Hence, the corticosteroid effect may be potentiated.

Antacids: During concomitant administration of aluminium hydroxide or magnesium hydroxide, glucocorticoid absorption may be diminished, resulting in reduced efficacy of Sterocort 4 mg. The glucocorticoid and antacid should therefore be taken separately, with an interval of 2 hours between them.

Medicinal products that induce CYP3A4, such as rifampicin, phenytoin, carbamazepine, barbiturates and primidone: The corticosteroid effect may be reduced.

Medicinal products that inhibit CYP3A4, such as ketoconazole and itraconazole: The corticosteroid effect may be potentiated.

Ephedrine: The metabolism of glucocorticoids may be accelerated, thereby reducing their efficacy.

ACE inhibitors: Increased risk for the onset of blood dyscrasias.

Cardiac glycosides: The glycoside effect may be potentiated by potassium deficiency.

Saluretics/laxatives: Potassium excretion may be increased.

Antidiabetics: The hypoglycaemic effect may be reduced.

Coumarin derivatives: The anticoagulant effect may be attenuated or potentiated. Adjustment of the anticoagulant dose may be required during concomitant use.

Non-steroidal anti-inflammatory drugs/antirheumatic agents (NSAIDs), salicylates and indomethacin: The risk of gastrointestinal ulceration and bleeding is increased.

Non-depolarising muscle relaxants: Muscle relaxation may be prolonged.

Atropine, other anticholinergics: Additional increases in intraocular pressure are possible with concomitant use of Sterocort 4 mg.

Praziquantel: Corticosteroids may cause a decrease in praziquantel blood concentrations.

Chloroquine, hydroxychloroquine, mefloquine: There is an increased risk that myopathy and cardiomyopathy may occur.

Somatropin: The effect of somatropin may be reduced during long-term therapy.

Protirelin: The increase in TSH upon protirelin administration may be reduced.

Immunosuppressants: Increased susceptibility to infections and possible exacerbation or manifestation of latent infections. Additionally, for ciclosporin: The blood levels of ciclosporin are increased: There is an increased risk of cerebral seizures.

Fluoroquinolones can increase the risk of tendinopathies.

During concomitant treatment with CYP3A inhibitors, including products containing cobicistat or ritonavir, an increased risk of systemic adverse reactions can be expected. The combination should be avoided, unless the benefit outweighs the increased risk of adverse systemic reactions to corticosteroids, in which case, patients should be monitored for adverse systemic reactions to corticosteroids.

Influence on testing methods:
Skin reactions to allergy tests may be suppressed.

4.6 Fertility, pregnancy and lactation

Pregnancy
Triamcinolone should not be used in the first 5 months of pregnancy, as animal studies have shown indications of teratogenic effects. Triamcinolone appears to have a higher teratogenic potential than other synthetic or natural glucocorticoids (see 5.3). The possibility of an increased risk of oral cleft formation in human fetuses as a result of glucocorticoid administration during the first trimester is under discussion. In long-term use, intrauterine growth disturbances cannot be ruled out. In the case of treatment at the end of pregnancy,

there is a fetal risk of adrenocortical atrophy, which may necessitate tapering replacement therapy in the neonate.

Breastfeeding
Glucocorticoids are excreted in human milk. Breastfeeding should cease if treatment with higher doses or long-term treatment is required.

4.7 Effects on ability to drive and use machines

To date, there is no evidence that Sterocort 4 mg impairs the ability to drive or use machines or to work without a safe foothold.

4.8 Undesirable effects

The following adverse reactions may occur, depending on the dose and duration of therapy.

Infections and infestations
Masking of infections; manifestation, exacerbation or reactivation of viral infections, fungal infections, bacterial, parasitic and opportunistic infections; activation of strongyloidiasis (see section 4.4).

Blood and lymphatic system disorders
Moderate leucocytosis, lymphopenia, eosinopenia, polycythaemia.

Immune system disorders
Hypersensitivity reactions (e.g. drug eruption), severe anaphylactic reactions such as arrhythmias, bronchospasms, hypo- or hypertension, circulatory collapse, cardiac arrest, weakening of the immune system.

Endocrine disorders
Adrenal suppression and induction of Cushing's syndrome (typical symptoms: moon face, truncal obesity and plethora).

Metabolism and nutrition disorders
Sodium retention with oedema formation, increased potassium excretion (caution: cardiac arrhythmias), weight gain, reduced glucose tolerance, diabetes mellitus, hypercholesterolaemia and hypertriglyceridaemia, increased appetite.

Psychiatric disorders
Depression, irritability, euphoria, increased drive, psychosis, mania, hallucinations, affect lability, feelings of anxiety, sleep disorders, suicidal ideation.

Nervous system disorders
Pseudotumor cerebri, manifestation of latent epilepsy, increased seizure susceptibility in patients with manifest epilepsy.

Eye disorders
Cataract, particularly with posterior subcapsular opacification, glaucoma, aggravation of corneal ulcer symptoms, promotion of viral, fungal and bacterial eye infections, exacerbation of bacterial corneal inflammation, ptosis, mydriasis, chemosis, iatrogenic scleral perforation, chorioretinopathy, blurred vision (see also section 4.4).

Vascular disorders
Hypertension, increased risk of arteriosclerosis and thrombosis, vasculitis (also as a withdrawal syndrome after long-term therapy), increased capillary fragility.

Gastrointestinal disorders
Gastrointestinal ulcers, gastrointestinal bleeding, pancreatitis, gastric complaints.

Skin and subcutaneous tissue disorders
Striae rubrae, atrophy, telangiectasia, petechiae, ecchymosis, hypertrichosis, steroid acne, rosacea-like (perioral) dermatitis, changes in skin pigmentation.

Musculoskeletal and connective tissue disorders
Myopathy, muscular atrophy and muscle weakness, osteoporosis (dose-dependent, possible even with short-term use), aseptic osteonecrosis, tendinopathies, tendinitis, tendon rupture, epidural lipomatosis, growth inhibition in children.

Note:
If the dose is reduced too rapidly after long-term treatment, complaints such as myalgia and arthralgia may occur.

Reproductive system and breast disorders
Impaired sex hormone secretion (resulting in onset of irregular menstruation and even amenorrhoea, hirsutism, impotence).

General disorders
Delayed wound healing.

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.

Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form at https://sideeffects.health.gov.il

4.9 Overdose
Symptoms:
There are no known cases of acute intoxication with triamcinolone. In the event of chronic overdose, increased undesirable effects can be anticipated (see section 4.8 "Undesirable effects"), particularly on the endocrine system, metabolism and electrolyte balance.

Treatment:
There is no known antidote to triamcinolone.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: glucocorticoid
ATC code: H02AB08

Triamcinolone is a synthetic glucocorticoid with marked anti-allergic, anti-inflammatory and membrane-stabilising properties, as well as effects on carbohydrate, protein and lipid metabolism.
Triamcinolone has less mineralocorticoid activity than prednisolone.

Glucocorticoids exert their biological effect by activating transcription of corticosteroid-sensitive genes. The anti-inflammatory, immunosuppressive and antiproliferative effects are induced by various factors, including reduced formation, release and activity of inflammatory mediators and inhibition of specific functions and migration of inflammatory cells. In addition, the effect of sensitised T-lymphocytes and macrophages on target cells may be prevented by corticosteroids.

If long-term corticosteroid medication is necessary, possible induction of transient adrenocortical insufficiency must be taken into consideration. Suppressibility of the hypothalamic-pituitary-adrenocortical axis depends, amongst other things, on individual factors.

5.2 Pharmacokinetic properties

Triamcinolone is rapidly absorbed after oral administration. In humans, it is bound exclusively to albumin. No binding to transcortin takes place. The plasma half-life in humans is approximately 300 minutes. The biological action of glucocorticoids goes far beyond the plasma half-life, due to enzyme induction and the subsequent specific corticosteroid effect. Metabolism in the liver as with all corticosteroids is about 70% conjugation with glucuronic acid and 30% sulphation. The excretion of inactive metabolites (including 6β hydroxy triamcinolone) is mostly renal (15% unchanged) and only to a lesser extent faecal.

5.3 Preclinical safety data

Acute toxicity
Acute toxicity studies on various animal species have shown low acute toxicity of triamcinolone.

Chronic toxicity
Chronic toxicity studies were performed on rats, dogs and monkeys.
Blood dyscrasias, disturbances in electrolyte balance, infections and hepatic changes were recorded in addition to several fatalities, depending on the dose, duration of treatment and method of administration.
Shrinkage of the adrenal cortex and lymphatic tissue was observed in direct association with the glucocorticoid effect. In rats and dogs, in addition to the phenomena mentioned above, interference with blood clotting factors was observed, as well as a reduction in the glycogen content of the liver, heart and skeletal muscle.

Mutagenic and carcinogenic potential
Study findings available for glucocorticoids do not indicate any clinically relevant genotoxic properties.

Reproductive toxicity
The embryotoxic properties of triamcinolone have been studied in rats, mice, hamsters, rabbits and three non-human primate species. Cleft palate and intrauterine growth disturbances were observed, induced in some cases by doses within the human therapeutic range. In the ape species, disturbances in chondrocranium cartilage formation were also

observed, which resulted in cranial anomalies (encephalocele) and dysmorphic facial features. In animal studies, the embryotoxic effect of triamcinolone was greater than that of other glucocorticoids. This might be partially attributable to the fact that triamcinolone is deactivated in the placenta to a lesser extent than other glucocorticoids.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate
Corn starch
Microcrystalline cellulose
Gelatin
Magnesium stearate

6.2 Incompatibilities

None known to date

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials.

6.4 Special precautions for storage

Store below 25°C.

6.5 Nature and contents of container

PVC/aluminium blister with 30 tablets.

6.6 Special precautions for disposal

No special requirements

7. MANUFACTURER AND REGISTRATION HOLDER

Taro Pharmaceutical Industries Ltd.
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Haifa Bay, 2624761

8. MARKETING AUTHORISATION NUMBER

024-58-21653-00

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