SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF MEDICINAL PRODUCT

SOLDESAM 4 mg/1 ml solution for injection
SOLDESAM 8 mg/2 ml solution for injection
SOLDESAM 0.2% oral drops, solution
SOLDESAM 0.2% ointment

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

SOLDESAM 4 mg/1 ml solution for injection - 1 ampoule of 1 ml
Each 1 ml ampoule contains 4 mg of dexamethasone sodium phosphate.
SOLDESAM 8 mg/2 ml solution for injection - 1 ampoule of 2 ml
Each 2 ml ampoule contains 8 mg of dexamethasone sodium phosphate.
SOLDESAM 0.2% oral drops, solution - 1 10 ml bottle
100 ml of oral drops contain 200 mg of dexamethasone sodium phosphate.
SOLDESAM 0.2% ointment - 1 tube of 30 g
100 g of ointment contain 200 mg of dexamethasone sodium phosphate.
Excipient with known effects: cetyl alcohol.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

SOLDESAM 4 mg/1 ml solution for injection and **SOLDESAM 8 mg/2 ml solution for injection**
Solution for injection
SOLDESAM 0.2% oral drops, solution
Oral drops, solution
SOLDESAM 0.2% ointment
Ointment

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

SOLDESAM 4 mg/1 ml solution for injection
Anti-inflammatory corticotherapy, degenerative and post-traumatic arthrosis, inflammatory arthritis, chronic developmental polyarthritis, ankylosing spondylarthrosis, asthmatic access.
SOLDESAM 8 mg / 2 ml solution for injection
Brain oedema, cerebral neoplasms (as an adjuvant), emergency states and various shocks: glutathione oedema, post-transfusion reactions, anaphylaxis; haemorrhagic, surgical, septic, cardiogenic traumas, and trauma from burns.
SOLDESAM 0.2% oral drops, solution

Anti-inflammatory and anti-allergy corticotherapy, degenerative and post-traumatic arthrosis, chronic developmental polyarthritis, ankylosing spondylarthrosis, asthmatic conditions, dermatitis and allergic dermatitis and in all cases requiring corticosteroid therapy.

SOLDESAM 0.2% ointment

Atopic dermatitis (allergic eczema, childhood eczema, numbing eczema, lichenitis, eczema dermatitis, food eczema); contact dermatitis (due to cosmetics, drugs, chemicals, tissues); itch also anomalous, not specific; seborrheic dermatitis, intertrigo.

4.2 Posology and method of administration

SOLDESAM 4 mg/1 ml solution for injection

- Intramuscularly and intravenously, depending on the case and therapeutic response: alternatively, one ampoule (4 mg) per day may be repeated. As soon as a positive result is achieved, gradually decrease the dose.
- Intra-synovially into soft tissues, to be performed under strictly aseptic conditions and with a good injection technique using the following indicative dosages:

large joints (knee) in some cases	2 mg 4 mg	0.5 ml 1 ml
small joints (inter-phalangeal tempero-mandibular)	0.8 - 1 mg	0.2 - 0.25 ml
synovial sacs	2 - 4 mg	0.5 - 1 ml
tendon sheaths	0.4 - 1 mg	0.1 - 0.25 ml
by soft tissue infiltration	2 - 4 mg	0.5 - 1 ml
callus	0.4 - 1 mg	0.1 - 0.25 ml
tendon cysts	1 - 2 mg	0.25 to 0.5 ml

SOLDESAM 8 mg/2 ml solution for injection

SOLDESAM 8mg/2ml dosage should be individualised based on the disease to be cured, its severity and the therapeutic response of the patient. Indicatively, in the treatments indicated, it is advisable to administer 32-96 mg per day divided into 4-6 doses.

SOLDESAM 0.2% oral drops, solution

To be adapted according to the case and therapeutic response.

It should be emphasised that dosage requirements are variable and need to be individualised according to the disease to be treated and the patient's response.

Indicatively, treatment can be started by administering 2 to 5 mg in 3 doses each day, to be dissolved in water by shaking before ingestion. As soon as an improvement occurs, gradually decrease the dosage to the minimum therapeutically active dose, which can vary from 0.25 to 2 mg daily. 1 ml = 32 drops = 2 mg.

SOLDESAM 0.2% ointment

Apply a thin layer of ointment, slowly massaging it in. The operation should be repeated 2-3 times a day. If occlusive bandage is required, apply the ointment to the area to be treated, cover with a sheet of waterproof material (plastic) and then wrap up normally. Repeat the application every 2 or 3 days.

4.3 Contraindications

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

SOLDESAM 4 mg/1 ml solution for injection, SOLDESAM 8 mg / 2 ml solution for injection, SOLDESAM 0.2% oral drops solution:

- systemic mycotic infections, systemic bacterial infections, except in cases where specific anti-infectious therapy is underway;
- local injections in:
  - bacteraemia
  - systemic mycotic infections
  - unstable joints
  - injection site infections, for example, in secondary septic goitre or tuberculosis;
- peptic ulcers;
- psychosis;
- ocular herpes simplex.

SOLDESAM 0.2% ointment
Skin tuberculosis, herpes simplex, laryngeal and fungal skin diseases; varicella, vaccine pustules.

4.4 Special warnings and precautions for use

SOLDESAM 4 mg/1 ml solution for injection, SOLDESAM 8 mg/2 ml solution for injection, SOLDESAM 0.2% oral drops solution
A maintenance dosage should always be the lowest capable of controlling the symptoms; any dosage reduction should always be made gradually.
Precautions should be taken when treating patients with acute and chronic infections. Corticosteroids can mask some signs of infections, and during their use, intercurrent infections can occur and there is a tendency for the infectious processes not to be local. In such cases, the opportunity to establish adequate antibiotic therapy should always be assessed. In addition, corticosteroids may influence the nitroblutetrazole test for bacterial infections and cause false negative results. Corticosteroids can activate latent amoebiasis. Therefore, it is recommended that no latent or active amoebiasis should be present before starting corticosteroid therapy in patients who have visited tropical regions or in patients with diarrhoea.
Corticosteroids can exacerbate systemic fungal infections and should not therefore be used in the presence of such infections unless they are needed to control medicines reactions due to amphotericin B. Conversely, there have been reports of cases where concomitant use with amphotericin B and hydrocortisone has been followed by congestive heart hypertrophy.
Suppression of both the inflammatory response and immune function increases susceptibility to infection and the severity of infections. The clinical picture may present itself atypically, and serious infections, like septicaemia and tuberculosis may be masked and reach an advanced stage before being diagnosed.
The use of SOLDESAM 4mg/1 ml solution for injection and SOLDESAM 8 mg/2ml solution for injection for tuberculosis should be limited to cases of fulminant or disseminated tuberculosis, in which corticosteroid is used to treat the disease in association with an appropriate anti-tuberculatory regime. When corticosteroids are administered to patients with latent tuberculosis or with a positive response to tuberculin, rigorous control is required, as disease reactivation can occur. During prolonged corticosteroid therapy, these patients should undergo a chemoprophylaxis.

Post-marketing experience reported tumour lysis syndrome (TLS) in patients with blood neoplasms following the administration of dexamethasone alone or in combination with other chemotherapeutic agents. High risk TLS patients, like those with high proliferation levels, high tumour loads, and high sensitivity to cytotoxic agents should be carefully monitored and appropriate precautions should be taken.
During corticosteroid treatment, psychic alterations may occur, ranging from euphoria, insomnia, mood swings, personality changes, severe depression, and actual psychotic manifestations. When present, psychiatric instabilities and psychotic tendencies can be aggravated by corticosteroids.
Intra-articular injections of a corticosteroid can provoke both systemic and local effects. The presence of fluid in the joints requires appropriate examinations, in order to exclude septic processes. A marked increase in pain - accompanied by local oedema, further limitation of joint mobility, fever and general illness - suggests the presence of septic arthritis. If this complication occurs and a diagnosis of sepsis is confirmed, appropriate anti-infective therapy will have to be initiated.
Local injection of a steroid in infected areas should be avoided. Corticosteroids should not be injected into unstable joints. It should be clearly underlined to patients that it is important that their joints are not abused where symptomatic improvement has been achieved, for as long as the inflammatory process activity persists. Avoid injecting corticosteroids into tendons. Frequent intra-articular injections may result in damage to the joints.
The lowest possible dose of corticosteroids should be used to control the disease and, where dose reduction is possible, this should be done gradually. During prolonged therapy, it may be appropriate, as a precautionary measure, to take an anti-ulcerative regime comprising an antacid.
Middle or high dose of hydrocortisone or cortisone can cause increased blood pressure, water and salt retention, or excessive depletion of potassium. Such effects are less likely to occur with synthetic derivatives, unless they are administered at high doses. A regime of low salt and potassium supplements may be necessary. All corticosteroids increase calcium excretion.
In patients on corticosteroid therapy who are exposed to particular stress, an increase in the posology of fast-acting corticosteroids is recommended before, during and after the stressful situation. The slowest absorption rate due to intramuscular administration should be taken into account.
A medicine induced secondary coronary insufficiency can be minimised by gradually reducing the dosage. However, this type of relative insufficiency may persist for a few months after the treatment is discontinued; in any stress situation that occurs during this period, it is therefore advisable to resume the hormone therapy again. If the patient is already on steroid treatment, it may be necessary to increase the posology. Since mineral corticoid secretion may be inadequate, simultaneous administration of salts and / or mineral corticoids is appropriate.
An adequate antimicrobial therapy should be combined with glucocorticoid treatment when necessary, as for example in viral and mycotic eye infections.
Varicella is of particular concern, because this usually mildly serious disease can be fatal in immunocompromised patients. Patients (or the parents of a child) without a clinical history to confirm the disease should avoid contact with people suffering from varicella or herpes zoster, and, if exposed, they should seek urgent medical treatment. Passive immunisation with the varicella zoster (VZIG) immunoglobulin is required in exposed non-immunised patients, who are on systemic corticosteroid treatment, or who were on the last 3 months; treatment should start within 10 days from the exposure to the varicella virus. On confirmation of a varicella diagnosis, the disease requires specialist care and urgent medical therapy.

Corticosteroids administration should not be interrupted, and the dosage may also be increased.
Patients should be advised to avoid exposure to measles virus and, in the event of exposure, to obtaining appropriate and urgent medical advice; intramuscular prophylaxis of immunoglobulins may be required.
Live vaccines should not be given to people with an insufficient immune response. The antibody response to other vaccines may be reduced.
In chronic treatment, cortical atrophy of the adrenal gland develops, which may persist for years after the suspension of therapy. In patients who received systemic corticosteroid doses higher than physiological levels (about 1 mg dexamethasone) for more than 3 weeks, discontinuation of treatment cannot occur suddenly. The gradual reduction in dosage depends on the risk of recurrence of the disease, a clinical evaluation of disease activity during treatment discontinuation from the potential degree of HPA axis suppression. When the daily dosage of 1 mg is reached, the dose reduction should be made more slowly to allow full recovery of HPA.
The sudden discontinuation of doses up to 6 mg / day of dexamethasone for treatments up to 3 weeks often results in clinically significant deletion of the HPA axis; however, there are some groups of patients in whom a gradual suspension of therapy is desirable even for therapy courses lasting 3 weeks or less. For example, in patients receiving a repeat treatment of systemic corticosteroids, in patients treated with short-term therapy within one year from the end of a chronic therapy, in patients with other adrenal insufficiency disorders, in patients treated with daily doses up to 6 mg dexamethasone and patients chronically treated with evening doses. A sudden drop in corticosteroid dosage after prolonged treatment can cause acute adrenal insufficiency, hypotension, and death. Suspension of corticosteroids after chronic therapy may cause symptoms (corticosteroid suspension syndrome) such as fever, myalgia, arthralgia, rhinitis, conjunctivitis, pruriginous and sore skin nodules, and decreased body weight. These symptoms may also occur in patients without adrenal insufficiency symptoms.
During chronic treatment, any inter current disease, trauma or surgery require a temporary increase in dosage; if corticosteroid has been discontinued after a prolonged therapy, it may be necessary to temporarily restore the treatment.
Patients should always have a health card that reports current steroid therapy and have clear guidelines on the precautions to be taken to reduce any risks with the prescriber's indications, medication, dosage and duration of the treatment.
Occasionally, cases of anaphylactic reactions have been reported in patients treated with systemic corticosteroids such as gluten oedema, urticaria and bronchospasm, especially where the patient's clinical medical history confirms allergies to several medicines. When these reactions occur, it is advisable to perform the following procedures: immediate and slow intravenous injection of adrenaline, intravenous administration of aminophylline and, if necessary, artificial respiration.
Corticosteroids should not be used in the management of brain damage or ictus, their clinical usefulness being uncertain and potentially hazardous for the patient.
Corticosteroids can suppress responses to skin tests. During corticosteroid therapy, patients should not be vaccinated against smallpox. Other immune procedures should not be used in patients treated with corticosteroids, especially at high doses, given the risk of neurological complications and lack of antibody response.
In the presence of hypo-prothrombinaemia, acetylsalicylic acid should be used with caution in corticosteroid therapy. In hypothyroid patients or those with liver cirrhosis, the response to corticosteroids may increase.

Steroids should be used with caution in the presence of: non-specific ulcerative colitis with a danger of perforation; abscesses or other pyogenic infections; diverticulitis; recent intestinal anastomosis; gastric ulceration, active or latent; renal failure; hypertension; osteoporosis; myasthenia gravis. Gaseous embolisms have been described as a possible complication of hyper-cortisonism.
In hypothyroid and cirrhotic patients, corticosteroids have a more marked effect. In some patients, steroids may increase or decrease the mobility and number of spermatozoa.
Care should be taken when evaluating the use of systemic corticosteroids in patients with the following pathologies, who need careful and frequent monitoring or their first-degree family members with a history of severe affective disorders including depression or manic depression or steroid psychosis:

- Osteoporosis (menopausal women are at greater risk)
- Hypertension or congestive heart failure
- Positive history of severe affective disorders (in particular with pre-existing steroid psychosis)
- Diabetes mellitus (or a family history of diabetes)
- Positive history of tuberculosis, because glucocorticoids may induce re-activation
- Glaucoma (or family history positive for glaucoma) with possible optic nerve damage
- Early corticosteroid-induced myopathy
- Hepatic insufficiency
- Renal insufficiency
- Epilepsy
- Gastrointestinal ulcerations
- Migraine
- Some forms of intestinal parasites such as amoebiasis
- Incomplete structural growth because glucocorticoids in chronic treatments can accelerate epiphyseal fusion
- Patients with Cushing's syndrome
- In the treatment of tendinitis or tenosynovitis, attention should be paid to injecting into the space between the covering and the tendon itself, as there have been reported cases of tendon rupture
- Prolonged use of corticosteroids can cause sub-capsular rear cataracts
- It may promote the emergence of secondary eye infections due to fungi or viruses
- In patients with a history of, or whose first-degree family have a history of severe affective disorders including depression or mania depressive disease or steroid psychosis.
- Patients and/or carers should be informed about the potential risk of serious psychiatric adverse reactions that can occur following systemic steroid therapy. Typically, the symptoms appear within days or weeks after the beginning of treatment. The risks may be higher with higher doses and after systemic exposures, although dosage levels do not allow to establish the onset, type, severity, or duration of the reactions to be established. Recovery from most reactions occurs after either dose reduction or suspension, although specific treatments may be required. In case of depression, suicidal ideation or after any psychological symptom, seek medical advice. Psychiatric disorders can occur both during and immediately after reduction/suspension of systemic steroid dose, although these reactions have only rarely been reported.

Paediatric patients
Children and adolescents undergoing chronic corticosteroid therapy should have their growth and development closely monitored.
Corticosteroids cause an irreversible growth delay in children and adolescents.
In very early childhood, the product should be administered in cases of actual need, under direct medical supervision.
Available evidence suggests a development of long-term adverse events on neurological development after the early treatment (< 96 hours) of premature babies with chronic pulmonary disease at baseline dexamethasone doses of 0.25 mg / kg twice a day.
Dexamethasone should not be used routinely in preterm babies with respiratory problems.

Use in the elderly
Common adverse effects of systemic corticosteroid therapy may be associated with more serious consequences in the elderly, particularly osteoporosis, hypertension, hypokalaemia, diabetes, susceptibility to infections and skin thinning. Careful clinical supervision is needed to ward off fatal reactions.

SOLDESAM 0.2% ointment
The epicutaneous application of cortisones in the treatment of extended dermatoses, and for prolonged periods may result in systemic absorption; this occurs more easily when occlusive bandages are used (babies diapers can act as occlusive bandage). In the presence of a skin infection, appropriate covering treatment should be established. The use, especially if prolonged, of topical products may give rise to sensitisation phenomena. Avoid ophthalmic use and application in the external ear canal in cases of tympanic perforation.
Cushing's syndrome and / or adrenal suppression associated with systemic absorption of cutaneous dexamethasone may occur after intensive or continued long-term therapy in patients with a predisposition, including children and patients treated with CYP3A4 inhibitors (including ritonavir). In these cases, treatment should be gradually suspended.

4.5 Interactions with other medicinal products and other forms of interaction

Medicines that induce cytochrome P450 3A4 (e.g. barbiturates, phenytoin, carbamazepine, diphenylhydantoin, phenobarbital, ephedrine, rifampicin, rifabutin, phenylbutazone, primidone, aminoglutetimide) may increase corticosteroid metabolism and necessitate a corticosteroid dosage increase. These interactions may interfere with dexamethasone suppression tests, which should be interpreted with caution when these drugs are being administered.
Medicines that inhibit cytochrome P450 3A4 (e.g. ketoconazole and macrolides such as erythromycin) may increase plasma concentrations of corticosteroids. Dexamethasone is a moderate inducer of CYP3A4. Concomitant administration with other medicines that are metabolised by CYP3A4 (e.g. indinavir, erythromycin) may increase clearance, resulting in a decrease in plasma concentration. Cardiac dilatation and congestive heart failure could occur with the concomitant use of amphotericin B and hydrocortisone. CYP3A4 inhibitors (including ritonavir) may decrease clearance of dexamethasone, resulting in enhanced effects and adrenal suppression/Cushing's syndrome. The combination should be avoided unless the benefit does not exceed the risk of systemic side effects of corticosteroids, in which case patients should be monitored for systemic effects of corticosteroids.
In myasthenia gravis, the effects of anticholinesterases are antagonised by corticosteroids.

The efficacy of coumarin anticoagulants can be exacerbated by the concomitant use of corticosteroids.
Prothrombin time and INR should be monitored frequently to avoid spontaneous bleeding in patients receiving corticosteroids and coumarin anticoagulants at the same time, as in some cases corticosteroids have altered the response to these anticoagulants. Some studies have shown that the effect usually caused by adding corticosteroids is inhibition of the response to coumarin compounds, although there have been some conflicting ratios indicating an enhancement. When corticosteroids are administered concurrently with potassium depleting diuretics, patients should be closely monitored for the development of hypokalaemia.
During corticosteroid therapy, patients should not be vaccinated against smallpox.
Other immunisation procedures should not be undertaken in patients receiving corticosteroids especially at high doses, due to possible risks of neurological complications and lack of antibody response.
The therapeutic effects of hypoglycaemic agents (including insulin), anti-hypertensives, cardiac glycosides and diuretics are antagonised by corticosteroids, while the hypokalaemic effects of acetazolamide, lactase diuretics, thiazide diuretics and carbenoxolone are increased.
Renal clearance of salicylates is enhanced by corticosteroids, steroid suspension may result in salicylated intoxication. In patients with hypo-prothrombinemia there may be an interaction with salicylates. In addition, concomitant use of acetylsalicylic acid (or other NSAIDs) and corticosteroids may increase the risk of adverse gastrointestinal effects.

The ointment contains cetyl alcohol among its excipients, which can cause local skin reactions (e.g. contact dermatitis).

4.6 Fertility, pregnancy and breastfeeding

Pregnancy
Since no adequate studies on human reproduction relating to corticosteroids are available, the use of these medicines in pregnant women or in women of childbearing age requires a careful consideration of the possible risks and benefits of the drug for the mother and the foetus.
Children born to mothers who have been treated with significant doses of corticosteroids during pregnancy should be subjected to accurate checks to ascertain any signs of hypo-adrenalism.
Corticosteroid administration to pregnant animals may cause foetal development abnormalities, including cleft palate, intrauterine growth delay and effects on growth and cerebral development. There is no evidence that corticosteroids cause a greater incidence of congenital anomalies, such as labio-palatoschisis in humans. When administered for prolonged periods or repeatedly during pregnancy, corticosteroids may increase the risk of delayed intrauterine growth.
As with all medicines, corticosteroids should be prescribed only if the benefits to the mother outweigh the risks to the foetus.
See also section 5.3.
The ability of corticosteroids to cross the placenta varies between medicine groups; however, dexamethasone crosses the placenta easily.

Breastfeeding
Corticosteroids have been found in breast milk, although no specific data for dexamethasone are available, and can stop growth, interfere with the production of endogenous corticosteroids or cause other undesired effects. Infants of mothers treated with high doses of

systemic corticosteroids and for prolonged periods may exhibit a certain degree of adrenal gland suppression.
Mothers undergoing corticosteroid therapy should be warned not to breastfeed.

Fertility
No data available.

4.7 Effects on ability to drive vehicles and use machineries

SOLDESAM does not affect the ability to drive vehicles and use machineries.

4.8 Undesired effects

SOLDESAM 4 mg/1 ml solution for injection, SOLDESAM 8 mg/2 ml solution for injection, SOLDESAM 0.2% oral drops solution
During cortisone therapy, especially for intense and prolonged treatments, some of the following effects may occur:
Metabolic and nutritional disorders: sodium retention; water retention; depletion of potassium; hypokalaemia alkalosis; reduced carbohydrate tolerance; de-latency of diabetes mellitus; increased insulin or oral hypoglycaemic requirements in diabetic patients. Protein catabolism with a negative nitrogen balance, while in prolonged treatments, the protein ratio should be increased accurately, increased body weight, and increased appetite. Increased calcium excretion.
Alterations of hydro-electrolytic balance which, rarely and in particularly predisposed patients, can lead to hypertension and congestive heart failure.
Cardiac disorders: in patients susceptible to congestive heart failure, congestive heart failure in predisposed subjects. There are reports of cardiac arrhythmias and / or circulatory collapse following rapid administration of high doses of intravenous corticosteroids.
Pathologies of the haemolipopoietic system: decreased lymphatic tissue, leucocytosis.
Vascular disorders: hypertension, hypotension or shock reactions, thromboembolism, haematoma.
Musculoskeletal and connective tissue disorders: muscular asthenia; steroid myopathy; reduced muscle mass; osteoporosis; compression fractures of the vertebrae; aseptic necrosis of the femoral and humeral head. Painless articular destruction (reminiscent of Charcot's arthropathy particularly after repeated intra-articular injections), premature closure of epiphyses, avascular osteonecrosis, proximal myopathy. Spontaneous fracture of long bones; tendon ruptures, bone fragility, exacerbations after intra-articular injection.
Traumas, poisoning and procedural complications: vertebral compression fractures, damage, poisoning and procedural complications such as tendon rupture.
Gastrointestinal disorders: gastric ulcer with possible perforation and haemorrhage; intestinal perforations, especially in patients with inflammatory bowel disease; pancreatitis; abdominal distension; ulcerative oesophagitis, nausea, malaise, dyspepsia.
Skin and subcutaneous tissue disorders: delayed wound healing; thin and delicate skin; reactions to skin tests may be inhibited; petecchia and bruises; rashes; increased perspiration; burning and itching, especially in the perineal region (after intravenous injection); other skin reactions such as allergic dermatitis, urticaria, angioneurotic oedema, hyper-pigmentation or hypo-pigmentation*;* hirsutism, teleangectasia, strokes and acne. Skin and subcutaneous atrophy. Sterile abscesses.

Psychiatric disorders: euphoria, insomnia, mood swings and personality disorders, suicidal thoughts, severe depression, mania, disappointments, hallucinations and aggravation of schizophrenia, irritability, anxiety, confusion, psychological dependence, symptoms of true psychosis, amnesia, a pre-existent emotional instability, or psychotic tendencies which may be aggravated by corticosteroids.
Nervous system disorders: convulsions; generally after the suspension of treatment; cognitive dysfunction, aggravation of epilepsy.
Endocrine disorders: Cushing's syndrome, adrenal suppression (see section 4.4); lack of secondary pituitary and cortico-adrenal responses, especially during periods of stress due to trauma, surgery or a serious illness.
Reduced carbohydrate tolerance; manifestations of latent diabetes mellitus; increased insulin or oral hypoglycaemic requirements in diabetic patients.
Reproductive system and breast disorders: irregularities in the menstrual cycle and amenorrhea; a momentary sensation of burning or tingling in the perineal area after the intravenous injection of high doses of phosphate corticosteroids.
Hepatobiliary disorders: increased levels of liver enzymes (in most cases reversible after discontinuation of treatment).
Eye disorders: sub-capsular rear cataracts; increased intra-ocular pressure; glaucoma; exophthalmoses, papilledema, corneal or scleral thinning. Chorio-retinopathy. Rare cases of blindness associated with intra-lesional therapy of the face and head.
Infections and infestations: increased susceptibility and severity of infections (with the suppression of symptoms and clinical signs), opportunistic infections, tuberculosis lymphadenitis, exacerbation of viral or mycotic ophthalmic diseases, candidiasis.
Immune system disorders: anaphylactic or hypersensitivity reactions, reduced immune response, reduced responses to vaccination and skin tests.

Paediatric patients
The frequency, type and severity of adverse reactions in children are expected to be the same in adults.
The following additional side effects have been reported in children and adolescents:
- arrested growth;
- raised endocranial pressure with papilledema in children (pseudotumour cerebri).

SOLDESAM 0.2% ointment
During epicutaneous cortisone therapy, particularly if intense and prolonged, some of the following effects may occur:
- sensations of burning, itching, irritation, skin dryness, skin atrophy, acne and hypo-pigmentation;
- atrophies and strokes located at intertriginous areas treated for a long time with occlusive dressings.

Reporting suspected adverse reactions
It is important to report any suspect adverse reactions that occur after the medicinal product has been authorised, as this allows the risk/benefit ratio to be continuously monitored. Healthcare professionals are required to report any suspected adverse reaction via the national alert system at www.aifa.gov.it/content/segnalazioni-reazioni-avverse.

4.9 Overdoses

In cases of overdose, the following symptoms occur: obesity, muscular atrophy, osteoporosis, hypertrichosis, purpura, acne (clinical symptoms); excitement, agitation (neuropsychiatric symptoms), glucosaemia, hyperglycaemia, hypokalaemia, (biological symptoms), Cushing's syndrome, arrested growth in children. In case of overdose, discontinue administration by gradual dose decreases.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

SOLDESAM 4 mg / 1 ml solution for injection, SOLDESAM 8 mg / 2 ml solution for injection, SOLDESAM 0.2% oral drops solution
Pharmaco-therapeutic category: non-combined systemic corticosteroids, glucocorticoids, ATC code: H02AB02
SOLDESAM 0.2% ointment
Pharmaco-therapeutic category: corticosteroids for topical use for the treatment of skin diseases, ATC code: D07AB19

Mechanism of action
Glucocorticoids are produced and secreted by the adrenal cortex and are an integral part of the hypothalamus-pituitary-adrenal (HPA) axis.
Glucocorticoids, both natural (cortisol) and synthetic (e.g. dexamethasone, triamcinolone) are easily absorbed by the gastrointestinal tract, exert various metabolic effects and modify the immune responses of the body to various stimuli.
Glucocorticoids are mainly used for their anti-inflammatory effects in many organ disorders.
Dexamethasone is a synthesis adrenocorticoid that possesses the actions and effects of other basic glucocorticoids and is among the most active compounds of its class.
Pharmacodynamic effects
Adrenocorticoids act on specific receptors of the HPA axis located on the cell membrane. In other tissues, adrenocorticoids spread through the cell membrane by means of cytoplasmic receptors, enter the cell nucleus and stimulate protein synthesis. Adrenocorticoids have anti-allergic, anti-toxic, anti-shock, anti-pyretic and immunosuppressive properties.
Dexamethasone has an anti-inflammatory effect that is 7 times higher than that of prednisolone, and about 30 times that of hydrocortisone.
Dexamethasone has little propensity to promote sodium and water retention by the kidneys, therefore it does not offer a complete replacement therapy and must be supplemented with a salt or deoxy corticosterone.
SOLDESAM contains the soluble derivative of dexamethasone, namely the ester disodium phosphoric salt.
SOLDESAM 4 mg/1 ml solution for injection and SOLDESAM 8 mg/2 ml solution for injection have a rapid effect and it is therefore recommended for the treatment of acute diseases that are susceptible to corticosteroid therapy. The drops pharmaceutical form allows to establish the most appropriate dosage for the treatment of every single morbid cases, in relation to the severity and reactivity of the individual. In addition, it is possible to establish a regularly decreasing dosage in order to administer the optimal dose and then gradually "weaning". The ointment 0.2% has good local therapeutic activity.

TOXICOLOGICAL DATA: acute toxicity: DL50 (in rats, orally): 40.81 mg / kg of dexamethasone sodium phosphate.

5.2 Pharmacokinetic properties

Absorption
Corticosteroids are generally absorbed through the gastrointestinal tract. They are absorbed even when administered locally. Corticosteroids can be absorbed and give systemic effects after topical use, especially under occlusive dressings or on skin lesions, or if they are used rectally (enemas).
Water-soluble corticosteroid forms are administered intravenously for a rapid response; by using liposoluble forms of corticosteroids intramuscularly, long lasting effects are observed.

Parenteral dexamethasone absorption (I.M. or I.V.)
After administration of dexamethasone solution by injection, sodium phosphate dexamethasone is rapidly hydrolysed to dexamethasone. After an intravenous dose of 20 mg of dexamethasone, the plasma peak is reached within 5 minutes. Dexamethasone is bound (approximately 77%) to plasma proteins, mainly albumin.

Oral absorption of dexamethasone
Glucocorticoids are well absorbed following oral administration and have a bioavailability of 60-100%. The % fraction systemically available after dexamethasone administration is 61-86%.

Absorption of dexamethasone by topical application
There are no data about the absorption of dexamethasone after topical application.

Distribution
Corticosteroids are generally absorbed through the gastrointestinal tract. Corticosteroids are rapidly distributed to all body tissues. Corticosteroids cross the placenta to varying degrees and can be distributed in small quantities through breast milk (or passed into breast milk). Most corticosteroids in circulation bound to plasma proteins, mainly to globulin and to a lesser extent, to albumin. Corticosteroid-binding globulin (transcortin) has high affinity and low binding capacity, while albumin has high binding capacity and low affinity. Synthetic corticosteroids compared to natural corticosteroids (cortisol) bind less to proteins and have longer half-lives.

Metabolism
Corticosteroids are metabolised mainly in the liver but in other tissues too, and are excreted through urine. The lower metabolic activity of synthetic corticosteroids and lower binding to proteins result in the higher potency of these compared to natural corticosteroids.
The plasma half-life is 3.5 to 4.5 hours, but since the effects of corticosteroids last longer than the significant plasma concentration of steroids, plasma half-life becomes less relevant, while the use of the biological half-life is more significant.
The biological half-life of dexamethasone is 36 to 54 hours; therefore, the action of dexamethasone is suitable under conditions where the continuous action of glucocorticoids is desired.

5.3 Preclinical safety data

In animal studies, palatoschisis was observed in rats, mice, hamsters, rabbits, dogs and primates, but not in horses and sheep. In some cases these anomalies were associated with defects in the central nervous system and the heart. In primates, effects on the brain were observed after exposure to the medicine. However intrauterine growth may be delayed. All of these effects were observed at high doses.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

SOLDESAM 4 mg/1 ml injectable solution, SOLDESAM 8 mg/2 ml injectable solution
Phenol, sodium citrate dihydrate, anhydrous citric acid, water for injections.
SOLDESAM 0.2% oral drops, solution
Sodium benzoate, propylene glycol, sodium dihydrogen phosphate dihydrate, sodium saccharin, hydroxypropyl betacyclodextrin, sodium EDTA, sodium hydroxide, purified water.
SOLDESAM 0.2% ointment
Polyethylene glycol 400, polyethylene glycol 4000, cetyl alcohol.

6.2 Incompatibilities

None noted.

6.3 Shelf life

SOLDESAM 4 mg/1 ml injectable solution: 5 years
SOLDESAM 8 mg/2 ml solution for injection: 4 years
SOLDESAM 0.2% oral drops solution: 3 years.
After first opening of the bottle: 60 days.
After this period, the remaining medicine should be discarded.
SOLDESAM 0.2% ointment: 5 years.

6.4 Special precautions for storage

SOLDESAM 0.2% oral solution drops
Do not store above 30°C.

6.5 Nature and contents of container

SOLDESAM 4 mg/1 ml solution for injection: 3 glass ampoules of 4 mg / ml.
SOLDESAM 8 mg/2 ml solution for injection: 3 glass ampoules of 8 mg / 2ml.
SOLDESAM 0.2% oral solution drops: one 10 ml glass bottle with dropper.
SOLDESAM 0.2% ointment: one aluminium tube of 30 g.

6.6 Special precautions for disposal and handling

The unused medicinal product and waste material derived from this medicine should be disposed of in accordance with local regulations.

7. MARKETING AUTHORISATION HOLDER

LABORATORIO FARMACOLOGICO MILANESE S.r.l.
Via Monterosso 273, 21042 Caronno Pertusella (VA)

8. MARKETING AUTHORISATION NUMBERS

SOLDESAM 4 mg /1 ml solution for injection: M.A. No. 019499019
SOLDESAM 8 mg /2 ml solution for injection: M.A. No. 019499084
SOLDESAM 0.2% oral solution drops: M.A. No. 019499072
SOLDESAM 0.2% ointment: M.A. No. 019499060

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

Date of first authorisation: December 21, 1961
Date of last renewal: November 2009

10. DATE OF LATEST TEXT REVISION: 25 June 2017