SUMMARY OF PRODUCT CHARACTERISTICS

Summary of Product Characteristics

1. NAME OF THE MEDICINAL PRODUCT

Diprofos Ampoule 5 mg + 2 mg/1 ml suspension for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Betamethasone dipropionate 6.43 mg/ml (equivalent to 5 mg of betamethasone) and betamethasone disodium phosphate 2.63 mg/ml (equivalent to 2 mg of betamethasone).

Excipients with known effect:
This medicinal product contains 9 mg of benzyl alcohol per mL.
Diprofos contains methyl parahydroxybenzoate (E218) and Diprofos contains propyl parahydroxybenzoate (E216)

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Suspension for injection

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Corticotherapy is an adjuvant treatment, not an alternative to conventional treatment.

Intramuscular administration
Diprofos is indicated for the treatment of various rheumatic, dermatological and allergic diseases, as well as collagen and other disorders, known for their response to treatment with corticosteroids.

Musculoskeletal administration (intraarticular and periarticular administration as well as direct administration into soft tissue)
As adjuvant treatment in short-term administration (to allow the patient to overcome an acute episode or exacerbation) for osteoarthritis, rheumatoid arthritis

Intralesional administration
For dermatological disorders

Local administration in the foot
As short-term adjuvant treatment (to allow the patient to overcome an acute episode or exacerbation) for bursitis under corns, calluses, heel spurs and hallux rigidus, and on a fifth toe; for synovial cysts, Morton's metatarsalgia, tenosynovitis and periostitis of the cuboid

Typical situations

Allergic conditions
Status asthmaticus, chronic bronchial asthma, seasonal and perennial allergic rhinitis, severe allergic bronchitis, contact dermatitis, atopic dermatitis, hay fever, angioneurotic edema, serum sickness, hypersensitivity reactions to medications or insect bites

Rheumatic diseases
Osteoarthritis, rheumatoid arthritis, bursitis, lumbago, sciatica, coccydynia, acute gouty arthritis, torticollis, ganglion cyst, ankylosing spondylitis, radiculitis, exostosis, fasciitis

Dermatological diseases
Atopic dermatitis (nummular eczema), neurodermatitis (circumscribed lichen simplex), contact dermatitis, severe solar actinitis, urticaria, hypertrophic lichen planus, necrobiosis lipoidica diabeticorum, alopecia areata, discoid lupus erythematosus, psoriasis, keloids, pemphigus, dermatitis herpetiformis, cystic acne

Collagen diseases
During an exacerbation or as maintenance treatment in selected cases of systemic lupus erythematosus, polyarteritis nodosa, scleroderma and dermatomyositis

Neoplastic diseases
Palliative treatment of leukemia and lymphoma in adults as well as acute leukemia in children

Other conditions
Adrenogenital syndrome, ulcerative colitis, Crohn's disease, sprue, blood dyscrasias sensitive to corticosteroids, nephritis, nephrotic syndrome

If a primary or secondary adrenocortical insufficiency is present, it can be treated by administering Diprofos, but mineralocorticoids should be added, if applicable.

4.2 Posology and method of administration

Shake before use.

THE DOSE IS VARIABLE AND MUST BE ADJUSTED TO THE NEEDS OF THE INDIVIDUAL PATIENT, BASED ON THE CONDITION TREATED, ITS SEVERITY AND THE CLINICAL RESPONSE OF THE PATIENT.

Posology

The dose should be as low as possible and the period of administration as shortest as possible.

The initial dose should be maintained or adjusted until a satisfactory response is obtained. If, after a reasonable time, no satisfactory clinical response is observed, treatment should be discontinued by a gradual reduction of the Diprofos dose, and another suitable treatment chosen.

In case of positive response, determining the appropriate maintenance dose can be done by gradually decreasing the initial dose in small steps at suitable intervals, until the lowest dose that provides an adequate clinical response is reached.

Method of administration

Diprofos cannot be used for intravenous or subcutaneous administration.

Systemic administration

For systemic treatment, the treatment of the majority of conditions is initiated with the injection of 1 to 2 ml, and repeated if necessary. The product is administered by deep intramuscular injection (IM) in the buttock. The dose and frequency of administration depends on the severity of the patient's condition and response to therapy. At first, it may be necessary to administer 2 ml during a critical illness such as systemic lupus erythematosus or status asthmaticus, which has been relieved by appropriate life-saving measures.

Various dermatological diseases respond well to an IM injection of 1 ml of Diprofos, which can be repeated depending on how the disorder responds.

In respiratory disorders, symptom relief has been obtained within a few hours after a Diprofos IM injection. Effective control of symptoms is obtained with 1 to 2 ml in the case of bronchial asthma, hay fever, allergic bronchitis and allergic rhinitis.

For the treatment of acute or chronic bursitis, excellent results are obtained with an IM injection of 1 to 2 ml of Diprofos, repeated if necessary.

Local administration

The co-administration of a local anesthetic is rarely needed (the injection is virtually painless). If coadministration of a local anesthetic is desired, Diprofos can be mixed (in the syringe, not in the vial), with lidocaine hydrochloride (1% or 2%), with procaine hydrochloride (1% or 2%) or with a similar local anesthetic, using formulations that do not contain parabens. Avoid the use of anesthetics containing methylparaben, propylparaben, phenol, etc. The required dose of Diprofos is first withdrawn from the vial into the syringe. Next, the local anesthetic is aspirated and the syringe briefly shaken.

For acute bursitis: (subdeltoid, subacromial and prepatellar)
an injection of 1 or 2 ml directly into the bursa relieves pain and restores the full range of motion within hours.

For chronic bursitis:
When a favorable response has been obtained after acute treatment, the dose can be reduced.

For tendinitis, tenosynovitis and peritendinitis:
acute: a single injection may already improve the patient's condition.
chronic: repetition may be necessary but this depends on the patient's condition.

For rheumatoid arthritis and osteoarthritis:
After intrarticular administration of 0.5 to 2 ml of Diprofos, two to four hours may be sufficient to relieve the pain, soreness and stiffness associated with rheumatoid arthritis and osteoarthritis. In most cases, the duration of relief thus obtained, which varies widely for both diseases, is four weeks or more.
Intraarticular injection of Diprofos is well tolerated by the joint and periarticular tissues.
Recommended dosages:

large joints (e.g., knee, hip)	: 1 ml to 2 ml
average joints (e.g., elbow)	: 0.5 to 1 ml
small joints (e.g., hand)	: 0.25 to 0.5 ml

For dermatological disorders:
Dermatological conditions may respond to intralesional administration of Diprofos. The response of certain lesions not directly treated may be due to a slight systemic effect of the medicinal product.
0.2 ml/cm^2 of Diprofos is injected intradermally (not subcutaneously) using a tuberculin syringe fitted with a 26 G needle. The total amount injected for all injection sites should not exceed 1 ml.

For foot disorders sensitive to corticosteroids. Bursitis under a corn can be overcome with two successive injections of 0.25 ml each. For conditions such as hallux rigidus (flexion deformity of the big toe), fifth toe varus (inward deflection of the fifth toe) and acute gouty arthritis, the onset of relief may occur rapidly. A tuberculin syringe fitted with a 25 G 1.9 cm needle is suitable for most injections in the foot.

Recommended doses at intervals of approximately one week:

bursitis	under a corn:	0.25 to 0.5 ml
	under a calcaneal spur:	0.5 ml
	under a hallux rigidus:	0.5 ml
	on a fifth toe varus:	0.5 ml
synovial cyst:		0.25 to 0.5 ml
Morton's metatarsalgia:		0.25 to 0.5 ml
tenosynovitis:		0.5 ml
periostitis of the cuboid:		0.5 ml
acute gouty arthritis:		0.5 to 1 ml

4.3 Contraindications

- Hypersensitivity to the active substances or to any of the excipients listed in section 6.1
- Hypersensitivity to corticosteroids;
- Systemic fungal infections.

In patients with idiopathic thrombocytopenic purpura, Diprofos CANNOT be administered intramuscularly.

4.4 Special warnings and precautions for use

Diprofos cannot be used for intravenous or subcutaneous administration.

Serious neurologic events, some resulting in death, have been reported with epidural injection of corticosteroids. Specific events reported include, but are not limited to, spinal cord infarction, paraplegia, quadriplegia, cortical blindness, and stroke. These serious neurologic events have been reported with and without use of fluoroscopy. The safety and effectiveness of epidural administration of corticosteroids have not been established, and corticosteroids are not approved for this use.

ANTISEPTIC TECHNIQUES ARE NECESSARY.

Diprofos contains two betamethasone esters, one of which, betamethasone sodium phosphate, disappears rapidly from the injection site. Therefore, when using this product, the physician must take into account that this soluble portion of Diprofos may have a systemic effect.

Eliminating or abruptly reducing administration during chronic use (at very high doses, after only a short time), or when an increase in corticosteroid requirements (following stress: infection, trauma, surgery) may precipitate adrenal insufficiency. It is therefore necessary to reduce the dose gradually. In stressful situations, it is sometimes necessary to administer corticosteroids again or to increase the dose.

The dose reduction should be achieved under close medical supervision and it is sometimes necessary to monitor the patient for up to 1 year after cessation of prolonged or high-dose treatment.

The symptoms of adrenal insufficiency are: discomfort, muscle weakness, mental disorders, lethargy, muscle and bone pain, desquamation of the skin, dyspnea, anorexia, nausea, vomiting, fever, hypoglycemia, hypotension, dehydration, and even death following abrupt discontinuation of the treatment. Treatment of adrenal insufficiency consists in administering corticosteroids, mineralocorticoids, water, sodium chloride and glucose.

Rapid intravenous injection of high doses of corticosteroids can cause cardiovascular collapse; this is why the injection has to be administered over a 10-minute period.

Rare instances of anaphylactoid/anaphylactic reactions with a possibility of shock have occurred in patients receiving parenteral corticosteroid therapy. Appropriate precautionary measures should be taken with patients who have a history of allergic reactions to corticosteroids.

During prolonged corticosteroid therapy, consider switching from parenteral to oral administration after weighing the potential benefits and risks.

For intra-articular injections, it is important to know that:
- This type of administration can have local and systemic effects.
- It is essential to examine any liquid that may be present in the joint, in order to exclude a septic process.
- Avoid local injection into a previously infected joint.
- A net increase in pain and local swelling, further decrease in joint mobility, fever and discomfort should raise the question of septic arthritis. If the diagnosis of infection is confirmed, appropriate antimicrobial treatment must be initiated.
- Do not inject corticosteroids in unstable joints, infected areas or intervertebral spaces.
- Repeated injections into osteoarthritis-affected joints can aggravate the destruction of the joint.
- Avoid injecting corticosteroids directly into tendons because tendon rupture may occur subsequently.

Intramuscular injection of corticosteroids should be performed deep in large muscle masses to avoid local tissue atrophy.

The administration of a corticosteroid in soft tissue, or intralesional and intra-articular administration, can induce systemic and local effects.

Specific groups at risk
In diabetics, betamethasone may be used only for a short period and only under close medical supervision, given its glucocorticoid properties (transformation of glucose into proteins).

There is an increase in the glucocorticoid effect in patients with hypothyroidism or cirrhosis.

The use of Diprofos in ocular herpes simplex should be avoided, given the possibility of perforation of the cornea.

Psychotic disorders can occur during treatment with corticosteroids. Predisposition to emotional instability or psychosis may worsen during treatment with corticosteroids.

Caution is advised in case of:
- nonspecific ulcerative colitis, impending perforation, abscess and other pyogenic infections;
- diverticulitis;
- intestinal anastomosis;
- gastroduodenal ulcer;
- renal insufficiency;
- hypertension;
- osteoporosis;
- myasthenia gravis;
- glaucoma;
- acute psychoses;
- viral and bacterial infections;
- growth retardation;
- tuberculosis;

- Cushing's syndrome;
- diabetes;
- heart failure;
- difficult-to-treat epilepsy;
- thromboembolism or thrombophlebitis tendencies;
- pregnancy.

Since the complications of corticosteroid treatment depend on the dose and duration of treatment, the risk/benefit ratio for each patient regarding the dose and duration of treatment needs to be considered.

Corticosteroids may mask certain signs of infection or make the detection of infection more difficult. Due to a decrease in resistance, new infections can occur during use.

Prolonged use can lead to a posterior subcapsular cataract (especially in children) or to glaucoma, which can damage the optic nerves and may exacerbate secondary ocular infections due to fungi or viruses.
In case of prolonged treatment (over 6 weeks), it is necessary to undergo regular ophthalmological examinations.
Average and large doses of corticosteroids can induce hypertension, fluid retention and increased potassium excretion. These effects are less likely to occur with the synthetic derivatives, except when used at high doses. A low sodium diet and potassium supplements may be considered. All corticosteroids increase calcium excretion.

PATIENTS ON CORTICOTHERAPY CANNOT RECEIVE THE FOLLOWING TREATMENTS:
- SMALLPOX VACCINATION;
- OTHER METHODS OF IMMUNIZATION (ESPECIALLY AT HIGH DOSE) BECAUSE OF THE RISK OF NEUROLOGICAL COMPLICATIONS AND INADEQUATE ANTIBODY RESPONSE.

However, patients receiving corticosteroids as replacement therapy may be immunized (e.g., Addison's disease).
Patients, especially children, receiving immunosuppressive doses of corticosteroids should be warned to avoid exposure to chickenpox or measles.

In case of active tuberculosis, corticosteroids should be limited to cases of fulminating or disseminated tuberculosis, in which corticosteroids are used in combination with a suitable anti-tubercular treatment regimen.

If corticosteroids are indicated in patients with latent tuberculosis or reacting to tuberculin, strict monitoring is necessary because disease reactivation can occur. During prolonged corticosteroid therapy, patients should receive chemoprophylaxis.

If using rifampicin in a chemoprophylaxis program, its enhancing effect on the metabolic hepatic clearance of corticosteroids must be remembered; it may be necessary to adjust the dose of the corticosteroid.

As corticosteroids can disturb the growth of infants and children and inhibit the endogenous production of corticosteroids, it is important to monitor their growth and development carefully in the event of prolonged treatment.

Corticosteroids may sometimes alter the motility and number of spermatozoa in some patients.

Diprofos contains benzyl alcohol
Benzyl alcohol may cause allergic reactions.
Benzyl alcohol has been linked with the risk of severe side effects including breathing problems (called “gasping syndrome”) in young children. The minimum amount of benzyl alcohol at which

toxicity may occur is not known. Do not administer to premature babies or newborns at term (up to 4 weeks). Do not administer for more than a week in young children (less than 3 years old).
Large amounts of benzyl alcohol may cause metabolic acidosis. Special precautions should be taken when prescribing Diprofos to neonates, pregnant or breast-feeding patients and patients with liver or kidney disease.

Diprofos contains sodium
This medicinal product contains less than 1 mmol sodium (23 mg) per injection, that is to say essentially 'sodium-free'.

Diprofos contains methyl parahydroxybenzoate (E218) and propyl parahydroxybenzoate (E216) which may cause allergic reactions (possibly delayed) and exceptionally, bronchospasm.

Visual disturbance

Visual disturbance may be reported with systemic and topical (including, intranasal, inhaled and intraocular) corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes of visual disturbances which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.

4.5 Interaction with other medicinal products and other forms of interaction

Interaction with other medicinal products:

Combination with phenobarbital, rifampin, phenytoin or ephedrine may enhance the metabolism of corticosteroids, resulting in a decrease in therapeutic effect.

PATIENTS ON CORTICOTHERAPY CANNOT RECEIVE THE FOLLOWING TYPES OF TREATMENT:
- SMALLPOX VACCINATION;
- OTHER METHODS OF IMMUNIZATION (ESPECIALLY AT HIGH DOSE) BECAUSE OF THE RISK OF NEUROLOGICAL COMPLICATIONS AND INADEQUATE ANTIBODY RESPONSE.

However, patients receiving corticosteroids as replacement therapy may be immunized (e.g., Addison's disease).

The combination with diuretics such as thiazides may increase the risk of glucose intolerance.

Patients simultaneously receiving a corticosteroid and an estrogen must be monitored for excessive corticosteroid effects.

The simultaneous administration of corticosteroids and cardiac glycosides may increase the risk of arrhythmias or digitalis toxicity related to hypokalemia. Often, patients using cardiac glycosides also take diuretics which induce potassium depletion; in this case, it is essential to conduct potassium level determinations. Corticosteroids may worsen the potassium depletion caused by amphotericin B. In all patients taking one of these medication combinations, serum electrolytes, particularly serum potassium, should be closely monitored.

The simultaneous use of corticosteroids and coumarin-type anticoagulants may increase or decrease the anticoagulant effects, which may require a dosage adjustment. In patients taking anticoagulants in

combination with glucocorticoids, the possibility of gastrointestinal ulceration induced by corticosteroids, or increased risk of internal bleeding, must be considered.

Corticosteroids may decrease the concentration of salicylates in the blood. When lowering the dose of corticosteroids or discontinuing treatment, patients should be checked for the presence of salicylism. The combination of glucocorticoids with salicylates may increase the frequency and severity of a gastrointestinal ulcer.

The combination with non-steroidal anti-inflammatories or alcohol can lead to an increased risk of developing a gastrointestinal ulcer or the worsening of an existing ulcer.

In diabetics, it is sometimes necessary to adjust the dose of oral antidiabetic agents or insulin, given the intrinsic hyperglycemic effect of glucocorticoids.

Combination with somatropin may inhibit the response to this hormone. Betamethasone doses greater than 300-450 µg (0.3 to 0.45 mg) per m^2 of body surface area per day should be avoided during administration of somatotropin.

Co-treatment with CYP3A inhibitors, including cobicistat-containing products, is expected to increase the risk of systemic side-effects. The combination should be avoided unless the benefit outweighs the increased risk of systemic corticosteroid side-effects, in which case patients should be monitored for systemic corticosteroid side-effects.

Other forms of interactions:
Laboratory tests

Corticosteroids may influence the nitro blue tetrazolium reduction test and produce false negative results.

When the patient is treated with corticosteroids, this fact should be taken into account when interpreting the parameters and laboratory tests (skin tests, thyroid hormone levels, etc.).

4.6 Fertility, pregnancy and lactation

Given the lack of adequate teratogenic studies in humans, glucocorticoids can only be administered during pregnancy, breast-feeding and in women of fertile age after having thoroughly evaluated the health benefits and potential risks of these medications for the mother, the embryo or the fetus.

Pregnancy

When prenatal corticotherapy is indicated, the advantages and disadvantages need to be weighed and the clinical benefit compared to the side effects (including the inhibition of growth and the increased risk of infection).

In some cases it is necessary to continue the corticosteroid treatment during pregnancy or even increase the dose (e.g., in replacement corticotherapy).

Intramuscular administration of betamethasone induces a significant decrease in the frequency of dyspnea in the fetus when the product is administered more than 24 hours before delivery (before the 32nd week of gestation).

Published data show that the prophylactic use of corticosteroids after the 32nd week of pregnancy is still controversial. Therefore, the physician should weigh the benefits and potential risks for the mother and fetus when using corticosteroids after the 32nd week of pregnancy.

Corticosteroids are not indicated to treat hyaline membrane disease after birth.

In prophylactic treatment of hyaline membrane disease in premature infants, do not administer corticosteroids to pregnant women with preeclampsia or eclampsia or with signs of placental lesions.

Children born to mothers given high doses of corticosteroids during pregnancy should be carefully monitored to detect any signs of adrenal insufficiency.

When betamethasone injections have been administered to mothers before birth, infants show a transient inhibition of fetal growth hormone and presumably of the pituitary hormones that regulate the production of steroids, both in the definitive zones and fetal zones of the fetal adrenals. However, inhibition of fetal hydrocortisone has not interfered with the pituitary-adrenal responses to stress after birth.

As corticosteroids readily cross the placenta, newborns and infants born to mothers who received corticosteroids during most or part of their pregnancy should be subject to careful examination in order to detect a possible, though very rare, congenital cataract.

Women who received corticosteroids during pregnancy should be monitored during and after contractions and during childbirth to detect adrenal insufficiency due to the stress caused by birth.

Studies have shown an increased risk of neonatal hypoglycaemia following antenatal administration of a short course of betamethasone to women at risk for late preterm delivery.

Breastfeeding

Corticosteroids cross the placental barrier and are excreted in breast milk.

Given that Diprofos may induce adverse reactions in breast-fed infants, a decision must be made whether to stop breast-feeding or stop the medicinal product, taking into account the importance of the medicinal product for the mother.

4.7 Effects on ability to drive and use machines

Caution should be exercised concerning the central effects when administered at high doses (euphoria, insomnia) and with regard to the vision disorders that can occur with prolonged treatment.

4.8 Undesirable effects

The adverse reactions observed with Diprofos, which are the same as those mentioned for other corticosteroids, are related to both dose and duration of treatment.

Among the adverse reactions to corticosteroids in general, the following effects are to be particularly noted:

Fluid and electrolyte disorders:
Sodium retention - Potassium loss - Hypokalemic alkalosis - Fluid retention - Congestive heart failure in susceptible patients - Hypertension;

Musculoskeletal disorders:
Muscular weakness - Loss of muscle mass - Aggravation of myasthenic symptoms in myasthenia gravis - Osteoporosis with sometimes severe bone pain and spontaneous fractures (vertebral compression

fractures) - Aseptic bone necrosis (femoral and humeral head) - Tendon rupture - Steroid myopathy - Pathological fractures - Joint instability;

Skin disorders:
Skin atrophy - Delayed healing - Thin and fragile skin - Petechiae - Bruising - Allergic dermatitis - Angioneurotic edema - Facial erythema - Increased sweating - Urticaria;

Digestive disorders:
Gastric ulcer with bleeding and possible perforation - Pancreatitis - Abdominal distension - Intestinal perforation - Ulcerative esophagitis - Nausea - Vomiting;

Neurological disorders:
Seizures - Vertigo - Headache - Migraines - Increased intracranial pressure (pseudotumor cerebri);

Psychiatric disorders:
Euphoria - Mood Disorders - Personality changes and severe depression - Hyperirritability - Insomnia - Psychotic reactions especially in patients with a psychiatric history - Depression;

Ophthalmic disorders:
Increased intraocular pressure (pseudotumor cerebri: see neurological); Glaucoma - Posterior subcapsular cataract – Exophthalmos- Vision blurred (see also section 4.4).

Endocrine disorders :
Clinical symptoms of Cushing's syndrome - Menstrual disorders - Increased need for insulin or oral antidiabetic agents in diabetics - Inhibition of fetal child growth - Reduced tolerance to carbohydrates - Signs of latent diabetes mellitus - Secondary inhibition of the pituitary and the adrenal cortex, especially harmful in case of stress (such as trauma, surgery and disease);

Metabolic disorders:
Negative nitrogen balance with protein degradation - Lipomatosis - Weight gain;

Immunity disorders :
Corticosteroids can cause an inhibition of skin tests, mask the symptoms of infection and active a latent infection. They can also decrease resistance to infection, especially when due to mycobacteria, tuberculosis, Candida albicans or viruses.

Other:
Anaphylactic or allergic reactions, hypotensive reactions or reactions related to shock.

THE FOLLOWING ADVERSE REACTIONS MAY BE OBSERVED DURING PARENTERAL CORTICOTHERAPY:
Rare cases of blindness associated with intralesional treatment of the face and head - Hyperpigmentation or hypopigmentation - Subcutaneous and cutaneous atrophy - Sterile abscess - Post-injection exacerbation (after intra-articular use) - Charcot arthropathy.

After repeated intra-articular administration, joint damage may occur. There is a risk of contamination.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.

4.9 Overdose

Symptoms:
Acute overdosage of glucocorticoids, including betamethasone, is not life-threatening.

Except in extreme doses, it is unlikely that a few days of glucocorticoid overdose will have negative consequences in the absence of specific contraindications such as diabetes, glaucoma, active peptic ulcer, or when administering medications such as digitalis, coumarin anticoagulants or potassium-sparing diuretics.

Measures:
The complications resulting from the metabolic effects of corticosteroids, or the deleterious effects of the main disease or concomitant diseases, as well as the complications resulting from medication interactions, must be treated appropriately. It is necessary to ensure adequate fluid intake and monitor electrolytes in the serum and urine, paying particular attention to the sodium and potassium balance. If necessary, any electrolyte imbalance must be treated.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Corticosteroids for systemic use, glucocorticoids, ATC code: H02A B01.

Betamethasone is a synthetic glucocorticoid (9 alpha-fluoro-16 beta-methylprednisolone).
Betamethasone has strong anti-inflammatory, immunosuppressive and anti-allergic activity.

Betamethasone has no clinically significant mineralocorticoid effect. Glucocorticoids diffuse across cell membranes and form complexes with specific cytoplasmic receptors. These complexes then enter the cell nucleus, bind to DNA (chromatin) and stimulate the transcription of messenger RNA and the protein synthesis of various enzymes. These are finally responsible for the effects observed in systemic glucocorticoid use. In addition to their significant effect on the inflammatory and immune processes, glucocorticoids also influence the metabolism of carbohydrates, proteins and lipids. Finally, they also have an effect on the cardiovascular system, skeletal muscles and the central nervous system.

Effect on inflammatory and immune processes:
The anti-inflammatory, immunosuppressive and anti-allergic properties of glucocorticoids are responsible for a very substantial part of their therapeutic applications. The main aspects of these properties are: reduction in the number of immuno-active cells at the inflammatory site, reduced vasodilation, stabilization of lysosomal membranes, inhibition of phagocytosis, reduced production of prostaglandins and related substances.
The anti-inflammatory activity is about 25 times greater than that of hydrocortisone, and 8 to 10 times greater than that of prednisolone (on a weight basis).

Effect on the metabolism of carbohydrates and proteins:
Glucocorticoids stimulate protein catabolism. In the liver, the released amino acids are converted into glucose and glycogen by the process of gluconeogenesis. Glucose uptake in peripheral tissues decreases, which leads to hyperglycemia and glucosuria, especially in patients with a diabetic predisposition.

Effect on lipid metabolism:
Glucocorticoids have lipolytic activity. This lipolysis is more pronounced in the limbs. Glucocorticoids also have a lipogenic effect that occurs mainly in the trunk, neck and head. As a whole, these effects lead to a redistribution of fat deposits.

The maximum pharmacological activity of corticosteroids appears later than the peak serum levels, suggesting that most effects of these medications are not based on direct activity of the medicinal product, but on the modification of enzyme activity.

5.2 Pharmacokinetic properties

Betamethasone disodium phosphate and betamethasone dipropionate are resorbed from the injection site and induce therapeutic effects and other pharmacological effects, both locally and systemically.

Betamethasone disodium phosphate is highly soluble in water and is metabolized in the body into betamethasone, the biologically active steroid. 2.63 mg of betamethasone disodium phosphate is equivalent to 2 mg of betamethasone.

Prolonged activity is obtained using betamethasone dipropionate. This practically insoluble product constitutes a deposit, so that it is less rapidly resorbed and relieves symptoms longer.

Blood levels	***Intramuscular injection***	
	betamethasone natrii phosphas	***dipropionas***
- Maximum plasma concentration	1 hour after administration	Slow absorption
- Plasma half-life after a single dose	from 3 to 5 hours	Progressive metabolism
- Excretion	24 hours	More than 10 days
- Biological half-life	36 to 54 hours	

Betamethasone is metabolized in the liver. Betamethasone binds primarily to albumin. In patients with a liver disorder, its clearance is slower or delayed.

5.3 Preclinical safety data

Not applicable.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Disodium phosphate dihydrate (disodium phosphate anhydrous for Diprofos Disposable Syringe), sodium chloride, disodium edetate, polysorbate 80, benzyl alcohol (E1519), methyl parahydroxybenzoate, propyl parahydroxybenzoate, sodium carboxymethylcellulose, macrogols, hydrochloric acid, water for injections, nitrogen

6.2 Incompatibilities

The concomitant use of a local anesthetic is rarely necessary. If coadministration of a local anesthetic is desired, Diprofos can be mixed (in the syringe, not in the vial), with lidocaine hydrochloride (1% or 2%), with procaine hydrochloride (1% or 2%) or with a similar local anesthetic, using formulations that do not contain parabens. Avoid the use of anesthetics containing methylparaben, propylparaben, phenol, etc.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Diprofos Disposable Syringe:
Store below 30°C.

Diprofos Ampoule:
Store below 25°C.

6.5 Nature and contents of container

Diprofos Ampoule:
Boxes of 1 ampoule of 1 ml
Boxes of 3 ampoules of 1 ml
Boxes of 1 ampoule of 2 ml
Boxes of 3 ampoules of 2 ml

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORIZATION HOLDER

Organon South Africa (Pty) Ltd,
Spaces, 1st Floor, 22 Magwa Crescent, Gateway West,
Waterfall City Midrand,
2090,
South Africa

8. NAME OF MANUFACTURER

Schering-Plough Labo N.V.
Industriepark 30
B-2220, Heist-op-den-Berg
Belgium

9. MARKETING AUTHORIZATION NUMBER(S)

COUNTRY	

Ethiopia	04631/07070/REN/2019
Kenya	6621
Tanzania	TAN 00 862 J03B S-P
Uganda	NDA/MAL/HDP/5256
Zambia	042/023

10. SCHEDULING STATUS

POM

11. DATE OF FIRST AUTHORISATION

COUNTRY	
Ethiopia	08/12/2010
Kenya	15/12/1985
Tanzania	08/07/2000
Uganda	18/01/2001
Zambia	19/01/2010

12. DATE OF REVISION OF THE TEXT

12 June 2023