SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICNAL PRODUCT

Dezacor 6 mg tablets
Dezacor 30 mg Tablets
Dezacor 22.75 mg/ml oral drops suspension

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Dezacor 6 mg tablets:
Each tablet contains 6 mg of deflazacort.
Excipients with effect: each tablet contains 153.0 mg of lactose monohydrate and 10.0 mg of corn starch.

Dezacor 30 mg Tablets:
Each tablet contains 30 mg of deflazacort.
Excipients with known effect: each tablet contains 313.0 mg of lactose monohydrate and 10.0 mg of com starch.

Dezacor 22.75 mg/ml oral drops suspension:
Each ml of suspension contains 22.75 mg of deflazacort, or each drop of suspension contains 1 mg of deflazacort.
Excipients with lamown effect: each ml of the suspension contains 100 mg of sorbitol and 2.4 mg of sodium.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets.

Dezacor 6 mg tablets: White, round, uncoated tablets, double-scored on one side and marked with the number 6 on the other.

Dezacor 30 mg Tablets: White, round, uncoated tablets, double-scored on one side and marked with the number 30 on the other. The tablets can be divided in equal doses.

Oral drops in suspension.

Dezacor oral drops, suspension: Homogeneous suspension with a whitish colour.

4. CLNICAL PARTICULARS

4.1 Therapeutic indications

Rheumatic and collagen disorders: treatment of exacerbations and/or maintenance therapy of rheumatoid arthritis and psoriatic arthritis when the failure of conservative treatments has been demonstrated; polymyalgia rheumatica; acute rheumatic fever; systemic lupus erythematosus; severe dermatomyositis; periarteritis nodosa; craneal arthritis and Wegener's granulomatosis.

Dermatological disorders: pemphigus, bullous pemphigoid, generalized exfoliative dermatitis, severe erythema multiforme, erythema nodosum and severe

Allergic disorders: Bronchial asthma resistant to conventional therapy
Pulmonary disorders: Pulmonary sarcoidosis, extrinsic allergic alveolitis (organic dustinduced pneumoconiosis), desquamative interstitial pneumonia (idiopathic pulmonary fibrosis).

Ocular pathologies: choroiditis, chorioretinitis, iritis, iridocyclitis.

Haematological disorders: idiopathic-thrombocytopenia, haemolytic anaemia and palliative treatment of leukaemias and lymphomas.

Gastrointestinal and hepatic pathologies: ulcerative colitis, Crohn's disease and chronic active hepatitis.

Renal disorders: nephrotic syndrome.

4.2 Dosage and method of administration

Dosage:
The initial dose can vary between 6 and 90 mg/day in adults and 0.25 and 1.5 mg/kg in children, depending on the severity of the disorder being treated and the evolution of each case. This initial dose may be maintained or modified to obtain a satisfactory clinical response.

The maintenance dose should always be the minimum necessary to control the symptoms. Reductions in the dose should be applied gradually, in order to allow the recovery of hypothalamic-pituitary axis function.

Dezacor oral drops suspension are of particular interest in paediatrics, given the ease of administration and acceptance, including in infants (1 drop contains I mg of deflazacort). No clinical data are available for the efficacy of deflazacort in children under 2 months.

Method of administration
Oral route.
With the oral drops suspension, the bottle should be shaken before use. The suspension to be administered can be diluted in sweetened water or non-carbonated drinks immediately before taking it.

4.3 Contraindications

- Hypersensitivity to the active drug substance or any of the excipients included in section 6.1.
- The use of corticosteroids for longer than the duration of a replacement treatment or short-term emergency therapy is contraindicated in the following cases:

Peptic ulcer, bacterial and viral infections such as active tuberculosis, ocular herpes simplex, shingles (viremic phase), chickenpox, as well as systemic fungal infections and in the period pre and post-vaccination.

4.4 Special warnings and precautions for use

A 6 mg tablet of Dezacor has the therapeutic equivalent of approximately 5 mg of prednisone. However, it is important to point out that the requirement for corticosteroid therapy is variable, and as such the posology should be personalised, and take into account the pathology and the patient's response to treatment.

In the following cases, special precautions must be taken before deciding to start a course of glucocorticoid therapy:
Heart diseases, or congestive heart failure (except in the case of active rheumatic carditis), hypertention, thromboembolic diseases, infections (where the appropriate anti-infection therapy must be instituted), gastritis or esophagitis, diverticulitis, ulcerative colitis if there is a risk of perforation or pyogenic infection, recent intestinal anastomosis, diabetes mellitus, emotional instability or psychotic tendency, epilepsy, glaucoma, hyperthyroidism and cirrhosis (in these latter two cases the effect of the glucocorticoid can be enhanced).

In stressful situations (such as infections, trauma or surgery) an increase in the dose may be required.

During the course of a prolonged treatment at high doses, possible alterations of the electrolyte balance should be monitored and the intake of sodium and potassium altered accordingly.

Changes in vision
Systemic topical use of corticosteroids may cause changes in vision. Patients experiencing symptoms such as blurred vision or other changes in eyesight should consult an ophthalmologist to assess the possible causes, which might include cataracts, glaucoma or rare diseases such as central serous chorioretinopathy (CSC), which have been reported following the use of systemic and topical corticosteroids.

Following the discontinuation of treatment, a secondary adrenal insufficiency may persist for some months, for which reason the abrupt interruption of chronic treatments should be avoided in order to reduce the risk of steroid withdrawal syndrome. In any situation of stress occurring during this period, adequate hormone therapy should be instituted. Since mineralocorticoid secretion may be impaired, salt and/or a mineralocorticoid should be administered concurrently

Long-term use of glucocorticoids can have negative effects on growth and development in children.

Warnings on excipients

Tablets of6 mg and 30 mg:
These medicines contains lactose. Patients with hereditary galactose intolerance, Lapp lactase deficiency (deficiency seen in some populations of Lapland) or glucose-galactose malabsorption should not take this medicinal product.

Oral drops:
This medicine contains sorbitol. Patients with hereditary fructose intolerance should not take this medicine,
This product contains less than 23 mg of sodium (1 mmol) per ml; i.e., it is essentially "sodium-free".

Notice to athletes
Patients are advised that this medicine contains deflazacort that could produce a positive result in an anti-doping test.

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant administration with non-steroidal anti-inflammatory drugs can increase the risk of gastrointestinal ulcers.

Serum levels of salicylates may decrease during treatment with glucocorticoids, and increase to toxic levels when therapy is interrupted without careful tapering to physiological levels.

Potassium-depleting diuretics can boost the hypokalaemic effects of glucocorticoids, while patients on digitalis glycosides may be at increased risk of hypokalemia-induced arrhythmias. It may be necessary to increase the dose of antidiabetic drugs.
Rifampicin, barbiturates, and phenytoin can increase the metabolism of the glucocorticoids, so that, in patients on stabilised glucocorticoid therapy, the addition - or withdrawal - of these drugs may require adjustment of the corticosteroid dose.

Concomitant use of anti-cholinesterase agents and glucocorticoids may produce severe muscle weakness in patients with myasthenia gravis.

In patients treated with systemic corticosteroids, the use of non-depolarising muscle relaxants can result in prolongation of the relaxing effect.

Glucocorticoids reduce the immune response to vaccines and toxoid vaccines, and may also potentiate the replication of some organisms contained in live attenuated vaccines.

In patients with hypoprothrombinemia caution is advised when associating acetyl salicylic acid (aspirin) and corticosteroids.

Serum levels of protein-bound iodine and thyroxine (T4) may decrease, as well as the uptake of 1^{131}.

Corticosteroids can increase or decrease the effects of anticoagulants.

The effect of the corticosteroids may be increased in women taking oestrogens or oral contraceptives; in these cases the dose of corticosteroids may need to be reduced.

Concomitant treatment with CYP3A inhibitors, including medication containing cobicistat, is expected to increase the risk of systemic adverse reactions. This combination should be avoided, unless the benefit outweighs the increased risk of corticosteroid-related systemic adverse reactions, in which case patients should undergo regular monitoring for such reactions.

4.6 Fertility, pregnancy and lactation

Pregnancy:
There is insufficient evidence to evaluate the safety in pregnant women. Studies in pregnant animals have shown that corticosteroids can cause abnormalities of foetal development including cleft palate and intra-uterine growth retardation.

Consequently there exists a small risk that these effects could appear in the foetus, for which reason deflazacort should only be used during pregnancy in humans when the benefits outweigh the possible risks.

Lactation:
Glucocorticoids are excreted in breast milk and could suppress growth and interfere with endogenous steroid production. For this reason their use is not recommended during lactation.

4.7 Effects on ability to drive and use machines

No studies have been conducted on the effects on ability to drive and use machines.

4.8 Undesirable effects

- Immune system disorders: Greater susceptibility to infections
- Gastrointestinal disorders: Peptic ulcer, perforation of peptic ulcer, gastrointestinal bleeding, dyspepsia, acute pancreatitis (especially in children).
- Nervous system disorders: Headache, vertigo, hypomania, insomnia, depression, euphoria and intracranial hypertension, idiopathic intracranial hypertension in children.
- Skin and subcutaneous tissue disorders: Thinning of the skin, striae and acne.
- Cardiac and vascular disorders: Hypertension, oedema, heart failure, thromboembolism, potassium depletion and sodium retention.
- Endocrine disorders: Relative adrenal insufficiency, that may persist for up to 1 year following cessation of treatment, weight gain with cushingoid appearance (moonfaced), amenorrhoea, diabetes mellitus, hypothalamic-pituitary-adrenal (HPA) axis suppression, decrease of growth in children.
- Musculoskeletal and connective tissue disorders: Myopathy (in patients treated with systemic corticosteroids, especially in high-dose and prolonged treatments, the use of non-depolarising muscle relaxants may precipitate an acute myopathy), aseptic necrosis of the hip, osteoporosis.
- Eye disorders: posterior subcapsular cataracts, mainly in children and increased intraocular pressure.

  Frequency unknown: blurred vision (see section 4.4).

Reporting suspected adverse drug reactions

It is important to report any suspected adverse reactions to the medicinal product following its authorisation. This enables continued supervision of its benefit/risk ratio. Doctors and other healthcare professionals are invited to report suspected adverse reactions to the Spanish System of Pharmacovigilance of Medicinal Products for 1--luman Use: www.notificaRAM.es.

4.9 Overdose

Cases of intoxication with Dezacor have not been reported, however if this does occur symptomatic measures are advised.

The ingestion of high doses of corticosteroids over a prolonged period of time can lead to hypothalamic-pituitary-adrenal (HPA) axis suppression.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: systemic corticosteroids, ATC code: H02AB 13.

Dezacor (deflazacort) is a synthetic glucocorticoid. It is similar to other corticoids in that it possesses anti-inflammatory properties, but has a different safety profile due to its reduced activity on bone and hydrocarbon metabolism.

When the physiological dose is exceeded, all glucocorticoids have a negative effect on the calcium balance; by reducing intestinal absorption and/or increasing its elimination via the urine: this initially produces a gradual loss of bone mass, which may progress to osteoporosis, the final stage of osteopenia.

In dual photon absorptiometry and iliac crest biopsy studies carried out on humans, in comparison with other glucocorticoids Dezacor was observed to interfere less with calcium absorption and urinary excretion of calcium, with the subsequent effec
shown by a less marked reduction in the volume of the trabecular bone and bone mineral content. Moreover, in 3 clinical studies carried out on 143 children receiving therapy for up to 26 months, Dezacor was observed to interfere less with their growth.

On the other hand, natural and synthetic corticoids tend to decrease glucose tolerance and clinically unmask latent diabetes mellitus, requiring treatment for diabetes to be instituted, or to exacerbate already clinical diabetes, consequently requiring an increase in the habitual dose of antidiabetic drugs. It has been observed in comparative studies that the interference of Dezacor on carbohydrate metabolism is significantly less than other glucocorticoids, with better metabolic control and glucose tolerance in diabetic patients.

5.2 Pharmacokinetic properties

Taken orally, deflazacort is absorbed well and immediately transformed by plasma esterases into its active metabolite (DF-210H). This metabolite reaches maximum plasma levels in I .5 to 2 hours. The metabolite, 40% of which is bound to plasma proteins, has no affinity for transcortin. The average plasma half-life of DF-21 OH is 1.1 to 1.9 hours.

It is eliminated mainly through the kidneys with 70% of the compound being excreted within 8 hours of being taken. The remaining 30% is eliminated in the faeces.

Deflazacort 21-0H is extensively metabolised: only 5% of urinary excretion consists of DF21 OH, while metabolites of deflazacort 6-beta-OH metabolites make up a third of the urinary excretion.

5.3 Preclinical safety data

Acute and chronic toxicology studies revealed findings consistent with other corticosteroids at comparable doses. Teratogenic effects in laboratory animals are consistent with the findings with other corticoids.

The oral LD50 in mice, rats and dogs (4,000-5,200 mg/kg) was 3,000-4,000 times superior to the maximum clinical daily dose administered to humans. Two full toxicity studies on oral doses, carried out on rats and macaca fascicularis monkeys, repeated over 12 months, and backed-up by short-term studies, showed changes consistent with typical glucocorticoid treatment.

As with other glucocorticoids, deflazacort demonstrated dose-dependent teratogenic effects in rats and rabbits at very high doses and did not reveal genotoxic properties in extensive in vivo and in vitro mutagenic battery testing. Deflazacort was not found to be carcinogenic in mice.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Dezacor 6 mg and 30 mg tablet

Lactose monohydrate,
Corn starch,
Microcrystalline cellulose,
Magnesium stearate.

Dezacor oral drops suspension

Sorbitol solution 70% (E-420)
Sodium carboxymethyl cellulose, Aluminium and magnesium silicate,
Polysorbate 80, Benzyl alcohol,
Sucralose,
Aroma of tropical fruit,
Citric acid monohydrate,
Sodium hydroxide (for pH adjustment),

Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Dezacqr 6 mg and 30 mg tablets
5 years

Dezacor oral drops suspension
3 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Dezacor tablets
Packed in PVC and aluminium foil blister packs.
Dezacor 6 mg tablets: packs containing 20 or 500 tablets
Dezacor 30 mg tablets: packs containing 10 or 500 tablets

Dezacor oral drops in suspension

In 20 ml tinted glass bottles, with a cap, including a glass dropper, and aluminium seal. The contents of the bottle are 13 ml of oral drops in suspension.

6.6 Special precautions for disposal.

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

7. HOLDER OF THE MARKETNG AUTHORISATION

FAES FARMA, S.A.
Maximum Aguirre, 14
48940 Leioa

8. MARKETING AUTHORISATION NUMBER(S)

Dezacor6 mg tablets: EMA Reg. No. 57.817
Dezacor 30 mg tablets: EMAReg. No. 57.816
Dezacor 22.75 mg/ml oral drops suspension: EMA Reg. No. 61.049

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Tablets of 6 mg and 30 mg:
Date of first authorisation: 02 March 1990 Date of last revalidation: September, 2009

Oral drops suspension:
Date of first authorisation: 4 November 1996
Date of last revalidation: September, 2009

10. DATE OF REVISION OF THE TEXT

September 1999

Detailed information on this medicinal product is available on the website of the Spanish Agency of Medicines and Medical Devices (AEMPS) http://www.aemps.gob.es./