Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

Defal 22,75 mg/mL oral drops suspension

2. Qualitative and quantitative composition

Each mL of suspension contains 22,75 mg of deflazacort, or each drop of suspension contains 1 mg of deflazacort.

Excipients with a known effect
Each ml of suspension contains 100 mg of sorbitol and 2,4 mg of sodium.
For full list of excipients see section 6.1.

3. Pharmaceutical form

Defal oral drops suspension.
Homogeneous suspension of a whitish colour

4. Clinical particulars

4.1 Therapeutic indications

Rheumatic and collagen disorders: treatment of acute episodes and/or maintenance therapy in rheumatoid arthritis, psoriatic arthritis when conservative treatment has been ineffectual; polymyalgia rheumatica; acute rheumatic fever; systemic lupus erythematosus; severe dermatomyositis; periarteritis nodosa; cranial arteritis and Wegener's granulomatosis.

Dermatological disorders: Pemphigus, bullous pemphigoid, exfoliative dermatitis in general, severe erythema multiforme, erythema nodosum and severe psoriasis.

Allergies: Bronchial asthma resistant to conventional treatment.

Lung disorders: pulmonary sarcoidosis, extrinsic allergic alveolitis (pneumonoconiosis due to inhalation of organic dust), desquamative interstitial pneumonia (idiopathic pulmonary fibrosis).

Ocular pathologies: choroiditis, chorioretinitis, iritis and iridocyclitis.

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

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

Renal disorders: nephrotic syndrome.

4.2 Posology and method of administration

Posology

The initial dose in adults may vary within ranges 6 – 90 mg/day and in children within ranged 0.25 – 1.5 mg/kg, depending on the severity of the illness and on its course. Its initial dose should be maintained or varied so as to achieve a satisfactory clinical response.

The maintenance dose should always be the smallest able to control the symptomatology. The reduction in dosage must be gradual, in order to enable the recovery of the hypothalamus – hypophysis axis function.

Defal oral drops suspension has a special interest in pediatrics, given the ease of administration and its acceptance, even in infants (1 drop contains 1 mg of deflazacort). No clinical data are available on the efficacy of deflazacort in children younger than 2 months.

Method of administration

Oral way. The bottle should be shaken before use. The suspension to be administered may be diluted immediately before making sugar water or non-carbonated beverages.

4.3 Contraindications

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

The use of corticoids for longer than the duration of replacement treatment or short term emergency therapy is contraindicated in the following cases:

- Peptic ulcer, bacterial and viral infections, active tuberculosis, ocular herpes, shingles (viremic phase), chickenpox, systemic mycotic infections; and in pre- and postvaccination periods.

4.4 Special warnings and precautions for use

Special care should be taken in the following cases before deciding to initiate treatment with glucocorticoids: heart disease (except for active rheumatic carditis), high blood pressure, thromboembolic disorders, infections (when the indicated anti-infective therapy should be applied), gastritis or oesophagitis, ulcerative colitis when there is a risk of perforation or pyogenic infection, recently-performed intestinal anastomosis, diabetes mellitus, emotional instability or psychotic tendencies, epilepsy, glaucoma, hypothyroidism and cirrhosis (in these latter two cases, the effect of the glucocorticoids may be enhanced).

Doses may need to be increased in stressful situations, such as infections, injuries or surgery.

Over prolonged treatment and at high doses, the electrolyte balance should be monitored and, if necessary, sodium and potassium intake adjusted.

Visual disturbance
Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient present 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 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.

After treatment is discontinued, secondary suprarenal insufficiency may persist for months. Accordingly, prolonged treatment should not be withdrawn suddenly, in order to avoid the risk of corticoid withdrawal syndrome. For any stressful situations which may arise during this period, the indicated hormonal treatment should be applied. In these situations, mineralcorticoid secretion may become compromised, and it may be necessary to supply concomitant salts and/or mineralcorticoids.

Prolonged use of glucocorticoids in children may inhibit growth and development.

Warnings on excipients
This medicine contains sorbitol. Patients with hereditary fructose intolerance should not take this medicine. This medicine contains less than 23 mg of sodium (1mmol) per mL, that is to say essentially "sodium-free".

Notice to athletes: this medicine contains deflazacort. Deflazacort may test positive in doping controls.

4.5 Interaction with other medicinal products and other forms of interaction.
Concomitant administration of this medicine with non-steroid anti-inflammatory drugs may increase the risk of suffering from gastrointestinal ulcers.

Levels of salicylates in the blood may drop when using glucocorticoids, and rise spontaneously to toxic levels when treatment is interrupted.

Potassium depleting diuretics may enhance the hypokalaemic action of glucocorticoids, while digitalis drugs can increase the possibility of hypokalaemia associated arrhythmia. It may be necessary to increase the dose of anti-diabetic drugs.

Rifampicin, barbiturates and phenytoin may accelerate glucocorticoid metabolism. Accordingly, addiction to or withdrawal from said drugs may require an adjustment to the corticoid dose.

In patients with myasthenia gravis, anticholinesterase drugs may interact with glucocorticoids and lead to severe muscular fatigue.

In patients under treatment with systemic corticoids, the use of non-depolarising muscle relaxants may lead to prolongation of the relaxant effect.

Glucocorticoids decrease the immunological response to vaccines and toxoids, and may also enhance germ growth in attenuated live vaccines.

Patients with hypoprothrombinemia are advised to be careful when associating acetylsalicylic acid and corticosteroids.

Levels of protein-linked iodine and thyroxine (T4) in plasma may decrease, as may I131 uptake.

Corticosteroids may increase or decrease the effects of anti-coagulants.

The effects of corticosteroids may be enhanced in women taking oestrogen or oral contraceptives; in these cases, the corticosteroid dose may need to be reduced.

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.

4.6 Pregnancy and Lactation

Pregnancy

Sufficient evidence is not available with regard to the safety of this medicine in pregnant women. Corticosteroids have been observed to cause foetal abnormalities in animals, including cleft palate and intrauterine growth retardation.

Consequently, there is a slight risk to the foetus and, when assessing the use of deflazacort in pregnant humans, the benefits of treatment need to be balanced against the possible risks.

Lactation

Glucocorticoids are excreted in breast milk. This may cause growth retardation and inhibit endogenous steroid production. Accordingly, their use during breastfeeding is not advised.

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: Greater susceptibility to infections, dyspepsia, peptic ulcer, perforated peptic ulcer, gastrointestinal bleeding, acute pancreatitis (particularly in children).
- Nervous system disorders: Headaches, dizziness, light-headedness, insomnia, mood swings, depression, pseudotumor cerebro in children.
- Disorders of the skin and subcutaneous tissue: Thinning of the skin, stretch marks, acne.
- Cardiac and vascular disorders: Sodium retention and high blood pressure, oedema and heart failure, intracranial hypertension, potassium depletion.
- Endocrine disorders: Relative adrenal insufficiency, which may persist up to 1 year after discontinuation of prolonged treatment. Cushingoid weight gain and moon face, amenorrhea, diabetes mellitus, suppression of the hypothalamus-hypophysaryadrenal axis function, growth retardation in children.
- Musculoskeletal and connective tissue disorders: myopathy (in patients treated with systemic corticosteroids, particularly during treatment with high doses and after prolonged treatment, the use of non-polarising muscle relaxants may trigger acute myopathy), avascular necrosis, clots, osteoporosis.
- Eye disorders: posterior subcapsular cataracts, particularly in children, and increased ocular pressure.
- With a frequency rare: Vision, blurred (see also section 4.4)

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions to the national reporting system via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS)https://pv.pharmacyboardkenya.org

4.9 Overdose

No cases of deflazacort intoxication have been described; in its event, symptomatic treatment is advised. High doses of corticosteroids, taken orally over a prolonged period of time, may suppress hypothalamus-hypophysary-adrenal axis function.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: systemic corticosteroids, ATC code: H02AB13.

Mechanism of Action

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 involve negativisation of the calcium balance, by means of reducing its intestinal absorption and/or increasing its elimination via the urine: this initially leads to a gradual loss of bone mass, which may progress to osteoporosis.

In dual photon absorptiometry and iliac crest biopsy studies carried out on humans, in comparison with other glucocorticoids deflazacort was observed to interfere less with calcium absorption and urinary excretion of calcium, with the subsequent effect on bone reabsorption 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 under treatment up to 26 months, deflazacort 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 diabetes drugs. In comparative studies, the interference of deflazacort on glucid metabolism has been observed to be significantly lower than other glucocorticoids, with better metabolic control and better glucose tolerance in diabetic patients.

5.2 Pharmacokinetic properties

Deflazacort taken orally is absorbed well and immediately transformed by plasma esterases into its active metabolite deflazacort 21-OH. This metabolite reaches maximum plasma levels in 1.5-2 hours. The metabolite, 40% of which is bound to plasma proteins, has no affinity for transcortin. The average plasma half-life of deflazacort 21-OH is 1.1-1.9 hours.

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

Deflazacort 21-OH is extensively metabolised, only 5% of urinary excretion consisting of 21-OH deflazacort; deflazacort 6-beta-OH metabolites make up a third of urinary excretion.

5.3 Preclinical safety data

Acute and chronic toxicology studies show findings similar to those found for other corticosteroids at equivalent anti-inflammatory doses. The teratogenic effects observed in laboratory animals are those observed for other corticoids.

Doses of DL50 (4000-5200 mg/kg) given to mice, rats and dogs were 3000-4000 times higher than the maximum daily clinical doses given to humans. Two full toxicity studies on oral doses repeated over 12 months, carried out on rats and macaca fascicularis monkeys and backed up by short-term studies, showed changes related with the typical treatment of glucocorticoids.

As with other glucocorticoids, deflazacort showed dose-dependent teratogenic effects in rats and rabbits at very high doses, with no genotoxic effects being observed throughout an extensive battery of mutagenic tests in vivo and in vitro. Deflazacort was not observed to induce or stimulate the development of tumors in mice.

6. Pharmaceutical Particulars

6.1 List of Excipients

Sorbitol solution 70% (E-420)
Carboxymethylcellulose sodium,
Aluminium magnesium silicate,
Polysorbate 80,
Benzyl alcohol,
Acetic acid,
Sucralose
Tropical flavour
Citric acid monohydrate
Sodium hydroxide (for pH adjustment),
Purified water

6.2 Incompatibilities

None described.

6.3 Shelf-Life

Three years
The shelf life of the suspension after first opening is 3 months.

6.4 Special Precautions for storage

Store below 30ºC.

6.5 Nature and Content of container

Defal drops is packed in an ambar glass container of 20 mL with a cap with aluminium seal including a glass dropper. The content of the container is 13 mL of oral drops in suspension.

6.6 Special precautions for disposal and other handling

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

7. Marketing Authorization Holder

FAES FARMA, S.A.
Máximo Aguirre, 14
48940 Leioa (Vizcaya)

8. Marketing Authorization Number

CTD9701

9. Date of first authorization/renewal of the authorization

16/06/2023

10. Date of revision of the text

11/05/2025