# SUMMARY OF PRODUCT CHARACTERISTICS

## 1. NAME OF THE MEDICINAL PRODUCT

DEKORT 0.50 mg Tablets

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

**Active substance:**
Each tablet contains 0.50 mg dexamethasone.

**Excipient(s):**
Lactose monohydrate 150.0 mg
For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Tablet.
White, round, slightly convex tablets scored in the middle on one side.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

DEKORT is used in cases responsive to corticosteroid therapy due to its anti-inflammatory, antirheumatic and anti-allergic effects.

Primary diseases DEKORT 0.50 mg is indicated for are as follows:
Rheumatic diseases (e.g. rheumatoid arthritis), allergic diseases (e.g. angioneurotic edema, anaphylaxis), dermatological diseases (e.g. pemphigus), arteritis collagenosis (e.g. polyarteritis nodosa), respiratory system diseases (e.g. bronchial asthma, aspiration pneumonia), ophthalmic diseases (e.g. anterior and posterior uveitis, optic neuritis), hematological disorders (e.g. hemolytic anemia, leukemia, myeloma), cardiovascular disorders (e.g. postmyocardial infarction syndrome), hypercalcemia (e.g. sarcoidosis), infections (e.g. miliary tuberculosis) (with suitable chemotherapy)), muscle diseases (e.g. polymyositis), diseases which cause edema (e.g. e.g., nephrotic syndrome caused by idiopathic or lupus erythematosus), gastrointestinal system diseases (e.g. ulcerative colitis, Crohn's disease), neurologic disorders (e.g. brain edema associated with cerebral tumors), endocrine disorders (e.g. brain edema associated with cerebral tumors).

### 4.2 Posology and method of administration

**Posology/frequency and duration of administration:**
Dose of the drug should be individualized according to the severity of the condition and response of the patient. Daily dose may change between 0.75-9 mg. In mild cases, it may be decreased below 0.75 mg; in more severe cases, it may be increased over 9 mg. Daily dose should be divided into 3 or 4 sections and administered. Clinical condition of the patients should be monitored well against remission or exacerbation of disease.

In chronic cases like rheumatoid arthritis and chronic asthma bronchial, daily dose is 1.5-3 mg while the maintenance dose is 0.75 mg. For severe seasonal asthma and acute diseases like acute

skin diseases, acute ulcerative colitis, daily dose is 2-3 mg.

In chronic diseases like rheumatism, disseminated lupus erythematosus, nephrotic syndrome, 2-4.5 mg is used daily. In severe cases such as life-threatening status asthmaticus and hemopathy, physician can administer 7.5-10 mg as the starting dose, if he/she deems it required. Maintenance dose is determined by reducing it up to the minimum dose required when the symptoms are sufficiently improved. Daily maintenance dose of dexamethasone is between 1-1.5 mg on an average; in some cases, 0.75 mg suffices as a daily dose.

In acute allergic reactions or when chronic allergic reactions are exacerbated, combination of oral and parenteral treatment and administration of following treatment are recommended.

Day 1 : 1-2 ml (4-8 mg) DEKORT injectable
Day 2 : 2 DEKORT tablets 0.75 mg twice daily
Day 3 : 2 DEKORT tablets 0.75 mg twice daily
Day 4 : 1 DEKORT tablet 0.75 mg twice daily
Day 5 : 1 DEKORT tablet 0.75 mg once daily
Day 6 : 1 DEKORT tablet 0.75 mg once daily
Day 7 : Treatment is discontinued.
Day 8 : Doctor is seen.

As such, risk of overdose is eliminated.

**In tests implemented with dexamethasone**
1. Cushing syndrome:
1 mg DEKORT is orally administered at 11 pm. Blood is drawn at 8 am in order to determine plasma cortisol level. For a more definite result, 0.5 mg DEKORT tablet is given every 6 hours for 48 hours. Urine within the subsequent 24 hours is collected and amount of 17-hydroksicorticosteroid excreted is determined.

2. In order to discriminate Cushing syndrome induced by Pituter ACTH hypersecretion from Cushing syndrome caused by other reasons:
2 mg DEKORT is orally administered every 6 hours for 48 hours. Urine within the subsequent 24 hours is collected and amount of 17-hydroksicorticosteroid excreted is determined.
DEKORT can be given as a substituent of another corticosteroid without suspending the treatment. Equivalent of the therapeutic effect of 0.75 mg DEKORT is shown below.

| DEKORT | Methyl prednisolone and triamcinolone | Prednisone ve prednisolone | Hydrocortisone | Cortisone |
|---|---|---|---|---|
| 0.75 mg | 4 mg | 5 mg | 20 mg | 25 mg |

**Method of administration:**
DEKORT tablet is for oral administration.

**Additional information on special populations:**

**Renal/Hepatic insufficiency:**
There is not a special dose adjustment for patients with renal or hepatic insufficiency.

**Pediatric population:**
Starting dose of dexamethasone may change according to severity of the disease in pediatric population. Starting dose range is 0.02-0.3 mg/kg/day and administered as divided into 3 or 4 doses. Maintenance dose is 0.01-0.1 mg/kg/day in children.

**Geriatric population:**
Clinical studies did not include sufficient number of patients aged 65 years and older to determine if this group of patients responds differently from young subjects. In other clinical trials reported, difference was not identified between old and young subjects. In general, dose should be chosen carefully for an elderly patient and the treatment should be started always with the lowest dose of dose range and decreasing hepatic, renal or cardiac function frequency, which is higher in this group, and concomitant disease or treatment with other drugs should be taken into consideration. Increased risk of diabetes mellitus, fluid retention and hypertension should be especially considered in elderly patients under corticosteroid treatment.

**4.3 Contraindications**
It is contraindicated in patients with known hypersensitivity to active ingredient of this product, acute infections, systemic fungal infections, in patients with ulcerative herpes simplex in their eye in herpes zoster as it intervenes with immunological response and inflammatory reactions. Live vaccine is contraindicated.

**4.4 Special warnings and precautions for use**
Side effects may occur at therapeutic doses. Therefore, dose should be increased gradually and slowly. Administration of corticosteroid may mask indications of some diseases which are about to develop. It may yield (-) result in nitro blue tetrazolium test used for bacterial infections.

Corticosteroids may activate latent amebiasis. Therefore; before initiating corticosteroid treatment, it should be controlled if latent or active amebiasis is present or not and caution should be taken against diarrhea the reason of which is unknown.

Long-term use of corticosteroid may cause damage to optic nerves. Subcapsular cataract and glaucoma may occur as a result. Oral corticosteroid is not recommended for use in optic neuritis and may cause increase in new risky events.

Corticosteroids should not be used in active ocular herpes simplex. In some patients, intraocular pressure may be increased. If steroid treatment lasts for more than 6 weeks, intraocular pressure should be monitored.

Administration of normal and high dose of hydrocortisone or cortisone may cause increased blood pressure, water and salt retention and increased potassium excretion. These effects may occur less in synthetic derivatives except for administration at high dose. Salt restriction and potassium supplement may be required. All of the corticosteroids increase calcium excretion. While potassium loss and water retention observed as a result of edema are caused by administration of corticosteriod, these agents should be used with caution in patients with congestive heart failure, hypertension or renal impairment.

Live virus vaccines are contraindicated in administration of corticosteroids at immunosuppressive doses. Again with the use of corticosteroids at these doses, serum antibody response expected after

administration of inactive bacteria and virus vaccines may not be obtained. As with Addison disease, immunization procedure can be implemented in patients under corticosteroid replacement treatment.

Chicken pox and measles may be very serious and even fatal when they occur in pediatric and adult patients using corticosteroid. Special caution should be taken in pediatric and adult patients with chicken pox and measles. Contribution of corticosteroid treatment, constituting the basis for disease and/or before the disease, to the risk is unknown. If one catches chicken pox, varicella zoster immune globulin (VZIG) can be indicated with prophylaxis. If one catches measles, immunglobulin (IG) with prophylaxis should be taken into consideration while treatment with antiviral agents should be considered if chicken pox develops.

In patients with suspected Strongyloides infections, corticosteroids should be used very carefully. In some immunosuppressive patients using corticosteroid, widespread larval migration is observed with strongyloides hyperinfections. These are accompanied by enterocolitis and potential fatal gram (-) septicemia.

In patients with active tuberculosis, corticosteroid can be used with suitable antitubercular agents. Patients with latent tuberculosis or tuberculosis re-activation and for whom corticosteroid is indicated should be seriously examined in respect of re-activation of the disease. Chemoprophylactic supplement should be administered to these patients if long-term corticosteroid treatment is to be applied.

Corticosteroids should not be suddenly discontinued; treatment should be withdrawn with gradual decrease of dose. Otherwise; symptoms such as fever, myalgia, arthralgia and malacia also accompanied by adrenal cortex insufficiency may be observed.

Effect of corticosteroids is increased in patients with hypothyroid and cirrhosis.

Corticosteroids should be used with caution in patients with ocular herpes simplex due to possibility of corneal perforation.

Physical disorders may occur upon use of corticosteroid. However; euphoria, insomnia, change of character, severe depression and visible psychotic manifestations may occur. Emotional heaviness or psychotic inclination condition may get severe upon use of corticosteroid.

In patients with hypoprothrombinemia, caution should be taken regarding co-administration of corticosteroid and aspirin. Steroids should be used with caution in cases of non-specific ulcerative colitis, pyogenic inflammations, diverticulitis, new intestinal anastomosis, active or latent peptic ulcer, diabetes mellitus, renal impairment, hypertension, osteoporosis and myasthenia gravis. High doses of peritoneal and gastrointestinal irritation were observed. Fat embolism has been reported as a complication of hypercortisolism.

It is reported that it is more suitable to take the drug after meals when high dose of corticosteroid is used and even taking antacid between meals will provide protection against peptic ulcer. Steroids may cause increase or decrease in motility and number of spermatosome. It may lead to exacerbation of systemic fungal infections. However; glucocorticoid treatment can be initiated if specific antifungal treatment is to be applied.

Efficacy and safety of corticosteroids in children depends on the course of effect of corticosteroids which is similar both in children and adults. Published studies have been proved in pediatric patients under treatment of nephrotic syndrome (patients above age of 2), aggressive lymphoma and leukemia (patients above age of 1 month).

For other indications such as severe asthma and wheezing, corticosteroid use in children is based on adequate and well-controlled studies in adults. As a result, it is thought that direction of disease and its pathophysiology are the same for both populations.

As with adults, also in children; clinical evaluation of blood pressure, weight, height, intraocular pressure and presence of infection; incidence of psychosocial disorder, thromboembolism, peptic ulcer, cataract and osteoporosis should be observed carefully. Growth rate retardation may be observed in children under treatment with corticosteroid, including corticosteroids which enter the systemic circulation.

Linear growth of children under treatment with corticosteroid should be monitored. Possible growth effect of continuous treatment should be evaluated against clinical benefit obtained and employability of alternative treatments. The lowest effective dose should be used in children in order to minimize the possible growth effect of corticosteroids.

In elderly patients 65 years and older, clinical study was not performed to detect if there is any difference from the adults regarding of response. In other clinical studies reported, there were no differences seen between elderly patients and adults.

Care should be taken in dose selection in the geriatric population, generally starting at the lower end of the dosage range, taking into account the increased frequency of decreased renal, hepatic, or cardiac function and of concomitant disease or other drug therapy. Especially in elderly patients under treatment with corticosteroids; risk of diabetes, fluid retention and hypertension should be taken into consideration.

DEKORT contains 150 mg lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, the Lapp lactose deficiency or glucose-galactose malabsorption should not take this medicine.

**4.5 Interaction with other medicinal products and other forms of interaction**

Rifampicin, rifabutin, carbamazepine, phenobartital, phenytoin, primidone, and aminoglutethimide enhance the metabolism of corticosteroids and its therapeutic effects may be reduced.

Ephedrine also accelerates the metabolism of dexamethasone.

The effects of anticholinesterases are antagonised by corticosteroids in myasthenia gravis.

The desired effects of hypoglycemic agents (including insulin), anti-hypertensives and diuretics are antagonised by corticosteroids, and the hypokalemic effects of acetazolamide, loop diuretics, thiazide diuretics and carbenoxolone are enhanced.

The efficacy of coumarin anticoagulants may be enhanced by concurrent corticosteroid therapy and close monitoring of the INR or prothrombin time is required to avoid spontaneous bleeding.

Oral contraceptives (oestrogens and progestogens) increase plasma concentration of corticosteroids.

The antiviral drug ritonavir also increases the plasma concentration of dexamethasone.
Dexamethasone reduces the plasma concentration of the antiviral drugs indinavir and saquinavir.

The renal clearance of salicylates is increased by corticosteroids and steroid withdrawal may result in salicylate intoxication.

Patients taking NSAIDs should be monitored since the incidence and/or severity of gastro-intestinal ulceration may increase.

Patients taking methotrexate and dexamethasone have an increased risk of hematological toxicity.

Antacids, especially those containing magnesium trisilicate have been reported to impair the gastrointestinal absorption of glucocorticoid steroids. Therefore, doses of one agent should be spaced as far as possible from the other.

**Additional information about special populations:**
Interaction study has not been performed for special populations.

**Pediatric population:**
Interaction study has not been performed for pediatric populations.

**4.6 P regnancy and lactation**

**General Recommendation**
Pregnancy category is C.

**Women of child-bearing potential/Birth control (Contraception)**
As sufficient data is not available as to use of dexamethasone in pregnant women, women of child-bearing potential are recommended to administer a suitable birth control method.

**Pregnancy**
There is not controlled and sufficient study regarding teratogenic effect of corticosteroids used in pregnant women. However; DEKORT should not be used during pregnancy unless it is necessary. Corticosteroids should be administered only under physician's supervision and only if the potential benefit justifies the potential risk to the fetus.

Symptoms of hypoadrenalism which may occur when high amount of corticosteroid is taken during pregnancy should be carefully monitored.

There is not sufficient data regarding usage of dexamethasone 21-phosphate in pregnant women.

Animal tests are not sufficient as to direct or indirect harmful effects on pregnancy/and-or/embryonal/fetal development/and-or/birth/and-or/post-natal development. DEKORT should not be taken during pregnancy unless it is necessary. Potential risk to human is unknown.

**Breast-feeding**

Corticosteroids is excreted in human milk. This leads to undesirable effects such as suppression of growth in children and harm endogenous corticosteroid production. Therefore; mothers taking corticosteroid at pharmacological dose are recommended not to breastfeed.

**Reproductive ability/Fertility**
Steroids may increase or decrease the number of sperm and ability to move in some patients.

**4.7 Effects on ability to drive and use machines**
DEKORT does not have any knoen negative effect on ability to drive and use machines.

**4.8 Undesirable effects**
Adverse events are listed based on the following approach according to system organ class and frequency:
Very common (1/10), Common (1/100 to <1/10), Uncommon (1/1,000 to <1/100), Rare (1/10,000 to <1/1,000), Very rare (<1/10,000), unknown (cannot be estimated from the available data).

The following adverse events have been reported for DEKORT and frequency is unknown (cannot be estimated from the available data).

**Immune system disorders**
*Unknown***:** Anaphylactic reactions, fatigue, exacerbation or masking of infections.

**Endocrine diseases**

*Unknown***:** Menstrual irregularities, development of a condition similar to Cushing's syndrome suppression of growth in pediatric patients, secondary adrenocortical and pituitary unresponsiveness particularly in times of stress, as in trauma, surgery and illness, decreased carbohydrate tolerance, manifestations of latent diabetes mellitus, increased requirements for insulin or oral hypoglycemic in diabetes, hirsutism.

Decreased carbohydrate and glucose tolerance, hyperglycemia, glycosuria.

**Metabolic and nutritional disorders**
*Unknown***:** Negative nitrogen balance due to protein catabolism.

**Nervous system disorders**
*Unknown***:** Convulsions, increased intracranial pressure and associated papilledema.

**Eye disorders**
*Unknown***:** Posterior subcapsular cataracts, increased intraocular pressure, glaucoma, exophthalmos.

**Cardiac disorders**
*Unknown***:** Congestive heart failure, thromboembolism.

**Vascular diseases**
*Unknown***:** Hypertension.

**Gastro-intestinal disorders**
*Unknown***:** Peptic ulcer with possible perforation and hemorrhage, perforation of the small and large intestine particularly in inflammatory bowel disease, pancreatitis, abdominal distention, ulcerative

esophagitis, elevation in liver enzyme levels, increased appetite, nausea.

**Skin and subcutaneous tissue disorders**
*Unknown***:** Delayed wound healing, thin fragile skin; ecchymoses, erythema, increased sweating, burning sensation and itching of perineal region, (after IV administration) allergic dermatitis, angioneurotic edema.

**Musculoskeletal disorders, connective tissue and bone diseases**
*Unknown***:** Muscle weakness, steroid myopathy, loss of muscle mass, osteoporosis, spinal compression fractures, aseptic necrosis of femoral and humeral heads, pathologic fracture of long bones, tendon rupture.

**Renal and urinary diseases**
*Unknown***:** Sodium retention, fluid retention, potassium loss, hypokalemic alkalosis.

**General disorders and administration site diseases**
*Unknown***:** Thromboembolism, increased weight and appetite, nausea, psychic disorders.

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. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system.

**4.9 Overdose**
Acute reactions and death are not encountered much with overdose of glucocorticoid. Symptoms of chronic toxicity does not also require treatment if there is not a special case which would lead to hypersensitivity to glucocorticoids. In case of such special condition, gastric lavage should be performed and symptomatic treatment should be administered. When hypersensitivity reactions and anaphylaxis are observed, adrenalin and aminophylline should be administered and the patient should be kept in a warm and quiet environment.
Dexamethasone does not have a special antidote. Its plasma half-life is approximately 190 minutes.

## 5. PHARMACOLOGICAL PROPERTIES

**5.1 Pharmacodynamic properties**
Pharmacotherapeutic group: Glucocorticoid
ATC code: H02AB02

The active substance of DEKORT, dexamethasone, is a glucocorticoid with high anti-inflammatory activity and is formed with the addition of a methyl group to position 16 of the fluoro-prednisolone molecule. As many side effects encountered in synthesized corticosteroids are less severe and occur less frequently with dexamethasone, corticosteroid treatment can be instituted in patients not tolerant to other corticosteroids.
Though it is superior to corticosteroids with known anti-inflammatory, anti-rheumatic and anti-allergic effect, its effect on electrolyte balance is negligible. Side effects such as loss of appetite, weight loss, severe headache, dizziness, muscle weakness which are observed during treatment with other corticosteroids do not occur in patients treated with dexamethasone and the drug product does not cause sodium retention and potassium loss (except for use at high doses); and these factors provide great convenience in clinical practice. As it does not cause hypertension in addition to not

leading to water and salt retention, it enables an effective treatment for most of the patients with cardiovascular diseases.

## 5.2 Pharmacokinetic properties

**General properties**
Dexamethasone is white or almost white crystal powder. It is slightly soluble in acetone, methanol, anhydrous ethanol or dioxane. It is very slightly soluble in chloroform. It is very very slightly soluble in ether, it is practically insoluble in water.

Absorption:
Dexamethasone is readily absorbed from the gastro-intestinal tract. Its biological half-life is approximately 190 minutes.

Distribution:
It binds to plasma proteins at a lower rate compared to other corticosteroids. Corticosteroids are rapidly distributed to body tissues.

Biotransformation:
Corticosteroids are mostly metabolized in liver.

Elimination:
Some of it is excreted in the urine.

Linearity/Non-linearity:
Data is not available.

**Characteristics in patients**
Geriatric population:
In elderly patients 65 years and older, clinical study was not performed to detect if there is any difference from the adults regarding to response. In other clinical studies reported, there were no differences seen between elderly patients and adults. Especially in elderly patients with diabetes mellitus, fluid retention and hypertension, corticosteroids should be used with caution.

Pediatric population:
Efficacy and safety of corticosteroids in pediatric population is based on well-known aspects of effects of corticosteroid as in adults.

## 5.3 Preclinical safety data
The active substance of the drug product is being used in clinic for many years. Studies about that have been completed. Negative effects which may arise from its use are included in related sections (4.4, 4.6, 4.8, 4.9).

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients
Lactose monohydrate
Maize (Corn) starch
Talc
Magnesium stearate

### 6.2 Incompatibilities
None known.

### 6.3 Shelf life
48 months

### 6.4 Special precautions for storage
Keep at room temperature below 25°C and protect from light.

### 6.5 Nature and contents of container
Blisters of 10 tablets coated with transparent PVC on one side and with printed aluminum foil on the other side.
Each cardboard box contains 20 tablets.

### 6.6 Special precautions for disposal and other handling
Any unused product or waste material should be disposed of in accordance with local requirements.

## 7. MARKETING AUTHORIZATION HOLDER

DEVA Holding A.Ş.
Halkalı Merkez Mah. Basın Ekspres Cad. No:1
34303 Küçükçekmece – ISTANBUL/TÜRKİYE

## 8. MARKETING AUTHORIZATION NUMBER

64/15

## 9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION

Date of first authorization : 28.06.1962
Date of last renewal : 23.02.2009

## 10. DATE OF REVISION OF THE TEXT