# SUMMARY OF PRODUCT CHARACTERISTICS

## 1. NAME OF THE MEDICINAL PRODUCT
DEKORT 8 mg Tablets

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each tablet contains:

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|---|---|
| **Active substance** | |
| Dexamethasone | 8 mg |
| **Excipients** | |
| Lactose monohydrate (from cow or bovine) | 118.985 mg |

For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM
Tablet
Round, biconvex, off-white colored tablet with a score on one side.

## 4. CLINICAL PARTICULARS
### 4.1 Therapeutic indications
DEKORT tablet is used as a corticosteroid treatment due to its anti-inflammatory, anti-rheumatic and anti-allergic effects. The indications of DEKORT tablet are as follows:

Allergic conditions: Control of severe or incapacitating allergic conditions not controlled by conventional treatment in hypersensitivity reactions, allergic rhinitis, and serum sickness.

Dermatological diseases: Treatment of extensive and severe diseases responding to glucocorticoids, e.g. erythroderma, pemphigus and eczema.

Endocrine disorders: Primary and secondary adrenocortical insufficiency (hydrocortisone or cortisone is the medicine of choice; synthetic analogues must be used in conjunction with mineralocorticoids where applicable; in infancy, mineralocorticoid supplementation is of particular importance); congenital adrenal hyperplasia; hypercalcemia associated with cancer; and nonsuppurative thyroiditis.

Hematological diseases: Use alone or in combination with other therapeutic agents, for the treatment of a variety of hematologic diseases, both non-malignant (e.g., idiopathic thrombocytopenic purpura) and malignant (lymphoma, leukemia, multiple myeloma).

Neoplastic diseases: Palliative treatment of malignant tumors (leukemia and lymphoma).

Nervous system: Primary or metastatic brain tumors with cerebral edema as evidenced by neuroimaging, neurosurgical interventions, cerebral abscesses.

Ophthalmic diseases: Ocular inflammatory conditions unresponsive to topical corticosteroids; anterior and posterior uveitis.

Respiratory diseases: Fulminating or disseminated pulmonary tuberculosis (when used concurrently with appropriate antituberculous chemotherapy), idiopathic eosinophilic pneumonia, symptomatic sarcoidosis, status asthmaticus, asthma attack.

Rheumatic diseases: Initial oral treatment of autoimmune diseases such as systemic lupus erythematosus; active phase of systemic vasculitis such as polyarteritis nodosa (treatment duration should be limited to 2 weeks in case of concomitant positive hepatitis B serology); severely progressive course of active rheumatoid arthritis (e.g. fast proceeding destructive forms and/or extra-articular manifestations); severe systemic course of juvenile idiopathic arthritis (Still's disease).

Active phases of systemic vasculitides like panarteritis nodosa (treatment duration should be limited to 2 weeks in cases of concomitant positive hepatitis B serology).

Severe systemic course of juvenile idiopathic arthritis (Still's disease).
Use alone or in combination for the treatment and prophylaxis of chemotherapy-induced nausea and vomiting.

Other: Diagnostic testing of adrenocortical hyperfunction, trichinosis with neurologic or myocardial involvement, tuberculous meningitis with subarachnoid block or impending block when used with appropriate antituberculous chemotherapy.

**4.2. Posology and method of administration**
**Posology/frequency and duration of administration**
Dexamethasone is given in usual doses of 0.5 to 10 mg daily, depending on the disease being treated. In more severe disease conditions doses above 10 mg per day may be required. The dose should be titrated to the individual patient response and disease severity. In order to minimize side effects, the lowest effective possible dose should be used.

Unless otherwise prescribed, the following dosage recommendations apply:

The following dosing recommendations are for guidance only for specific clinical conditions. The initial and maintenance doses should always be determined based on individual patient response and disease severity.

Cerebral edema: Initial dose and duration of treatment depending on the cause and severity, 6-16 mg/day (up to 24 mg) orally, divided into 3-4 individual doses.

Acute asthma: *Adults*: 16 mg/day for 2 days.

Acute skin diseases: Depending on the nature and extent of the disease daily doses of 8-40 mg, in some cases up to 100 mg, which should be followed by down titration according to clinical need.

Active phase of rheumatic system disorders: Systemic lupus erythematosus, 6-16 mg/day.
Severe progressive rheumatoid arthritis: Fast destructive forms 12-16 mg/day, with extra-articular manifestations 6-12 mg/day.

Idiopathic thrombocytopenic purpura: 40 mg for 4 days in cycles.

Tuberculous meningitis: Patients with grade II or III disease received intravenous treatment for 4 weeks (0.4 mg per kilogram per day for the 1st week; 0.3 mg per kilogram per day for the 2nd week; 0.2 mg per kilogram per day for the 3rd week; and 0.1 mg per kilogram per day for the 4th week) and then oral treatment for 4 weeks, starting at a total of 4 mg per day and decreasing by 1 mg each week. Patients with grade I disease received 2 weeks of intravenous therapy (0.3 mg per kilogram per day

for week 1 and 0.2 mg per kilogram per day for week 2) and then 4 weeks of oral therapy (0.1 mg per kilogram per day for week 3, then a total of 3 mg per day, decreasing by 1 mg each week).

Palliative treatment of neoplastic diseases: Initial dose and duration of treatment depending on the cause and severity, is 3-20 mg/day. Very high doses up to 96 mg may also be used for palliative treatment. Low-dose combination forms (4 mg and 8 mg) and high-dose forms (20 mg or 40 mg) can be used for proper dosing and to reduce the number of doses or tablets.

Treatment and prophylaxis of emesis induced by cytotoxic, emetogenic chemotherapy within antiemetic treatment: 8-20 mg dexamethasone prior to chemotherapy treatment, then 4-16 mg/day on day 2 and 3.

Treatment and prevention of postoperative vomiting, within antiemetic treatment: Single dose of 8 mg before the surgery.

Treatment of symptomatic multiple myeloma, acute lymphoblastic leukemia, Hodgkin's disease and non-Hodgkin's lymphoma in combination with other medicinal products: the usual posology is 40 mg or 20 mg once per day.

Although there is no harm in using high doses of glucocorticoids for a short period of time (up to 10 days) in some emergencies (e.g., acute cerebral edema, anaphylactic shock, status asthmaticus, increasing the dose up to 1 g of prednisolone in acute transplant rejection), the high dose (usually 40-80 mg) given at the beginning of treatment should be reduced to a maintenance dose (less than 2 times the Cushing's threshold dose) in a short period of time.

Maintenance treatment should be administered every other day (spread over 24 hours).

It is advisable to give the entire dose to the patient before 8 o'clock in the morning in order not to interfere with the secretory rhythm of the adrenal glands.

It is even better if the dose is alternated every 2 days.

In the treatment of cerebral edema, as well as in palliative and antiemetic therapy, it may be necessary to give the daily dose 2-4 times.
Long-term treatment should not be discontinued abruptly. Instead, it is recommended to discontinue the medication gradually.

Because adrenal insufficiency may occur on exertion due to adrenal dysfunction, a new supplemental dose (equivalent to 5 mg prednisolone/day) should be given in these cases (e.g., trauma, surgery).

*Long-term treatment*
For the long-term treatment of several conditions, after initial therapy, glucocorticoid treatment should be switched from dexamethasone to prednisone/prednisolone to reduce suppression on the function of the adrenal cortex.

*Discontinuation of treatment*
Acute adrenocortical failure may occur after abrupt discontinuation of long-term treatment with high doses of glucocorticoids. Therefore, glucocorticoid doses should be gradually reduced in such cases and treatment should be discontinued gradually (see section 4.4).

**Method of administration**
DEKORT should be taken with or after food to minimize irritation to the gastrointestinal tract. Drinks containing alcohol or caffeine should be avoided.

When alternate-day therapy is not possible, the entire daily dose of glucocorticoid can usually be administered as a single morning dose; however, some patients will require divided daily doses of glucocorticoids.

The tablets can be divided into equal halves.

**Additional information on special populations**
Renal impairment
Patients undergoing active hemodialysis may show an increased clearance of drug via the dialysate and thus require an adjustment of steroid dose.

Hepatic impairment
In patients with severe hepatic impairment, dose adjustment may be necessary, and the biological effects of dexamethasone may be potentiated due to its slower metabolism (prolonged plasma half-life) and hypoalbuminemia (increased plasma levels of free drug), which may also cause more side effects.

Pediatric population
The usual dose is 0.01-0.1 mg/kg of body weight daily. The excretion of dexamethasone is approximately equal in children and adults if dosage is adjusted to their body area. Dosage should be planned bearing in mind possible effects upon growth and development and for signs of adrenal suppression.

Elderly
Treatment of elderly patients, particularly if long-term, should be planned taking into account the more serious consequences of the common side effects of corticosteroids in the elderly (osteoporosis, diabetes mellitus, hypertension, hypokalemia, decreased immunity, psychological changes, susceptibility to infection, and thinning of the skin). In such patients, the plasma concentrations of dexamethasone may be higher and its excretion slower than in younger patients, therefore its dose should be reduced accordingly.

**4.3. Contraindications**
- Hypersensitivity to dexamethasone or any of the excipients of DEKORT tablet
- Systemic mycosis

**Avoid live vaccines in patients receiving immunosuppressive doses (serum antibody response diminished).**
In general, no contraindications apply in conditions where the use of glucocorticoids may be lifesaving.

With the following diseases, DEKORT should not be used for a long time, except for emergency treatment and additional treatment:
- Gastrointestinal ulcer
- Severe osteoporosis
- Severe myopathies (except Myasthenia Gravis)

- Viral diseases, viroses (e.g. herpes simplex and herpes zoster [viremic phase]), varicella, poliomyelitis (except bulbar encephalitic form)
- HBsAG-positive chronic active hepatitis
- Rosacea
- Approximately 8 weeks before and 2 weeks after preventive vaccination
- Lymphoma formation after tuberculosis vaccination (BCG)
- Angle-closure and open-angle glaucoma

It is contraindicated in systemic infections unless anti-infective treatment is employed.

**4.4. Special warnings and precautions for use**

There is an increased risk of systemic adverse events with CYP3A inhibitors (see section 4.5).

In post-marketing experience, tumor lysis syndrome (TLS) has been reported in patients with hematological malignancies following the use of dexamethasone alone or in combination with other chemotherapeutic agents. Patients at high risk of TLS, such as patients with high proliferative rate, high tumor burden, and high sensitivity to cytotoxic agents, should be monitored closely and appropriate precaution taken.

Undesirable effects can be minimized by using the lowest effective dose for the shortest duration and administering it as a single morning dose according to the daily requirement, or on alternate days if possible. Frequent patient review is required to appropriately titrate the dose against disease activity. If dose reduction is possible, it should be done gradually (see section 4.2).

Corticosteroids may aggravate systemic fungal infections and should not be used in the presence of such infections unless necessary to control life-threatening drug reactions due to amphotericin. In addition, cases of cardiac enlargement and heart failure have been reported with concomitant use of amphotericin and hydrocortisone.

One report shows that the use of corticosteroids in cerebral malaria is associated with prolonged coma and increased incidence of pneumonia and gastrointestinal bleeding.

Discontinuation of long-term corticosteroid treatment may cause withdrawal symptoms such as fever, myalgia, arthralgia, and malaise. This may occur in patients even when there is no evidence of adrenal insufficiency.

The use of dexamethasone in active tuberculosis should be limited to cases of fulminant or disseminated tuberculosis where the corticosteroid is used to treat the disease in conjunction with an appropriate antituberculosis regimen. If corticosteroids are indicated in patients with latent tuberculosis or tuberculin reactivity, close monitoring of the disease is necessary because reactivation may occur. During long-term corticosteroid therapy, patients should receive prophylactic chemotherapy.

Corticosteroids may activate latent amebiasis or strongyloidiasis or exacerbate the active disease. Therefore, it is recommended that latent or active amebiasis and strongyloidiasis be ruled out before initiating corticosteroid therapy in any patient at risk or with symptoms suggestive of either condition.

Steroids can increase or decrease the motility and number of sperm.

Special precautions

Special caution and frequent patient review is required when considering the use of systemic corticosteroids in patients with renal failure, hypertension, diabetes or a family history of diabetes, congestive heart failure, osteoporosis, previous steroid-induced myopathy, glaucoma (or family history of glaucoma), myasthenia gravis, non-specific ulcerative colitis, diverticulitis, recent intestinal anastomosis, active or latent peptic ulcer, current or previous history of severe affective disorder (especially previous steroid-induced psychosis), hepatic impairment and epilepsy. Signs of peritoneal irritation after gastrointestinal perforation may be minimal or absent in patients receiving high doses of corticosteroids. Fat embolism has been reported as a possible complication of hypercortisonism.

*Adrenocortical insufficiency*

An adrenocortical insufficiency, which is caused by glucocorticoid treatment, can, depending on the dose and length of treatment, remain for many months, and in some cases more than a year, after discontinuation of treatment. During treatment with dexamethasone for specific physical stress conditions (trauma, surgery, childbirth, etc.), a temporary increase in dose may be required. Because of the possible risk in stressful conditions, a corticosteroid identification should be made for patients undergoing long-term treatment. Even in cases of prolonged adrenocortical insufficiency after discontinuation of treatment, the administration of glucocorticoids can be necessary in physically stressful situations. Acute therapy-induced adrenocortical insufficiency can be minimized by slow dose reduction until a planned discontinuation time, but it may persist for up to one year after discontinuation. In any stressful situation during this period, corticosteroid therapy should be restarted. If the patient is already receiving corticosteroids, the current dosage may need to be temporarily increased. Because mineralocorticoid secretion may be impaired, salt and/or a mineralocorticoid should be given concurrently.

The effect of corticosteroids is increased in patients with hypothyroidism or liver cirrhosis.

Treatment with dexamethasone should only be implemented in the event of the strongest indications and, if necessary, additional targeted anti-infective treatment administered for the following diseases:

- Acute viral infections (Herpes zoster, Herpes simplex, Varicella, herpetic keratitis)
- HBsAG-positive chronic active hepatitis
- Approximately 8 weeks prior through 2 weeks after vaccinations with live vaccines (see sections 4.3 and 4.5).
- Systemic mycoses and parasitosis (e.g. Nematodes)
- Poliomyelitis
- Lymphadenitis (inflammation of the lymph nodes) after BCG vaccination
- Acute and chronic bacterial infections
- With a history of tuberculosis (reactivation risk) use only under tuberculostatic protection
- Known or suspected Strongyloidiasis (threadworm infestation). Treatment with glucocorticoids may lead to Strongyloides hyper-infection and dissemination with widespread larval migration.

In addition, treatment with dexamethasone should only be implemented under strong indications and, if necessary, additional specific treatment must be implemented for:

- Gastrointestinal ulcers
- Severe osteoporosis (as corticosteroids have a negative effect on the calcium balance)
- Difficulty to regulate high blood pressure
- Difficulty to regulate diabetes mellitus

• Psychiatric disorders (including history)
• Angle-closure glaucoma and wide-angle glaucoma
• Corneal ulcerations and corneal injuries
• Severe heart failure.

*Anaphylactic reaction*
Serious anaphylactic reactions may occur.

*Tendinitis*
The risk of tendinitis and tendon rupture is increased in patients treated concomitantly with glucocorticoids and fluoroquinolones.

*Myasthenia gravis*
Pre-existing myasthenia gravis may initially deteriorate in the beginning of dexamethasone treatment.

*Ocular disorders*
Systemic treatment with glucocorticoids can induce chorioretinopathy which may result in impaired vision including loss of vision.
Prolonged use of corticosteroids may cause posterior subcapsular cataracts, glaucoma with possible damage to the optic nerve and can increase the risk of secondary ocular infections due to fungi or viruses.

Corticosteroids should be used cautiously in patients with ocular herpes simplex because of possible corneal perforation.

*Intestinal perforation*
Because of the risk of an intestinal perforation, dexamethasone must only be used under urgent indication and under appropriate monitoring for:
• Severe ulcerative colitis with threatened perforation
• Diverticulitis
• Entero-anastomosis (immediately postoperative)

Signs of peritoneal irritation after gastrointestinal perforation may be minimum or absent in patients receiving high doses of glucocorticoids.

*Diabetes*
A higher need for insulin, or oral antidiabetics, must be taken into consideration when administering dexamethasone to diabetics.

*Cardiovascular disorders*
Regular blood pressure monitoring is necessary during treatment with dexamethasone, particularly during administration of higher doses and with patients with difficult to regulate high blood pressure.
Because of the risk of deterioration, patients with severe cardiac insufficiency should be carefully monitored.

Bradycardia may occur in patients treated with high doses of dexamethasone.
A clear association between corticosteroid use and left ventricular free-wall rupture after a recent myocardial infarction has been reported; therefore, corticosteroids should be used with extreme caution in these patients.

Caution should be exercised when using corticosteroids in patients who have recently suffered myocardial infarction as myocardial rupture has been reported.

*Infections*
Corticosteroids may conceal some symptoms of an infection, and new infections may occur during their use. Suppression of the inflammatory response and immune function increases susceptibility to and severity of infection. The clinical presentation can often be atypical, and serious infections such as septicemia and tuberculosis can occur at any stage and may be concealed in the advanced stages before being noticed. Patients using corticosteroids may experience situations such as decreased resistance and inability to localize the infection. The prolonged use of even small amounts of dexamethasone leads to an increased risk of infection, even by microorganisms which otherwise rarely cause infections (so-called opportunistic infections).

*Vaccination*
Vaccinations with an inactivated vaccine are always possible. However, it should be noted that the immune reaction and thereby the success of the inoculation can be affected by high doses of corticoids.

Regular checkups with doctors (including vision checkups in three-month intervals) are advised during long-term treatment with dexamethasone.
Vaccination with live virus vaccines is contraindicated in individuals receiving immunosuppressive doses of corticosteroids. Individuals receiving immunosuppressive doses of corticosteroids who are vaccinated with inactivated viral or bacterial vaccines may not achieve the expected serum antibody response. However, vaccination may be performed, for example, in patients receiving corticosteroids as replacement therapy for Addison's disease.

*Metabolic disorders*
At high doses, sufficient calcium intake and sodium restriction, as well as serum potassium levels should be monitored. Depending on the length and dosage of the treatment, a negative influence on calcium metabolism can be expected, so that an osteoporosis prophylaxis is recommended. This applies, above all, to co-existing risk factors like familial disposition, increased age, postmenopausal insufficient protein and calcium intake, heavy smoking, excessive alcohol intake, as well as insufficient exercise. Prevention consists of sufficient calcium and vitamin D intake and physical activity. Additional medical treatment should be considered in the event of pre-existing osteoporosis.
Corticosteroids should be used cautiously in patients with migraine, as they may cause fluid retention.
Moderate and high doses of hydrocortisone or cortisone can cause increased blood pressure, salt and water retention, and increased potassium excretion, but these effects are less likely to be seen with synthetic derivatives except at high doses. Dietary salt restriction and potassium supplementation may be needed. All corticosteroids increase calcium excretion.

*Psychological changes*
Patients and/or caregivers should be warned that potentially severe psychiatric adverse reactions might occur with systemic steroids (see section 4.8). Symptoms typically appear several days or weeks after starting treatment. Risks may be higher with high dose/systemic exposure (see also section 4.5 Interactions with other medicinal products and other forms of interaction). However, the onset, type, severity, or length of the reaction cannot be predicted from the dose levels. Most reactions resolve with dose reduction or discontinuation, but specific treatment may be required.

Patients/caregivers should be encouraged to seek medical advice if worrisome psychological symptoms develop, especially if depressed mood or suicidal ideation is suspected. Patients/caregivers should be aware of possible psychiatric disorders that may occur immediately or right after dose reduction/withdrawal of systemic steroids. Such reactions have rarely been reported. Particular caution should be exercised when considering the use of systemic corticosteroids in patients who have or have had a history of severe affective disorders in themselves or in first-degree relatives. These include depressive or manic depressive illness and previous steroid-induced psychosis.
Psychological changes are manifested in various forms, the most common being euphoria. Depression, psychotic reactions and suicidal tendencies may also appear. These illnesses can be serious. Usually they start within a few days or weeks of starting the medicine. They are more likely to happen at high doses. Most of these problems disappear when the dose is lowered or the medicine is stopped. However, if problems do happen, they might need treatment. In a few cases, mental health problems have happened when doses are being lowered or stopped.

*Cerebral edema or increased intracranial pressure*
Corticosteroids should not be used in head trauma as they are unlikely to benefit patients or may even cause harm.

*Discontinuation of treatment*
Glucocorticoid doses should be gradually reduced.
The following risks should be considered upon interruption or discontinuation of long-term glucocorticoid administration:
• Exacerbation or recurrence of the underlying disease, acute adrenal insufficiency, corticosteroid withdrawal syndrome (a 'withdrawal syndrome' may include fever, muscle and joint pain, inflammation of the nose lining [rhinitis], weight loss, itchy skin and inflammation of the eye [conjunctivitis]).
• Certain viral diseases (chickenpox, measles) in patients treated with glucocorticoids may be very severe.
• Children and immunocompromised persons without previous chickenpox or measles infection are particularly at risk. If these people have contact with people infected with measles or chickenpox while undergoing treatment with dexamethasone, a preventative treatment should be introduced if necessary.

Chickenpox is of particular concern since this normally minor illness may be fatal in immunosuppressed patients. Patients (or parents of children) without a definite history of chickenpox should be advised to avoid close personal contact with people who have chickenpox or herpes zoster and if exposed they should seek urgent medical attention. Passive immunization with varicella zoster immunoglobulin (VZIG) is needed by exposed non-immune patients who are receiving systemic corticosteroids or who have used them within the previous 3 months; this should be given within 10 days of exposure to chickenpox. If a diagnosis of chickenpox is confirmed, the disease requires specialized care and emergency treatment. Corticosteroids should not be discontinued, and the dose may need to be increased.
Measles can be more serious and even fatal in immunocompromised patients. Special care should be taken in order to avoid exposure to measles in such children or adults. In case of exposure, prophylaxis with intramuscular mixed immunoglobulin (IG) may be indicated. Exposed patients should be advised to seek medical attention without delay.

In patients who have received higher than physiological doses of systemic corticosteroids (approximately 1 mg dexamethasone) for more than 3 weeks, treatment should not be abruptly discontinued. How the dose is reduced depends largely on whether the disease is likely to recur as the

systemic corticosteroid dose is reduced. Clinical evaluation of disease activity may be required during discontinuation. If recurrence is unlikely with discontinuation of systemic corticosteroids, but there is uncertainty about hypothalamic-pituitary-adrenal (HPA) suppression, the dose of systemic corticosteroids may be rapidly tapered to physiologic doses. Once a daily dose of 1 mg of dexamethasone is reached, the dose should be tapered more slowly to allow the HPA axis to recover. Abrupt discontinuation of systemic corticosteroid therapy for up to 3 weeks is appropriate if a recurrence of disease is considered unlikely.

In most patients, abrupt discontinuation of dexamethasone doses up to 6 mg per day for 3 weeks is unlikely to result in clinically significant HPA axis suppression. Gradual discontinuation of systemic corticosteroid therapy should be considered in the following groups of patients, even after 3 weeks or less of treatment:
• Patients who have received repeated courses of systemic corticosteroids, especially if they have been taken for more than 3 weeks.
• When a short course is prescribed within one year after discontinuation of long-term treatment (months or years).
• Patients who may have causes of adrenocortical insufficiency other than exogenous corticosteroid therapy.
• Patients receiving systemic corticosteroids at doses more than 6 mg dexamethasone per day.
• Patients taking repeated doses in the evening.

**Patients should carry "steroid treatment" cards that provide clear guidance on risk minimization measures and identify the prescribing physician, medication, dosage, and duration of treatment.**

Adrenal Suppression
Abrupt discontinuation of long-term corticosteroid therapy may result in acute adrenal insufficiency, hypotension, or death. Adrenal atrophy develops during prolonged therapy with corticosteroids and may persist for years after discontinuation of treatment. Discontinuation of treatment may also be associated with fever, myalgia, arthralgia, rhinitis, conjunctivitis, painful itchy skin nodules, and weight loss. To compensate for a diminished adrenocortical response caused by prolonged corticosteroid treatment, any significant intercurrent illness, trauma or surgical procedure requires a temporary increase in corticosteroid dose, or if already stopped, a temporary re-introduction of corticosteroid treatment. Therefore, the anesthesiologist must know if the patient is taking or has previously taken corticosteroids to prevent a rapid drop in blood pressure during anesthesia or in the immediate postoperative period. An appropriate corticosteroid replacement regimen for patients who have received more than 1.5 mg of dexamethasone daily in the 3 months prior to surgery is as follows:

*Minor surgery under general anesthesia:* Usual dose of oral corticosteroids or initial 25-50 mg of intravenous hydrocortisone (usually sodium succinate) on the morning of surgery; usual dose of oral corticosteroids is recommended postoperatively.

*Moderate or major surgery:* The usual dose of oral corticosteroids on the morning of surgery is 25-50 mg intravenous hydrocortisone initially, followed by 25-50 mg intravenous hydrocortisone 3 times daily for 24 hours after moderate surgery or 48-72 hours after major surgery; the usual preoperative dose of oral corticosteroids is recommended if hydrocortisone injections are discontinued.

For a short dexamethasone suppression test, 1 mg of dexamethasone is given at 11 p.m. and plasma cortisol is measured the next morning. Patients who do not show a decrease in cortisol may have a

longer test: 500 micrograms of dexamethasone is given every 6 hours for 48 hours, followed by 2 mg every 6 hours for more than 48 hours. 24-hour urine collections are performed before, during, and at the end of testing in order to detect 17-hydroxycorticosteroids.

*Others*
Pheochromocytoma crisis, which can be fatal, has been reported after administration of systemic corticosteroids. Corticosteroids should only be administered to patients with suspected or identified pheochromocytoma after an appropriate risk/benefit evaluation.

Pediatric population
Corticosteroids cause a dose-dependent inhibition of growth in infancy, childhood, and adolescence since corticosteroids may give rise to early closing of the epiphyses, which may be irreversible. Therefore, during long-term treatment with dexamethasone, the indication should be very strongly presented in children and their growth rate should be checked regularly. Treatment should be limited to the minimum dose for the shortest possible duration.
To minimize suppression of the hypothalamic-pituitary-adrenal axis and growth retardation, treatment should be limited to a single dose on alternate days, if possible.

*Preterm newborns*: Available evidence suggests long-term neurodevelopmental adverse events after early treatment (< 96 hours) of premature infants with chronic lung disease at starting doses of 0.25 mg/kg twice daily.

Elderly
The common adverse effects of systemic corticosteroids may be associated with more serious consequences in the elderly, especially osteoporosis, hypertension, hypokalemia, diabetes, susceptibility to infection and skin atrophy. Close clinical supervision is required to avoid life-threatening reactions.

Influence of diagnostic tests
Glucocorticoids can suppress skin reaction to allergy testing. They can also affect the nitroblue tetrazolium test for bacterial infections and cause false-negative results.

Note on doping
The use of doping tests when taking dexamethasone can lead to positive results.

DEKORT contains 118.985 mg lactose monohydrate (of cow or bovine origin). Patients with rare hereditary problems of galactose intolerance, Lapp-lactase deficiency or glucose-galactose malabsorption should not take this medicine.

**4.5. Interactions with other medicinal products and other forms of interaction**
**Pharmacodynamic interactions**
Patients taking NSAIDs should be monitored, as NSAIDs may increase the incidence and/or severity of gastric ulcers. Acetylsalicylic acid should be used carefully in combination with corticosteroids in hypoprothrombinemia.

Aspirin should be used carefully in combination with corticosteroids in hypoprothrombinemia. The renal clearance of salicylates is increased by corticosteroids. Therefore, the dosage of salicylates may

be reduced once the steroids are discontinued. Steroid discontinuation may result in salicylate intoxication due to the increase of salicylate concentration in the serum.
Corticosteroids reduce the effect of antidiabetic agents such as insulin, sulfonylurea, and metformin. Hyperglycemia and diabetic ketoacidosis may occur occasionally.

Therefore, at the beginning of treatment, diabetics should have more frequent blood and urine tests.
The hypokalemic effect of acetazolamide, loop diuretics, thiazide diuretics, kaliuretics, amphotericin B injections (glucomineral)-corticosteroids, tetracosactide and laxatives will increase. Hypokalemia promotes cardiac arrhythmias, especially torsade de pointes, and increases the toxicity of cardiac glycosides. Before the start of corticosteroid treatment, hypokalemia should be corrected and patients should be monitored clinically, for electrolytes and by electrocardiography. Furthermore, there are case reports in which the simultaneous use of amphotericin B and hydrocortisone led to an enlarged heart and heart failure.

Antiulcer drugs: Carbenoxolone increases the risk of hypokalemia.

Chloroquine, hydroxychloroquine and mefloquine: Increased risk of myopathies and cardiomyopathies.
Concomitant administration of ACE inhibitors creates an increased risk of blood disorders.

The blood pressure-lowering effects of antihypertensive drugs may be affected by corticosteroids. The dose of anti-hypertensive therapy should be adjusted during the treatment with dexamethasone.

Thalidomide: Extreme caution should be exercised during co-administration with thalidomide, as there have been reported cases of toxic epidermal necrolysis.

The effect of vaccinations may be reduced during treatment with dexamethasone.

Vaccination with live vaccines during treatment with large therapeutic doses of dexamethasone (and other corticosteroids) is contraindicated due to the possibility of viral infection. In this case, vaccination should be postponed for at least 3 months after the completion of treatment with corticosteroids. Other types of immunization during treatment with large therapeutic doses of corticosteroids are dangerous due to the risk of neurological complications and decreased or absent increase in the antibody titers (in comparison with expected values) and therefore a smaller protective effect. However, patients who have received corticosteroids locally (parenteral) or for a short period of time (less than 2 weeks), in smaller doses may be immunized.

Cholinesterase inhibitors: Concomitant use of cholinesterase inhibitors and corticosteroids may cause serious muscle weakness in patients with myasthenia gravis. If possible, cholinesterase inhibitors should be discontinued at least 24 hours before the start of corticosteroid therapy.
The risk of tendinitis and tendon rupture is increased in patients treated concomitantly with glucocorticoids and fluoroquinolones.
Concomitant treatment with CYP3A inhibitors, including cobicistat-containing products, is expected to increase the risk of systemic adverse 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.

**Pharmacokinetic interactions**
Effects of other medicinal products on dexamethasone:
Dexamethasone is metabolized via the cytochrome P450 3A4 (CYP3A4).

The administration of dexamethasone with inducers of CYP3A4, such as ephedrine, barbiturates, rifabutin, rifampicin, phenytoin, and carbamazepine can lead to reduced plasma concentrations of dexamethasone, so the dose must be increased. The effects of other drugs on dexamethasone metabolism may interfere with dexamethasone suppression tests and should be interpreted with caution when administering such drugs.

Aminoglutethimide can accelerate the reduction of dexamethasone and reduce its efficacy. If necessary, the dexamethasone dosage should be adjusted.

Bile acid resins such as cholestyramine may decrease the absorption of dexamethasone.

Topically applied gastrointestinal drugs, antacids, activated charcoal: Decreased glucocorticoid resorption has been described during co-administration of prednisolone and dexamethasone. Therefore, the administration of glucocorticoids and topically applied gastrointestinal drugs, antacids, activated charcoal should be postponed (with an interval of at least 2 hours).

The administration of dexamethasone with inhibitors of CYP3A4, such as azole antifungals (e.g. ketoconazole, itraconazole), HIV protease inhibitors (e.g. ritonavir) and macrolide antibiotics (e.g. erythromycin) may lead to increased plasma concentrations and reduced clearance of dexamethasone. If required, the dexamethasone dose should be reduced.

Concomitant treatment with CYP3A inhibitors, including cobicistat-containing products, is expected to increase the risk of systemic adverse 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.

Ketoconazole may not only increase the plasma concentration of dexamethasone by inhibition of CYP3A4, but also suppress adrenal corticosteroid synthesis and cause adrenal insufficiency upon discontinuation of corticosteroid treatment.
Estrogens, including oral contraceptives, may inhibit the metabolism of certain corticosteroids and thus enhance their effect.

Effects of dexamethasone on other medicinal products:
Dexamethasone is a moderate inducer of CYP3A4. The administration of dexamethasone with substances metabolized by CYP3A4 (e.g. erythromycin and anti-HIV drugs such as indinavir, ritonavir, lopinavir, saquinavir) can lead to increased clearance and decreased plasma concentrations of these substances. Post-marketing experience has reported both increases and decreases in phenytoin levels with co-administration of dexamethasone, resulting in changes in seizure control.
Tuberculostatics: A reduction of isoniazid plasma concentrations was observed during concurrent use of prednisolone. Patients taking isoniazid should be monitored closely.

Cyclosporine: Concomitant administration of cyclosporine and corticosteroids may lead to an increased effect of both substances. There is an increased risk of cerebral seizures.

Praziquantel: Reduced praziquantel plasma concentrations create a risk of treatment failure due to the increased hepatic metabolism of dexamethasone.

Oral anticoagulants (coumarin): Concomitant corticosteroid therapy may either potentiate or lead to a weakening of the effect of oral anticoagulants. In case of high doses or of treatment lasting over 10

days there is a risk of bleeding specific to corticosteroid therapies (gastrointestinal mucosa, vascular fragility). Patients who use corticosteroids combined with oral anticoagulants should be closely monitored (controls on day 8, then every 2 weeks during and after treatment).

Atropine and other anticholinergics: Intraocular pressure increases may be noted during co-administration with dexamethasone.

Non-depolarizing muscle relaxants: The muscle relaxing effect may last longer.

Somatotropin: The effect of growth hormone can be reduced.

Protirelin: Reduced increase in TSH may be noted during administration of protirelin.
The desired effects of hypoglycemic agents (including insulin) are antagonized by corticosteroids.
Patients should be closely monitored for the development of hypokalemia when corticosteroids are administered concurrently with potassium-depleting diuretics.
Corticosteroids may can also affect the nitroblue tetrazolium test for bacterial infections and cause false-negative results.

**Additional information on special populations:**
No interaction study has been conducted in special populations.

**Pediatric population**
No interaction study has been conducted on the pediatric population.

**4.6. Pregnancy and lactation**
**General recommendation**
Pregnancy category is C.

**Women of child-bearing potential/Birth control (Contraception)**
Birth control should be implemented while using DEKORT.

**Pregnancy**
Data obtained from animal studies are insufficient to draw conclusions with regard to the effects on pregnancy and/or embryonic/fetal development and/or postnatal development. Potential risk for humans is unknown.

DEKORT should not be used during pregnancy unless necessary.

When administered for prolonged periods or repeatedly during pregnancy, the risk of uterine growth restriction may increase.

Any adrenal suppression in the neonate following prenatal exposure usually resolves spontaneously and is rarely clinically important.

Systemic effects in the newborn are unlikely with maternal dexamethasone doses up to 6 mg per day (≡ 40 mg prednisolone). Infant adrenal function should be monitored at higher doses.

Administration of corticosteroids to pregnant animals can cause abnormalities of fetal development, including cleft palate, intrauterine growth restriction, and effects on brain growth and development.

There is no evidence that corticosteroids cause an increased incidence of congenital abnormalities such as cleft palate/lip in humans (see section 5.3).

However, when administered for prolonged periods or repeatedly during pregnancy, corticosteroids may increase the risk of intra-uterine growth restriction. Hypoadrenalism may, in theory, occur in the neonate following prenatal exposure to corticosteroids but usually resolves spontaneously following birth and is rarely clinically important. As with all drugs, corticosteroids should only be prescribed when the benefits to the mother and child outweigh the risks. When corticosteroids are essential however, patients with normal pregnancies may be treated as though they were in the non-gravid state.

Dexamethasone should not be prescribed during pregnancy, especially in the first trimester, unless the benefits outweigh the risks to the mother and baby.

**Lactation**
Glucocorticoids are excreted in breast milk. There is insufficient information on the excretion of dexamethasone in human milk. A risk to newborns/infants cannot be excluded. Corticosteroids can be excreted from the body in small amounts through breast milk. Infants of mothers taking high doses of systemic corticosteroids for prolonged periods may have a degree of adrenal suppression.

A decision on whether to continue/discontinue breastfeeding or to continue/discontinue therapy with dexamethasone should be made taking into account the benefit of breastfeeding to the child and the benefit of dexamethasone therapy to the woman.

**Reproductive ability/Fertility**
Dexamethasone decreases testosterone biosynthesis and endogenous ACTH secretion, which has an effect on the spermatogenesis and the ovarian cycle.

**4.7. Effects on the ability to drive and use machines**
There have been no studies on the effects on the ability to drive and use machines.
Dexamethasone may cause confusional state, hallucinations, dizziness, somnolence, fatigue, syncope, and blurred vision (see section 4.8). If affected, patients should be instructed not to drive, use machines, or perform hazardous tasks while being treated with dexamethasone.

**4.8 Undesirable effects**
Summary of the safety profile
The incidence of anticipated adverse effects correlates with the relative potency of the substance, dose, time of day of administration and duration of treatment. During a short-term therapy, in compliance with the dosage recommendations and close monitoring of patients, the risk of side effects is low.

The usual side effects of short-term dexamethasone treatment (days/weeks) include weight gain, psychological disturbances, glucose intolerance and transient adrenocortical insufficiency. Long-term dexamethasone treatment (months/years) usually causes central obesity, skin fragility, muscle atrophy, osteoporosis, growth retardation and long-term suprarenal insufficiency (see also section 4.4).
Adverse events are listed by system organ class and frequency using the following convention:
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); not known (cannot be estimated from available data)

Tabulated list of adverse reactions

| | |
|---|---|
| | Frequency not known (cannot be estimated from the available data) |
| Infections and infestations | Increased susceptibility to, or exacerbation of (latent) infections* (including septicemia, tuberculosis, eye infections, chickenpox, measles, fungal and viral infections) with masking of clinical symptoms, opportunistic infections, recurrence of dormant tuberculosis |
| Blood and lymphatic system disorders | Leukocytosis, lymphopenia, eosinopenia, polycythemia, abnormal coagulation |
| Immune system disorders | Hypersensitivity reactions including anaphylaxis, immunosuppression (see also “Infections and infestations”) |
| Endocrine disorders | Suppression of hypothalamic-pituitary-adrenal axis and induction of Cushing's syndrome (typical symptoms: full-moon face, plethora, truncal obesity), secondary adrenal and pituitary insufficiency* (especially in stress such as trauma or surgery), growth suppression in infancy, childhood and adolescence, menstrual irregularity and amenorrhea, hirsutism, adrenocortical insufficiency, decreased glucose tolerance, manifestation of latent diabetes mellitus, hyperglycemia, increased need for insulin or oral hypoglycemic agents in diabetics |
| Metabolism and nutrition disorders | Weight gain, negative protein and calcium balance*, increased appetite, sodium and water retention*, potassium loss* (caution: rhythm disorders), hypokalemic alkalosis, manifestation of latent diabetes mellitus, impaired carbohydrate tolerance with increased dose requirements of antidiabetic therapy*, hypercholesterolemia, hypertriglyceridemia, negative nitrogen balance due to protein catabolism |
| Psychiatric disorders | Psychological dependence, depression, insomnia, aggravated schizophrenia, mental illness, from euphoria to manifest psychosis, emotional disorders (such as irritability, euphoric, depressive mood and mood swings and suicidal ideation), psychotic reactions (mania, delusions, hallucinations), a wide range of psychiatric reactions, including behavioral disorders, irritability, anxiety, sleep disturbances, and cognitive dysfunction, including confusion and amnesia, have been reported. Reactions are common and can occur in both adults and children. The frequency of severe reactions in adults is estimated to be 5-6%. Psychological effects have been reported with discontinuation of corticosteroids with unknown frequency. |
| Nervous system disorders | Increased intracranial pressure with papilledema in children (pseudotumor cerebri) usually following discontinuation of treatment; manifestation of latent epilepsy, increased seizures in overt epilepsy, vertigo, headache, convulsions |
| Eye disorders | Elevated intraocular pressure; glaucoma*; papilledema*, posterior subcapsular cataract*, mainly with posterior subcapsular opacity; corneal and scleral atrophy; increased risk of ophthalmic viral, fungal and bacterial infections; corneal ulcers; worsening of symptoms associated with central serous chorioretinopathy; |

| | |
|---|---|
| | exophthalmos; chorioretinopathy. |
| Cardiac disorders | Cardiac muscle rupture after recent history of myocardial infarction*, congestive heart failure in predisposed patients, cardiac decompensation* |
| Vascular disorders | Hypertension, vasculitis, increased risk of atherosclerosis and thrombosis/thromboembolism (increase in coagulability of blood may lead to thromboembolic complications) |
| Respiratory, thoracic and mediastinal disorders | Hiccough |
| Gastrointestinal disorders | Dyspepsia, abdominal distension*, gastric ulcers with perforation and bleeding, peptic ulcers and hemorrhage, acute pancreatitis, ulcerative esophagitis, esophageal candidiasis, flatulence, nausea, vomiting, perforation of the small and large intestine, especially in patients with inflammatory bowel disease, abdominal distension, dyspepsia |
| Skin and subcutaneous tissue disorders | Hypersensitivity reactions such as hypertrichosis, skin atrophy, telangiectasia, striea, erythema, steroid acne, petechiae, ecchymosis, allergic dermatitis, urticaria, angioneurotic edema, thinning hair, pigment disorders, increased capillary fragility, perioral dermatitis, hyperhidrosis, tendency to bruise, delayed wound healing, thin sensitive skin, increased sweating, suppressed reaction to skin tests |
| Musculoskeletal and connective tissue disorders | Premature epiphyseal closure, osteoporosis (especially in postmenopausal women), fractures of the spine and long bones, aseptic necrosis of the femoral and humeral bones, tendon tears*, proximal myopathy, muscle weakness, loss of muscle mass, steroid-induced myopathy, vertebral compression fractures |
| Reproductive system and breast disorders | Impotence |
| General disorders and administration site conditions | Reduced response to vaccination and skin tests. Delayed wound healing, discomfort, malaise, steroid withdrawal syndrome: a too rapid reduction in corticosteroid dose after prolonged treatment can lead to acute adrenal insufficiency, hypotension and death. A withdrawal syndrome may present with fever, myalgia, arthralgia, rhinitis, conjunctivitis, painful itchy skin nodules, and weight loss. |

* See also section 4.4

Description of selected side effects

*Adrenocortical insufficiency*

An adrenocortical insufficiency, which is caused by glucocorticoid treatment, can, depending on the duration and length of treatment, remain for many months, and in some cases more than a year, after discontinuation of treatment (see section 4.4).

*Psychological changes*

Psychological changes are manifested in various forms, the most common being euphoria. Depression, psychotic reactions and suicidal tendencies may also appear. These illnesses can be serious. Usually they start within a few days or weeks of starting the medicine. They are more likely to happen at high doses. Most of these problems disappear when the dose is lowered or the medicine is stopped (see section 4.4).

*Infections*
Treatment with dexamethasone can conceal the symptoms of an existing, or developing infection thereby making a diagnosis more difficult and can lead to an increased risk of infection (see section 4.4).

*Intestinal perforation*
Corticosteroids can be associated with an increased risk of colonic perforation in severe ulcerative colitis with threatened perforation, diverticulitis and entero-anastomosis (immediately postoperative).

Signs of peritoneal irritation after gastrointestinal perforation may be absent in patients receiving high doses of glucocorticoids (see section 4.4).

*Cardiovascular disorders*
Bradycardia, deterioration of severe cardiac insufficiency and difficult to regulate high blood pressure may occur. Caution should be exercised when using corticosteroids in patients who have recently suffered myocardial infarction as myocardial rupture has been reported (see section 4.4).

Pediatric population
Corticosteroids cause a dose-dependent inhibition of growth in infancy, childhood, and adolescence since corticosteroids may give rise to early closing of the epiphyses, which may be irreversible (see section 4.4).

Elderly
The adverse effects of systemic corticosteroids can have serious consequences especially in old age, mainly osteoporosis, hypertension, hypokalemia, diabetes, susceptibility to infection and skin atrophy (see section 4.4).

Withdrawal symptoms and signs
A too rapid reduction in corticosteroid dose after prolonged treatment can lead to acute adrenal insufficiency, hypotension and death (see section 4.4).
In some cases, withdrawal symptoms may simulate a clinical relapse of the disease for which the patient is being treated.

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 and treatment**
Symptoms
Reports of acute toxicity and/or death in overdosage with glucocorticoids are rare.
Overdose or prolonged use may exaggerate glucocorticoid side effects.

Management
No antidote is available. Treatment should be symptomatic and supportive with the dosage of dexamethasone being reduced or slowly withdrawn. Treatment is probably not indicated for reactions due to chronic poisoning unless the patient has a condition that would render him unusually

susceptible to ill effects from corticosteroids. In this case, the stomach should be emptied and symptomatic treatment should be instituted as necessary. Anaphylactic and hypersensitivity reactions may be treated with epinephrine (adrenaline), positive-pressure artificial respiration and aminophylline. The patient should be kept warm and quiet. The biological half-life of dexamethasone in plasma is about 190 minutes.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Corticosteroids for systematic use, Glucocorticoids
ATC code: H02AB02

**Mechanism of action**

Dexamethasone is a highly potent and long-acting glucocorticoid with negligible sodium retaining properties, has the effects of other essential glucocorticoids and is among the most active members, and is therefore particularly suitable for use in patients with heart failure and hypertension.

Its anti-inflammatory potency is 7 times greater than prednisolone and, like other glucocorticoids, dexamethasone also has anti-allergic, antipyretic and immunosuppressive properties.
Dexamethasone has a biological half-life of 36 - 54 hours and therefore is suitable in conditions where continuous glucocorticoid action is required.

Glucocorticoids are adrenocortical steroids, both naturally occurring and synthetic, that are readily absorbed from the gastrointestinal tract. They have profound and diverse metabolic effects and also alter the body's immune responses to various stimuli.
Naturally occurring glucocorticoids (hydrocortisone and cortisone), which also have salt-retaining properties, are used as replacement therapy for adrenocortical insufficiency. Synthetic analogues, including dexamethasone, are used primarily for their potent anti-inflammatory effects in many organ system disorders.

Dexamethasone is a synthetic 9α-fluorinated glucocorticoid and is approximately 30 times more potent than cortisone. However, it has almost no mineralocorticoid effect. Cushing's threshold dose is 1.5 mg/day.

### 5.2. Pharmacokinetic properties

**General properties**

Absorption:
Dexamethasone is rapidly and completely absorbed in the stomach and proximal small intestine immediately after oral administration. It reaches its maximum blood level between one and two hours. The bioavailability rate of dexamethasone after oral administration is approximately 80-90%.

Distribution:
Depending on the dose, dexamethasone is mainly bound to plasma albumin. When it reaches very high concentrations, most of it is found free in the blood, not bound to protein. In case of hypoalbuminemia, the rate of unbound (active) corticoid increases.

*Pass to the cerebrospinal fluid:*

Four hours after intravenous administration of radiolabeled dexamethasone to humans, the maximum level of dexamethasone in the cerebrospinal fluid was measured to be approximately 1/6 of the plasma concentration.

*Pass to the placenta:*
As with all glucocorticoids, it is possible for dexamethasone to cross the placental barrier (in an unmetabolized state, unlike many other corticoids).

*Pass to the breast milk:*
No data are available for dexamethasone. Glucocorticoids pass into breast milk in small amounts. This means that less than 1/100 of the systemic dose in the mother is usually passed on to the breastfed infant. However, with higher doses or prolonged use, breast-feeding should be discontinued.

Biotransformation:
Its metabolism occurs in the liver, partly in the form of glucorone or sulfuric acid conjugation, and then in the form of excretion through the kidney.

Elimination:
The half-life of dexamethasone in serum is between 168 and 324 minutes in adults (mean: 4.1 +/- 1.3 hours). Dexamethasone is largely excreted via the kidneys in the form of free dexamethasone alcohol in the urine. Renal impairment do not significantly affect the elimination of dexamethasone. Glucocorticoid half-life is prolonged in severe liver diseases such as hepatitis, liver cirrhosis, pregnancy and estrogen administration. Up to 65% of a dose is excreted in the urine within 24 hours, with an increased rate of excretion when phenytoin is co-administered.

Linearity and non-linearity:
There is no data.

**Patient characteristics**
Elderly:
Clinical trials have not been conducted in people 65 years of age and older to determine if there is a difference in response compared to adults. In other reported clinical studies, no differences were seen between elderly and adult patients. Caution should be exercised in the use of corticosteroids, especially in elderly patients with diabetes mellitus, fluid retention and hypertension.

Pediatric population:
The efficacy and safety of corticosteroids in the pediatric population, as in adults, are based on well-established aspects of corticosteroid effects.

**5.3. Preclinical safety data**
The acute toxicity of glucocorticoids is low. No chronic toxicity data are available in humans or animals. There are no known cases of corticoid-induced intoxication. However, it should be noted that significant side effects may occur with long-term therapeutic use in humans above a daily dose of >1 mg. There is insufficient animal data on its teratogenic and mutagenic potential. It remains unclear whether it is relevant to humans.

In animal studies, dexamethasone has caused cleft lip and a small number of other developmental defects in several species. There is no evidence of an increased risk of developmental defects in

human cases published to date. However, the number of cases mentioned is not sufficient to conclude that such a risk does not exist. To date, clinical experience with glucocorticoids in the first trimester has not provided evidence of a high teratogenic risk. It cannot be assumed that long-term treatment during pregnancy will not result in intrauterine developmental defects.

There is a risk of adrenal atrophy in the fetus with treatment given late in pregnancy, and the newborn may require treatment with a gradual tapering of the drug.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1. List of excipients

Lactose monohydrate (cow or bovine origin)
Maize starch
Microcrystalline cellulose (Type 102)
Crospovidone
Yellow iron oxide
Talc
Magnesium stearate

### 6.2. Incompatibilities

No known incompatibilities.

### 6.3. Shelf life

36 months.

### 6.4. Special precautions for storage

Store at room temperature below 25°C.

### 6.5. Nature and contents of the container

Transparent PVC/Aluminum foil blister material was used as the primary packaging material.
Presented in packages of 20 tablets in a cardboard box.

### 6.6. Special precautions for disposal and other handling

No special requirements.
Any unused medicinal 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 / İSTANBUL / TÜRKİYE

## 8. MARKETING AUTHORIZATION NUMBER

2017/618

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

Date of first authorization: 23.08.2017
Date of renewal of authorization:

## 10. DATE OF REVISION OF THE TEXT

05.06.2023