SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Dexamethasone 2 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 2 mg of Dexamethasone.

Excipient with known effect

Each tablet contains approximately 116.00 mg Lactose (as lactose monohydrate).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet

White, round and flat tablets bevelled edges tablets with coded ‘DM2’ on one side and plain on other side with approximately 6 mm diameter.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Neurology

Cerebral oedema caused by brain tumours, neurosurgery, bacterial meningitis, brain abscess.

Pulmonary and respiratory diseases

Severe acute asthma attack.

Dermatology

Oral initial treatment of extensive, severe, acute skin diseases that respond to glucocorticoids, such as erythroderma, pemphigus, vulgaris, acute eczema.

Autoimmune disorders/rheumatology

Oral initial treatment of autoimmune diseases, such as systemic lupus erythematosus (especially visceral forms).

Severely progressive form of active rheumatoid arthritis, e.g. rapidly destructive forms and/or with extra-articular manifestations.

Infectology

Severe infections with toxic conditions (e.g. tuberculosis, typhoid) only with concomitant anti-infective therapy.

Oncology

Palliative treatment of malignant tumours.

Endocrinology

Congenital adrenogenital syndrome in adulthood.

4.2 Posology and method of administration

Posology

Dosage depends on the nature and severity of the disease and the individual response of the patient to treatment. In general, relatively high initial doses are administered, and they should be significantly higher in acute severe forms than in chronic diseases.

Unless otherwise prescribed, the following dosage recommendations apply:

- Cerebral oedema: Depending on the cause and severity, initial dose of 8–10 mg (up to 80 mg) i.v., followed by 16–24 mg (up to 48 mg)/day orally, divided into 3–4 (up to 6) individual doses for 4–8 days. A longer-term, lower-dose administration of Dexamethasone may be required during irradiation and in the conservative treatment of inoperable brain tumours.

- Cerebral oedema due to bacterial meningitis: 0.15 mg/kg body weight every 6 hours for 4 days, children: 0.4 mg/kg body weight every 12 hours for 2 days, starting before the first antibiotics.

- Severe acute asthma attack: Adults: 8–20 mg, then, if necessary, 8 mg every 4 hours. Children: 0.15–0.3 mg/kg body weight.

- Acute skin diseases: Depending on the nature and extent of the disease, daily doses of 8–40 mg. Followed by treatment with decreasing doses.

- Active phases of rheumatic systemic diseases: systemic lupus erythematosus 6–16 mg/day.

- Severely progressive form of active rheumatoid arthritis: in rapidly destructive forms 12–16 mg/day, in extra-articular manifestations 6–12 mg/day

- Severe infectious diseases, toxic states (e.g. tuberculosis, typhoid): 4–20 mg for a few days, only with concomitant anti-infective therapy.

- Palliative treatment of malignant tumours: initially 8–16 mg/day, in prolonged treatment 4–12 mg/day.

- Congenital adrenogenital syndrome in adulthood: 0.25–0.75 mg/day as a single dose. If necessary, addition of a mineralcorticoid (fludrocortisone). In cases of particular physical stress (e.g. trauma, surgery), intercurrent infections, etc., a 2- to 3-fold dose increase may be required and under extreme stress (e.g. birth) a 10-fold increase.

- The tablets should not be split to adjust doses. If patients need a dose that cannot be provided by one or more tablets of 0.5mg, other appropriate formulations should be used.

Method of administration

The tablets should be taken during or after a meal. They should be swallowed whole, with a sufficient amount of liquid. The daily dose should be administered as a single dose in the morning, if possible (circadian therapy). In patients who require a high-dose therapy because of their disease, multiple daily dosing is often required to achieve maximum effect.

Depending on the underlying disease, clinical symptoms and response to therapy, the dose can be reduced at a faster or slower rate and the therapy stopped, or the patient is stabilised on a maintenance dose as low as possible and, if necessary, adrenal axis monitored. Basically, the dose and duration of treatment should be kept as high and long as necessary, but as low and short as possible. In principle, the dose should be reduced gradually.

In long-term therapy which is deemed necessary following initial treatment, patients should be switched to prednisone/prednisolone, because this leads to lower adrenal suppression.

In hypothyroidism or liver cirrhosis, low doses may be sufficient or a dose reduction may be necessary.

4.3 Contraindications

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

Systemic infection unless specific anti-infective therapy is employed. Stomach ulcer or duodenal ulcer.

Avoid live vaccines in patients receiving immuno suppressive doses (serum antibody response diminished).

In general no contraindications apply in conditions where the use of glucocorticoids may be life saving.

4.4 Special warnings and precautions for use

In post-marketing experience tumour lysis syndrome (TLS) has been reported in patients with haematological 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 tumour burden, and high sensitivity to cytotoxic agents, should be monitored closely and appropriate precaution taken.

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 steroid emergency card 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. An acute therapy-induced adrenocortical insufficiency can be minimized by slow dose reduction until a planned discontinuation time.

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 illnesses:

- Acute viral infections (Herpes zoster, Herpes simplex, Varicella, herpetic keratitis)
- HBsAG-positive chronic active hepatitis
- Approximately 8 weeks prior to 2 weeks after vaccinations with live vaccines
- Systemic mycoses and parasitoses (e.g. nematodes)
- In patients with suspected or confirmed strongyloidiasis (infection with threadworms), glucocorticoids can lead to activation and mass proliferation of these parasites
- Poliomyelitis
- Lymphadenitis after BCG vaccination
- Acute and chronic bacterial infections
- In a history of tuberculosis (reactivation risk), use only under tuberculostatic protection
- Known or suspected Strongyloidiasis (threadworm infestation). Treatment with glucocorticoids may lead to lead to Strongyloides hyperinfection 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
- Osteoporosis
- Severe cardiac insufficiency
- High blood pressure that is difficult to regulate
- Diabetes mellitus that is difficult to regulate
- Psychiatric disorders (also in the past), including suicidality: neurological or psychiatric monitoring is recommended
- Narrow- and wide-angle glaucoma, ophthalmic monitoring and adjunctive therapy are recommended
- Corneal ulcerations and corneal injuries, ophthalmic monitoring and adjunctive therapy are recommended

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 may only be used under urgent indication and under appropriate monitoring for:

- Severe ulcerative colitis with threatened perforation, possibly without peritoneal irritation
- Diverticulitis
- Enteroenterostomy (immediately postoperatively)

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

Diabetes

The possibility of 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 in patients with high blood pressure that is difficult to regulate.

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

Infections

Treatment with dexamethasone can conceal the symptoms of an existing, or developing infection thereby making a diagnosis more difficult. 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 inactivated vaccine are always possible. However, it should be noted that the immune reaction and thereby the success of inoculation, can be affected by higher doses of corticoids.

Regular checkups with doctors (including vision checkups in three-month intervals) are advised during long-term treatment with dexamethasone.

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, after menopause, 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 corticosteroids may cause fluid retention.

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 go away if 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 oedema or increased intracranial pressure

Corticosteroids should not be used in conjunction with a head injury since they will probably not be of benefit or may even do 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.

Other

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.

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

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. Close clinical monitoring is required to prevent 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 falsenegative results.

Note on doping

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

Dexamethasone contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.

4.5 Interaction with other medicinal products and other forms of interaction

Oestrogens (e.g. oral contraceptives): The half-life of glucocorticoids may be prolonged. Therefore, the effect of corticoids may be increased.

Antacids: Concomitant administration of aluminum hydroxide or magnesium hydroxide can lead to a reduction in the absorption of glucocorticoids with reduced efficacy of Dexamethasone. There should be a 2-hour interval between the intake of one and the other drug.

Drugs that induce CYP3A4, such as rifampicin, phenytoin, carbamazepine, barbiturates and primidone: The effect of corticoids may 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.

Drugs that inhibit CYP3A4, such as ketoconazole and itraconazole: The effect of corticoids may be increased.

Ephedrine: The metabolism of glucocorticoids may be accelerated and thus their effectiveness reduced.

ACE inhibitors: Increased risk of blood count changes.

Cardiac glycosides: The effect of glycosides may be increased by potassium deficiency.

Saluretics/laxatives: Potassium excretion may be increased.

Antidiabetics: The hypoglycaemic effect may be reduced.

Coumarin derivatives: The anticoagulant effect may be reduced or increased. Dosage adjustment of the anticoagulant may be necessary when co-administered.

Nonsteroidal anti-inflammatory drugs (NSAIDs), salicylates and indomethacin: The risk of gastrointestinal ulcers and bleeding is increased.

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

Atropine, other anticholinergics: Additional intraocular pressure increases are possible during concomitant use.

Praziquantel: Corticosteroids may cause a fall in praziquantel concentration in the blood.

Chloroquine, hydroxychloroquine, mefloquine: There is an increased risk of myopathies, cardiomyopathies.

Somatropin: The effect of somatropin may be reduced under long-term therapy.

Protirelin: Reduced increase in TSH may be noted during administration of protirelin.

Immunosuppressive agents: Increased susceptibility to infections and possible aggravation or manifestation of latent infections. Additionally, for ciclosporin: The blood levels of cyclosporine are increased: There is an increased risk of seizures.

Fluoroquinolones may increase the risk of tendon disorders.

Effect on investigation methods: Skin reactions in allergy tests can be suppressed.

4.6 Fertility, pregnancy and lactation

Pregnancy

Dexamethasone crosses the placenta. During pregnancy, especially in the first trimester, the drug should only be administered after careful benefit-risk assessment.

In long-term treatment with glucocorticoids during pregnancy, foetal growth disorders cannot be excluded. Administration of corticosteroids to pregnant animals can cause abnormalities of foetal development including cleft palate, intra-uterine growth retardation and effects on brain growth and development. There is no evidence that corticosteroids result in an increased incidence of congenital abnormalities, such as cleft palate/lip in man. See also section 5.3 of the SmPC. If glucocorticoids are administered towards the end of pregnancy, there is a risk of atrophy of the foetal adrenal cortex, which may necessitate replacement therapy in the newborn, which has to be slowly reduced.

Breast-feeding

Dexamethasone is excreted in breast milk. There are no known cases of harm to the infant. Nevertheless, the drug should be strongly indicated during lactation. If the disease requires higher doses, breast-feeding should be discontinued.

Fertility

Dexamethasone decreases testosterone biosynthesis and endogenous ACTH secretion which has an effect on the spermatogenesis and the ovarian cycle.

4.7 Effects on 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

- 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 the available data)

Hormone replacement therapy:

Low risk of undesirable effects with the use of recommended doses.

Pharmacotherapy:

The following undesirable effects may occur; they are highly dependent on the dose and duration of treatment, so their frequency cannot be specified:

Infections and infestations	Masking of infections, manifestation and exacerbation of viral infections, fungal infections, bacterial, parasitic and opportunistic infections,

	activation of strongyloidiasis.
Blood and lymphatic system disorders	Moderate leukocytosis, lymphocytopenia, eosinopenia, polycythemia.
Immune system disorders	Hypersensitivity reactions (e.g. drug eruption), severe anaphylactic reactions, such as arrhythmias, bronchospasm, hypo- or hypertension, circulatory collapse, cardiac arrest, weakening of the immune system.
Endocrine disorders	Adrenal suppression and induction of Cushing's syndrome (typical symptoms: moon face, central obesity and plethora).
Metabolism and nutrition disorders	Sodium retention with oedema, increased potassium excretion (risk of arrhythmias), weight gain, reduced glucose tolerance, diabetes mellitus, hypercholesterolemia and hypertriglyceridemia, increased appetite.
Psychiatric disorders	Depression, irritability, euphoria, increased drive, psychoses, mania, hallucinations, emotional lability, anxiety, sleep disorders, suicidality.
Nervous system disorders	Pseudotumor cerebri, manifestation of latent epilepsy, increase in seizure susceptibility in manifest epilepsy.
Eye disorders	Cataract, especially with posterior subcapsular opacity, glaucoma, deterioration of symptoms associated with corneal ulcer, increased occurrence of viral, fungal and bacterial inflammation of the eye, deterioration of bacterial inflammation of the cornea, ptosis, mydriasis, chemosis, iatrogenic scleral perforation, chorioretinopathy, vision, blurred (see also section 4.4).
Vascular disorders	Hypertension, increased risk of atherosclerosis and thrombosis, vasculitis (also as withdrawal syndrome after long-term therapy), increased capillary fragility.
Gastrointestinal disorders	Gastrointestinal ulcers, gastrointestinal bleeding, pancreatitis, stomach discomfort, hiccups.
Skin and subcutaneous tissue disorders	Striae rubra, atrophy, telangiectasias, petechiae, ecchymosis, hypertrichosis, steroid acne, rosacea-like (perioral) dermatitis, changes in skin pigmentation.
Musculoskeletal and connective tissue disorders	Myopathy, muscle atrophy and weakness, osteoporosis (dose-dependent, possible also in short-term administration), aseptic bone necrosis, tendon disorders, tendinitis, tendon rupture, epidural lipomatosis, growth inhibition in children. Note: Too rapid dose reduction after long-term treatment

	may cause symptoms such as muscle and joint pain.
Reproductive system and breast disorders	Disorders of sexual hormone secretion (consequently: irregular menstruation up to amenorrhea, hirsutism, impotence).
General disorders and administration site conditions	Delayed wound healing.

Description of selected adverse reactions

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. (see section 4.4 Special warnings and precautions for use)

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 go away if the dose is lowered or the medicine is stopped. (see section 4.4 Special warnings and precautions for use)

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 Special warnings and precautions for use)

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 Special warnings and precautions for use)

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 Special warnings and precautions for use)

<u>Paediatric population</u>

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 Special warnings and precautions for use)

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 Special warnings and precautions for use)

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 via Yellow Card Scheme, Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Symptoms

Acute intoxications with dexamethasone are not known. In case of chronic overdosing, an increase in undesirable effects, especially endocrine, metabolic and electrolyte-related effects, can be expected (see section 4.8).

Management

There is no known antidote to dexamethasone.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Corticosteroids for systemic use, Glucocorticoids, ATC code: H02AB02.

Mechanism of action

Dexamethasone is a mono-fluorinated glucocorticoid with pronounced antiallergic, anti-inflammatory and membrane-stabilizing properties and effects on carbohydrate, protein and fat metabolism.

Dexamethasone has an approximately 7.5 times greater glucocorticoid effect than prednisolone, and compared to hydrocortisone it is 30 times more effective, lacking mineralocorticoid effects.

Glucocorticoids, such as dexamethasone, exert their biological effects by activating the transcription of corticosteroid-sensitive genes. The antiinflammatory, immunosuppressive and anti-proliferative effects are caused by decreased formation, release and activity of inflammatory mediators, by the inhibition of specific functions and the migration of inflammatory cells. In addition, the effect of sensitized T lymphocytes and macrophages on target cells may be prevented by corticosteroids.

When long-term corticoid treatment is required, the possibility of induction of transient adrenal insufficiency must be considered. The suppression of the hypothalamic-pituitary-adrenal axis also depends on individual factors.

5.2 Pharmacokinetic properties

Absorption and distribution

After oral administration, dexamethasone is rapidly and almost completely absorbed in the stomach and small intestine. Its bioavailability is 80–90%. Maximum blood levels are reached between 60 and 120 minutes. The binding of dexamethasone to plasma albumins is dose-dependent. At very high doses, the largest portion circulates freely in the blood. In hypoalbuminaemia the proportion of the unbound (active) corticoid rises.

Biotransformation

The average (serum) elimination half-life of dexamethasone in adults is 250 minutes (+ 80 minutes). Due to its long biological half-life of more than 36 hours, daily continuous administration of dexamethasone can lead to accumulation and overdosing.

Elimination

The elimination is largely renal in the form of free dexamethasone alcohol. Dexamethasone is partly metabolised, the metabolites are excreted as glucuronates or sulfates, also mainly by the kidneys.

Renal and hepatic impairment

Renal function impairment has no relevant effect on the clearance of dexamethasone. However, the elimination half-life is prolonged in severe liver disease.

5.3 Preclinical safety data

Acute toxicity:

In mice and rats, the LD50 for dexamethasone after a single oral dose is 16 g/kg body and over 3 g/kg body weight, respectively, within the first 7 days. Following a single subcutaneous dose, the LD50 in mice is more than 700 mg/kg body weight and in rats about 120 mg/kg body weight, within the first 7 days.

Over a period of 21 days, these values become lower, which is interpreted as a consequence of serious infectious diseases caused by the hormone-induced immunosuppression.

Chronic toxicity:

There are no data on chronic toxicity in humans and animals. Corticoid induced intoxications are not known. In longer-term treatment with doses above 1.5 mg/day, pronounced undesirable effects can be expected (see section 4.8).

Mutagenic and tumorigenic potential:

The available study findings for glucocorticoids show no evidence of clinically relevant genotoxic properties.

Reproductive toxicity:

In animal studies, cleft palate was observed in rats, mice, hamsters, rabbits, dogs and primates; not in horses and sheep. In some cases these divergences were combined with defects of the central nervous system and of the heart. In primates, effects in the brain were seen after exposure. Moreover, intrauterine growth can be delayed. All these effects were seen at high dosages.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate,

Potato starch

Magnesium stearate

6.2 Incompatibilities

Not applicable

6.3 Shelf life

48 months

6.4 Special precautions for storage

This medicine does not require any special temperature storage conditions. Store in the original package in order to protect from light and moisture.

6.5 Nature and contents of container

PVC/PVdC/Aluminium foil blister packs, with blister packs contained in a carton together with the patient information leaflet.

Dexamethasone 2 mg tablets are sold in pack of 50 and of 100 tablets.

6.6 Special precautions for disposal

No Special requirements for disposal.

7 MARKETING AUTHORISATION HOLDER

ACIUM LTD

Business Technology Centre, Bessemer Drive,

Stevenage, United Kingdom,

SG1 2DX

8 MARKETING AUTHORISATION NUMBER(S)

PL 52914/0002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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