INSTRUCTION
for medical use
of medicinal product
LEKTHASONE®

Composition:
active ingredient: dexamethasone sodium phosphate;
Each 1 ml of solution contains 4 mg of dexamethasone sodium phosphate on a dry substance basis;
excipients: propylene glycol, glycerol, disodium edetate, phosphate buffer solution pH 7.5, methylparaben (E 218), propylparaben (E 216), water for injections.

Pharmaceutical form. Solution for injections.
Main physicochemical properties: clear colourless liquid.

Pharmacotherapeutic group. Corticosteroids for systemic administration. ATC code H02A B02.

Pharmacological properties.
Pharmacodynamics.
Dexamethasone is the semisinthetic hormone of the adrenal gland (corticosteroid) with glucocorticoid activity. It has anti-inflammatory and immunosuppressive effect and affects energy metabolism of glucose and (via negative feedback) secretion of the hypothalamus activation factor and trophic hormone of the adenohypophysis.
Mechanism of action of glucocorticoids has not yet been completely established. Currently, there are enough reports about mechanism of action of glucocorticoids supporting their action on the cellular level. There are two well-established systems of receptors in the cellular cytoplasm. Due to the binding to glucocorticoid receptors, corticoids have anti-inflammatory and immunosuppressive effect, and regulate glucose metabolism, and as a consequence of binding to mineralocorticoid receptors they regulate sodium and potassium metabolism as well as water-electrolytic balance. Glucocorticoids are soluble in lipids and easily penetrate target cells through the cellular membrane. Hormone binding to receptors leads to receptor conformation change that promotes reinforcement of its affinity to DNA. Hormone/receptor complex enters into the cell nucleus and binds to regulating centre of DNA molecule that is also referred to as the glucocorticoid response element (GRE). Activated receptor bound to GRE or specific genes regulates transcription of mRNA that can be increased or decreased. Newly-formed mRNA is transported to the ribosomes with subsequent formation of the new proteins. Depending on the target cells and processes in the cell, protein synthesis can be increased (e.g., formation of tyrosine transaminase in the hepatic cells) or decreased (e.g., formation of IL-2 in the lymphocytes). Since glucocorticoid receptors are present in all types of tissues, it can be assumed that glucocorticoids influence most of the body cells.
Effect on the energy metabolism and glucose homeostasis.
Dexamethasone along with insulin, glucagon, and catecholamines regulate energy conservation and consumption. Formation of glucose from pyruvates or aminoacids and formation of glycogen increases in the liver. In the peripheral tissues, especially in muscles, glucose consumption and mobilization of aminoacids (from proteins) that are the substrates for gluconeogenesis in liver is reduced. Direct effect on lipid metabolism is the centrical distribution of the fatty tissue and increase of the lipolytic direction on catecholamines.
With the help of receptors in the renal proximal tubules, dexamethasone increases renal circulation and glomerular filtration, inhibits formation and secretion of vasopressin, improves ability of the kidneys for acids elimination from the body.
Due to the increased amount of β-adrenoreceptors and affinity to β-adrenoreceptors that deliver positive inotropic effect of catecholamines, dexamethasone directly increases cardiac contractile function and tone of the peripheral vessels.
High dexamethasone doses inhibit fibroblastic production of type I and type III collagen, and formation of the glycosaminoglycans. Therefore, delay in wound healing occurs due to the inhibition of extracellular collagen and matrix formation. Continuous administration of the high

doses leads via indirect effect to the progressive bone resorption and reduces osteogenesis via direct effect (increased secretion of parathyroid hormone and decreased secretion of calcitonin) and it is also responsible for negative calcium balance due to the reduction of calcium absorption in the intestine and increase of its elimination with urine. Generally, this leads to the secondary hyperparathyroidism and phosphaturia.

Effect on hypophysis and hypothalamus.

Dexamethasone shows 30-fold higher effect than cortisol. Therefore, it is more potent inhibitor of the corticotropin-releasing factor (CRF) and secretion of the adrenocorticotropic hormone (ACTH) compared with endogenous cortisol. This leads to the reduced secretion of cortisol, and following continuous inhibition of CRF and ACTH secretion − to the atrophy of the adrenal gland. Adrenal cortex insufficiency can occur on the Day 5 and 7 of dexamethasone administration at the dose equivalent to 20-30 mg of prednisone daily or following 30-day treatment with low doses. Following discontinuation of the short-term treatment (up to 5 days) with high doses, function of the adrenal cortex should restore during 1 week, and after continuous treatment normalization occurs later, in general, up to 1 year. Non-reversible atrophy of the adrenal gland may develop in some patients.

Anti-inflammatory and immunosuppressive effect of glucocorticoids is based on their molecular and biochemical influence. Molecular anti-inflammatory effect occurs as the result of binding to glucocorticoid receptors and change of the expression of several genes that regulate formation of the different information molecules, proteins and enzymes participating in the inflammatory reaction. Biochemical anti-inflammatory effect of glucocorticoids is the result of blockade of formation and functioning of the humoral inflammatory mediators: prostaglandins, thromboxanes, cytokines, and leukotrienes. Dexamethasone reduces formation of leukotrienes via reduced release of the arachidonic acid form cellular phospholipides that is associated with inhibition of phospholipase A_2 activity. Effect on phospholipases is achieved as the result of increase of lipocortin (macrocortin) concentration that inhibits phospholipase A_2 rather than via indirect effect. Dexamethasone inhibits formation of prostaglandins and thromboxane via reduced formation of the specific mDNA and consequently reduces formation of cyclooxygenase. Dexamethasone also reduces production of platelet activation factor (PAF) due to the increased concentration of lipocortin. Other biochemical anti-inflammatory effects include reduction of formation of tumour necrosis factor (TNF) and interleukin (IL-1).

Pharmacodynamics.

Absorption.

Dexamethasone achieves plasma peak concentration during the first 5 minutes following intravenous administration and during 1 hour following intramuscular administration. Following local administration into the joint or soft tissues (inflammatory focus), absorption is slower compared with intramuscular administration. Onset of action is immediate following intravenous administration, and clinical effect occurs after 8 hours following intramuscular administration. Effect lasts for 17 to 28 days following intramuscular administration and 3 days to 3 weeks following local administration.

Distribution.

Transformation of dexamethasone phosphate to dexamethasone in the blood plasma and synovial fluid occurs very quickly. Approximately 77% of dexamethasone in the blood plasma binds to plasma proteins, predominantly, to albumin. Only small amount of dexamethasone binds to the other proteins. Dexamethasone is lipid-soluble, therefore it freely penetrates cells and intercellular space. In the central nervous system (hypothalamus, hypophysis) it binds to the membrane receptors and acts through them. In peripheral tissues it binds to the cytoplasmic receptors and acts through them.

Biotransformation.

Dexamethasone degradation occurs in the site of action, that is in the cell. Dexamethasone is primarily metabolized in the liver, and possibly also in kidneys and other tissues.

Elimination.

Biological elimination half-life of dexamethasone is 24 to 72 hours. It is primarily excreted in the urine.

Clinical particulars.

Indications.

Dexamethasone is administered intravenously or intramuscularly in emergency cases and if it is not possible to administer it orally.

Endocrine disorders:

− replacement therapy of the primary and secondary (hypophyseal) insufficiency of the adrenal glands (excluding acute insufficiency of the adrenal glands upon which hydrocortisone or cortisone are the most reasonable considering their more pronounced hormonal effect);

− acute insufficiency of the adrenal glands (hydrocortisone or cortisone are the drugs of choice, and concomitant administration with mineralocorticoids, especially, in case of administration of the synthetic analogues may be required);

− before surgery and in case of serious injuries or diseases in patients with established adrenal insufficiency or in case of unspecified adrenocortical reserve;

− shock resistant to the conventional therapy, in case of existing or suspecting insufficiency of the adrenal glands;

− congenital insufficiency of the adrenal glands;

− non-purulent inflammation of the thyroid gland and severe forms of the radiation thyroiditis.

Rheumatologic disorders

(as the supportive therapy during the period when the background therapy had no effect, i.e., in patients with unsatisfactory analgesic and anti-inflammatory effect of NSAIDs):

− rheumatoid arthritis, including juvenile rheumatoid arthritis and extra-articular manifestations of the rheumatoid arthritis (rheumatoid lung disease, changes in the heart and eyes, cutaneous vasculitis);

− synovitis in case of osteoarthrosis, post-traumatic osteoarthrosis; epicondylitis, acute non-specific tendosynovitis; acute gouty arthritis; psoriatic arthritis; ankylosing spondylitis; systemic diseases of the connective tissue; vasculitis.

Skin disorders:

− pemphigus, severe erythema multiform (Stevens-Johnson syndrome); exfoliative dermatitis; bullous dermatitis herpetiformis; severe forms of exudative erythema; erythema nodosum; severe forms of seborrheic dermatitis; severe forms of psoriasis; urticaria resistant to the standard treatment; mycosis fungoides; dermatomyositis.

Allergic disorders:

(resistant to the conventional treatment):

− bronchial asthma; contact dermatitis; atopic dermatitis; serum disease; chronic or seasonal allergic rhinitis; drug allergy; urticaria following blood transfusion.

Eye disorders:

− inflammatory diseases of the eyes (acute central chorioiditis, optic neuritis); allergic diseases (conjunctivitis, uveitis, scleritits, keratitis, iritis); systemic immune diseases (sarcoidosis, temporal arteritis); proliferative changes in the orbital cavity (endocrinous ophthalmopathy, pseudotumour); immunosuppressive therapy following keratoplasty.

Solution can be administered systemically or locally (administration under conjunctive and retrobulbar or parabulbar administration).

Gastrointestinal disorders:

in order to treat emergency condition in case of:

− ulcerative colitis (severe development), Crohn's disease (severe development); chronic autoimmune hepatitis; rejection reaction following liver transplantation.

Respiratory system disorders:

− symptomatic sarcoidosis (symptomatic treatment); acute toxic bronchiolitis; chronic bronchitis and asthma (in case of exacerbation); focal or disseminated pulmonary tuberculosis (along with the appropriate antituberculous therapy); berylliosis (granulomatous inflammation); radiation or aspiration pneumonitis.

Haematological disorders:

− acquired or congenital chronic aplastic anaemia; autoimmune hemolytic anaemia; secondary thrombocytopenia in adults; erythroblastopenia; acute lymphoblastic leukaemia (induction therapy);

− idiopathic thrombocytopenic purpura in adults (only intravenous administration − intramuscular administration is contraindicated).
Renal disorders:
− immunosuppressive therapy in case of kidney transplantation; diuresis stimulation or reduction of the proteinuria in case of idiopathic nephrotic syndrome (without uraemia) and renal impairment in case of systemic lupus erythematosus.
Malignant oncological diseases:
− palliative treatment of leukemia and lymphoma in adults; acute leukemia in children, hypercalcemia in case of the malignant diseases.
Cerebral oedema:
− cerebral oedema due to the primary or metastatic tumour of the brain, craniotomy and craniocerebral injuries.
Shock:
− shock resistant to the standard treatment; shock in patients with insufficiency of the adrenal glands; anaphylactic shock (intravenously following adrenalin administration), before surgery in order to prevent shock if insufficiency of the adrenal glands is suspected or established.
Other indications:
− tuberculous meningitis with subarachnoid blockade (along with the appropriate antituberculous therapy); trichinellosis with neurological symptoms or myocardial trichinellosis; cystic tumour of aponeurosis or tendon (ganglion).
Indications for intra-articular administration or administration into the soft tissues:
− rheumatoid arthritis (severe inflammation of the separate joint); ankylosing spondylitis (when inflamed joints are resistant to the conventional treatment); psoriatic arthritis (oligoarticular form and tendovaginitis); monoarthritis (following evacuation of the synovial fluid), joint osteoarthritis (only in case of synovitis and exudation); extra-articular rheumatism (epicondylitis, tendovaginitis, bursitis); acute and gouty arthritis.
Local administration (administration into the site of lesion):
− keloid lesions; hypertrophic, inflammatory, and infiltrated lesions in case of lichen, psoriasis, granuloma annulare, sclerogenous folliculitis, discoid lupus, and cutaneous sarcoidosis; discoid lupus erythematosus, Urbach-Oppeheim disease, localized alopecia.

Contraindications.
Hypersensitivity to the active ingredient or to the any other drug ingredient.
Acute viral, bacterial or systemic fungal infections (if appropriate treatment is not administered).
Cushing syndrome.
Vaccination with live vaccine.
Breast-feeding (excluding emergency cases).
Intramuscular administration is contraindicated in patients with severe disorders of the blood coagulation.
Local administration is contraindicated in case of the bacteraemia, systemic fungal infections, in patients with unstable joints, infections in the administration site, including septic arthritis as a result of gonorrhoea or tuberculosis.

Interaction with other medicinal products and other forms of interactions.
Concomitant administration of dexamethasone and non-steroidal anti-inflammatory drugs increases the risk of the gastrointestinal bleeding and ulceration.
Dexamethasone effect is reduced following co-administration with the drugs activating CYP 3A4 enzyme (phenytoin, phenobarbital, carbamazepine, primidone, rifabutin, rifampicin) or increasing metabolic clearance of the glucocorticoids (ephedrine and aminogluthetimide). In these cases, dexamethasone dose should be increased. Interaction between dexamethasone and all mentioned above medicinal products can falsify findings of the dexamethasone suppression test. This should be considered upon evaluation of the results.
Co-administration of dexamethasone and drugs inhibiting activity of CYP 3A4 (ketoconazole, macrolides) can lead to increased serum dexamethasone concentration. Dexamethasone is moderate

CYP 3A4 inductor. Co-administration with the drugs that are metabolized by CYP 3A4 (indinavir, erythromycin) can increase their clearance leading to the reduced serum concentration.
By inhibition of CYP 3A4 enzymatic action, ketoconazole can increase serum concentration of dexamethasone. On the other hand, ketoconazole can inhibit adrenal synthesis of glucocorticoids, therefore, due to the reduction of dexamethasone concentration, insufficiency of the adrenal glands can develop.
Dexamethasone reduces therapeutic effect of the antidiabetic drugs, antihypertensive drugs, praziquantel, and natriuretics (therefore, the dose of these drugs should be increased), however, it increases activity of heparin, albendazole, and kaliuretic diuretics (the dose of these drugs should be reduced, if required).
Dexamethasone can change the effect of coumarine anticoagulants, therefore, prothrombin time should be controlled more frequently in case of such drug combination.
Co-administration of high doses of glucocorticoids and β_2-adrenoreceptor agonists increases the risk of hypopotassemia development. In patients with hypopotassemia, cardiac glycosides promote arrhythmias to a greater extent and have higher toxicity.
Dexamethasone reduces therapeutic effect of anticholinesterase agents administered in case of myasthenia.
Antacids reduce dexamethasone absorption in the stomach. Effect of dexamethasone following co-administration with meals and alcohol was not studied, however, co-administration of the drugs and food with high sodium content is not recommended. Smoking does not affect dexamethasone pharmacokinetics.
Glucocorticoids increase renal clearance of salicylates, therefore, sometimes it is difficultly to obtain their therapeutic concentrations in the serum. Caution should be taken in patients who gradually reduce the dose of corticosteroids as increased concentration of salicylates in serum and intoxication can be observed.
In case of oral contraceptives co-administration, elimination half-life of glucocorticoids may elongate enhancing their biological effect and increasing the risk of adverse effects.
Co-administration of ritordin and dexamethasone is contraindicated during delivery as this can lead to fatal outcome for parturient woman associated with the pulmonary oedema. Fatal outcome in the parturient woman due to the development of such condition was reported.
Co-administration of dexamethasone and thalidomide can cause toxic epidermal necrolysis.
Types of interaction that have therapeutic benefits: concomitant prescription of dexamethasone and metoclopramide, dyphenhydramide, prochlorperazine, or 5-HT_3 receptor antagonists (receptors of serotonin or 5-hydroxytryptamine, type 3 such as ondasetron or granisetron) is efficient for prevention of nausea and vomiting caused by chemotherapy with cisplatin, cyclophosphamide, methotrexate, fluorouracil.

Special warnings and precautions for use.
During parenteral treatment with corticoids, occasional hypersensitivity reactions can be observed, therefore, appropriate measures should be taken before initiation of treatment with dexamethasone, considering possibility of allergic reactions (especially, in patients with the history of allergic reactions to the any drug products).
Severe psychic reactions may accompany systemic administration of the corticosteroids. Generally, symptoms occur several days or week following treatment initiation. The risk of development of such symptoms is increased following administration of the high doses. Most of the reactions disappear following dose reduction or drug discontinuation. Changes in the psychic condition, especially, depressed mood, suicidal thoughts and intents should be monitored and timely identified. Corticosteroids should be used with special care in patients with the history of affective disorders, especially, in patients with the history of allergic reactions to any other drugs, including family history. Development of the adverse effects can be avoided by administering minimal effective doses during short period of time or by administering required drug dose once daily in the morning.
In patients who received treatment with dexamethasone for a long time, withdrawal syndrome (without visible signs of insufficiency of the adrenal glands) with the following symptoms can be observed: increased temperature, rhinorrhoea, redness of conjunctiva, headache, dizziness,

somnolence or irritability, muscular and articular pain, vomiting, body weight loss, general weakness, and commonly seizures. Therefore, dexamethasone dose should be reduced gradually. Sudden drug discontinuation can be fatal. If the patients is in severe stress condition (due to the injury, operation, or severe disease) dexamethasone dose should be increased during therapy, if however such condition develops during treatment discontinuation, hydrocortisone or cortisone should be administered.
In patients who received dexamethasone continuously and who suffered from severe stress following treatment discontinuation, treatment with dexamethasone should be repeated as insufficiency of the adrenal glands caused by its administration can last during several months following treatment discontinuation.
Treatment with dexamethasone or natural glucocorticoids may mask symptoms of the existing or new infection as well as symptoms of the intestinal perforation.
Dexamethasone can exacerbate systemic fungal infection, latent amebiasis, and pulmonary tuberculosis.
Patients with active pulmonary tuberculosis should receive dexamethasone (along with the antituberculous drugs) only in case of transitory or very disseminated pulmonary tuberculosis.
Patients with inactive pulmonary tuberculosis who are treated with dexamethasone or patients who respond to tuberculin should receive chemical preventive agents.
Caution and medical follow-up is recommended in patients with osteoporosis, arterial hypertension, heart failure, tuberculosis, glaucoma, hepatic or renal failure, diabetes, active peptic ulcer, with recent intestinal anastomosis, ulcerative colitis, and epilepsy. Special care is required in patients during the first weeks following myocardial infarction, in patients with thromboembolism, myasthenia gravis, glaucoma, hypothyroidism, psychosis or psychoneurosis as well as in elderly patients.
Exacerbation of diabetes or transition from latent to clinical manifestation of the diabetes can be observed during treatment.
Serum potassium level should be controlled in case of continuous treatment.
Vaccination with live vaccine is contraindicated during treatment with dexamethasone. Vaccination with non-live viral or bacterial vaccine does not lead to the expected antibody synthesis and has no expected protective effect. Dexamethasone is not usually prescribed 8 week before vaccination and treatment is not initiated earlier than 2 weeks following vaccination.
Patients who received continuous treatment with high dexamethasone doses and who have never suffered from measles should avoid contact with infected persons, and in case of accidental contact preventive treatment with immunoglobulin is recommended.
Caution is recommended in patients who are recovering following surgery or bone fracture as dexamethasone can delay wound healing and formation of the bone tissue.
Effect of glucocorticoids is increased in patients with hepatic cirrhosis or hypothyroidism.
Intra-articular administration of corticosteroids can lead to the local and systemic effects. Frequent administration can lead to the cartilage damage or bone necrosis.
Synovial fluid should be removed from the joints and examined (tests for infections) before intra-articular administration. Administration of corticoids into the infected joints should be avoided. If joint infection is developed following injection, appropriate treatment with antibiotics should be initiated.
Patients should be informed that they must avoid physical loading on the affected joints until inflammation is cured.
Administration of the drugs into the unstable joints should be avoided.
Corticoids can confound findings of the skin allergic tests.
Special warnings regarding excipients.
The drug contains 1 mmol (23 mg) of sodium per dose that is very low amount.

Pregnancy and Lactation.
Pregnancy. Harmful effect on the foetus and new-born child cannon be excluded. Medicinal product inhibits prenatal development of the child. Dexamethasone can be prescribed in pregnant women only in the isolated emergency cases when expected benefit for the mother outweighs potential risk for the foetus. Special caution is recommended in case of preeclampsia. According to

the general recommendations, minimal effective dose for control of the main disease should be administered in case of treatment with glucocorticoids during pregnancy. Those children who were born from mothers receiving glucocorticoids during pregnancy should be examined for adrenal insufficiency.
Glucocorticoids penetrate placenta and achieve high concentrations in foetus. Dexamethasone is less active metabolized in placenta compared, for example, with prednisone. On this basis, high concentrations of dexamethasone may be observed in the blood serum of the foetus. According to some reports, even pharmacological doses of glucocorticoids can increase the risk of placental insufficiency, oligohydramniosis, delayed fetal development or its intrauterine death, increased number of white blood cells (neutrophils) in foetus and adrenal insufficiency. There is no evidence supporting teratogenic effect of the glucocorticosteroids.
Additional doses of glucocorticosteroids are recommended during delivery in those women who received glucocorticosteroids during pregnancy. In case of the prolonged delivery or if Caesarian operation is planned, intravenous administration of 100 mg of hydrocortisone every 8 hours is recommended.
Lactation. Administration during the period of breast-feeding is contraindicated (excluding emergency cases).
Slight amount of glucocorticoids enter into the breast milk, therefore, breast-feeding is not recommended during treatment with dexamethasone, especially, if higher than physiological norms are used (about 1 mg). This can lead to delayed growth of the child and reduced secretion of the endogenous corticosteroids.

Effects on ability to drive and use machines.
Dexamethasone has no effects on ability to drive and use machines.

Posology and method of administration.
Lekthasone®, solution for injections, can be prescribed to adults and children since birth.
Solution for injections can be administered intravenously (via injection or infusion with glucose solution or sodium chloride solution) intramuscularly or locally (via injection in to the joint or injection into the site of lesion on the skin or into the infiltrate in the soft tissues). 0.9% sodium chloride or 5% glucose solution is used as the solvent for intravenous infusion.
Solutions designed for intravenous administration or subsequent drug dissolution should not contain preservatives in case of administration in babies, especially, premature.
The drug should be mixed with solvent for infusion under the sterile conditions. Mixture should be used during 24 hours as solutions for infusions generally contain no preservatives. Drugs for parenteral administration should be visually inspected for presence of the extraneous impurities and discoloration before each administration.
Dose should be determined individually in accordance with the disease of the certain patient, required treatment period, tolerability of corticosteroids and body response.
Parenteral administration.
Dexamethasone should be administered parenterally in emergency cases, if oral therapy is impossible, and in cases specified in section Indications.
Solution for injections is designed for intravenous and intramuscular administration or via infusion (with glucose solution or sodium chloride solution).
Recommended mean initial daily dose for intravenous and intramuscular administration is 0.5 to 9 mg daily, and dose can be increased, if required. Initial drug doses should be administered before development of the clinical reaction then the dose should be gradually decreased to the lowest clinically effective dose.
If high doses are prescribed during several days, the dose is gradually reduced during subsequent several days or longer period.
Local administration.
Doses from 0.4 mg to 4 mg are recommended for intra-articular administration. Dose depends on the size of the affected joint. Generally, 2 to 4 mg should be administered into the large joints and 0.8 to 1 mg into the small joints. Repeated administration into the joint is possible following 3-4 months. Administration can be done three or four times into one joint throughout life and not

more than into 2 joints concomitantly. More frequent intra-articular administration can damage articular cartilage and lead to bone necrosis.
Dexamethasone dose that is administered into the synovial bursa is 2 to 3 mg, into the tendon sheath − 0.4 to 1 mg, into the ganglion − from 1 to 2 mg in general.
Dexamethasone dose that is administered into the site of lesion is equal to the intra-articular dose.
Dexamethasone can be concomitantly administered into not more than two sites of lesion.
Doses for administration into the soft tissues (around the joint) are 2 to 6 mg.
Paediatric doses.
In case of intramuscular administration, recommended dose upon replacement therapy is 0.02 mg/kg body weight or 0.67 mg/m^2 body surface area, divided into 3 doses that is administered on the every third day, or 0.008 to 0.01 mg/kg body weight or 0.2 to 0.3 mg/m^2 body surface area daily.
For all other indications recommended dose is 0.02 to 0.1 mg/kg body weight or 0.8 to 5 mg/m^2 body surface area every 12-24 hours.
Equivalent doses of corticosteroids:

Dexamethasone 0.75 mg	Prednisone 5 mg
Cortisone 25 mg	Methylprednisolone 4 mg
Hydrocortisone 20 mg	Triamcinolone 4 mg
Prednisolone 5 mg	Betamethasone 0.75 mg

Paediatric population.
It is administered in children since neonatal period, but only in emergency cases. Careful monitoring of growth and development of the children and adolescents is required during treatment with dexamethasone.
Overdose.
There are isolated reports about acute overdose or fatal outcome due to the acute overdose. Generally, overdose occurs several weeks following administration. Overdose can cause most adverse effects, specified in section Adverse Reactions, first of all, Cushing syndrome. There is no specific antidote. Treatment of the overdose should be supportive and symptomatic. Haemodialysis is not the efficient method of rapid elimination of dexamethasone from the body.
Adverse reactions.
Adverse events during short-term treatment with dexamethasone:
Immune system disorders: hypersensitivity reactions.
Endocrine disorders: transient inhibition of the adrenal glands function.
Metabolism and nutrition disorders: reduced tolerance to carbohydrates, increased appetite and body weight gain, hypertriglyceridaemia.
Psychiatric disorders: psychiatric disorders.
Gastrointestinal disorders: peptic ulcer and acute pancreatitis.
Adverse events during continuous treatment with dexamethasone:
Immune system disorders: reduced immune response and increased susceptibility to infections.
Endocrine disorders: permanent inhibition of the adrenal glands function, growth retardation in children and adolescents, early closing of the epiphyseal growth zones.
Metabolism and nutrition disorders: obesity.
Eye disorders: cataract, glaucoma.
Vascular disorders: hypertension, telangiectasia.
Skin and subcutaneous tissue disorders: skin thinning.
Musculoskeletal and connective tissue disorders: muscular atrophy, osteoporosis, aseptic bone necrosis, fractures of the tubular bones.
Adverse events that also occur in the separate organs and systems during treatment with dexamethasone:
Blood and lymphatic system disorders: thromboembolic complications; reduced number of monocytes and/or lymphocytes; leukocytosis; eosinophilia (as well as with other glucocorticosteroids); thrombocytopenia and non-thrombocytopenic purpura.

Immune system disorders: rash, bronchospasm, anaphylactic reactions, development of the opportunistic infections, hypersensitivity reactions.
Cardiac disorders: multifocal ventricular extrasystole, temporal bradycardia, heart failure, cardiac arrest, myocardial perforation due to the earlier myocardial infarction.
Vascular disorders: hypertensive encephalopathy.
Respiratory thoracic and mediastinal disorders: relapse of the inactive tuberculosis.
Nervous system disorders: optic nerve oedema and increased intracranial pressure (benign intracranial hypertension) following treatment discontinuation; dizziness; vertigo, headache, seizures.
Psychiatric disorders: personality and behavioural disorders that are commonly manifest as euphoria, insomnia, irritability, hyperkinesis, depression, nervousness, psychic tension, maniacal-depressive psychosis, delirium, disorientation, hallucinations, paranoia, mood instability, suicidal thoughts, psychosis, sleep disturbances, confused consciousness, amnesia, aggravation of schizophrenia course, deterioration of epilepsy course.
Endocrine disorders: inhibition of the adrenal glands function and atrophy of the adrenal glands (reduced response to stress), Cushing syndrome, menstrual disorders, hirsutism.
Metabolism and nutrition disorders: transition from latent form to clinical manifestation of diabetes; increased demand for insulin and oral antidiabetic drugs in patients with diabetes mellitus; sodium and water retention; increased consumption of potassium; hypokalaemic alkalosis; negative nitrogen balance due to the protein catabolizm; hypopotassemia.
Gastrointestinal disorders: dyspepsia, nausea, vomiting, hiccup, peptic ulcer of the stomach or duodenum, oesophagitis, perforations and bleedings in the gastrointestinal tract (vomiting with admixed blood, melena), pancreatitis, gall bladder perforation and intestinal perforation (especially, in patients with inflammatory bowel diseases).
Musculoskeletal and connective tissue disorders: muscular weakness, steroidal myopathy (muscular weakness due to the muscular catabolizm), spinal fractures upon compression, tendon ruptures (especially, in case of co-administration with some quinolones), articular cartilage damage and bone necrosis (in case of frequent administrations into the joint).
Skin and subcutaneous tissue disorders: delayed wound healing, striae, petechiae and bruises, increased sweating, acne, suppressed reaction to skin tests, oedema, Quincke oedema, allergic dermatitis, urticaria, skin itching.
Eye disorders: increased intraocular pressure, exophthalm, exacerbation of bacterial, fungal and viral infections of the eyes, corneal thinning.
Disorders of the reproductive system and mammary glands: erectile dysfunction, amenorrhea.
General disorders and disorders in administration site: transient burning and tingling sensation in the perineum following intravenous administration or following administration of the high doses; oedema, hyper- or hypopigmentation of the skin, atrophy of the skin and subcutaneous tissue, sterile abscess and skin redness.
Signs of glucocorticoids withdrawal syndrome.
In patients who received dexamethasone for a long time, withdrawal syndrome can be observed during very quick dose reduction, resulted in possible cases of the insufficiency of the adrenal glands, arterial hypotension or fatal outcome. In some cases, signs of the withdrawal syndrome can be similar with the signs of deterioration or relapse of the disease against which the patients is treated. In case of severe adverse reactions treatment should be discontinued.

Shelf life. 2 years.

Storage. Store away from children in the original package at temperature not exceeding 25 °C.

Incompatibilities.
The drug should not be mixed with the other drugs except following: 0.9% sodium chloride solution or 5% glucose solution.
If dexamethasone is mixed with chlorpromazine, diphenhydramine, doxapram, doxorubicin, daunorubicin, idarubicin, hydromorphone, ondasetron, prochlorperazine, potassium nitrate, and vancomycin sediment is formed.

About 16% of dexamethasone is degraded in 2.5% glucose solution and 0.9% sodium chloride solution with amikacin.
Some medicinal products such as lorazepam should be mixed with dexamethasone in glass vials and not in the plastic bags (lorazepam concentration is reduced to the values lower than 90% within 3 to 4 hours of storage in the polyvinyl chloride bags under room temperature).
So called incompatibility is developed with some drugs such as metharaminol, and it is developed slowly following 24 hours upon mixing with dexamethasone.
Dexamethasone and glycopyrrolate: pH of the final solution is 6.4 that is beyond the stability range.

Package. 1 ml per ampoule, 5 or 100 ampoules in the pack or 5 ampoules in blister, 1 blister in the pack.

Prescription status. By prescription.

Manufacturer. Joint Stock Company «Lekhim-Kharkiv».

Location of the manufacturer and address of carrying out its activities.
Ukraine, 61115, Kharkiv region, Kharkiv, Severyna Pototskoho street, building 36.

Date of the last revision.