SLIDERON

1. Product Name
Generic name: Methylprednisolone
Brand name: Slideron
2. Name and Strenght of Active Ingredient(s|
Methylprednisolone 4 mg
3. Product Description
Slideron (Methylprednisolone 4 mg) tablets:
Round, flat tablets, bevelled and scored on one side, with diameter of 8 mm.
4. Pharmacodynamics/Pharmacokinetics
Pharmacodynamic properties
Pharmacotherapeutic group: Corticosteroids for systemic use, Glucocorticosteroids; ATC code: H02AB04
Mechanism of action
Methylprednisolone is a synthetic glucocorticoid with a pronounced action. Corticosteroids pass through cell membranes via diffusion to form complexes with specific cytoplasmic receptors which penetrate into the cell nucleus, bind the DNA and stimulate the transcription of the tRNA and subsequent protein synthesis of various enzymes with different functions in the body.
Pharmacological effects
Maximum pharmacological effects are observed for some time after reaching the maximum plasma concentration, which is an indication that the effect is mainly due to a change in the enzymatic activity and to a lesser extent, a direct effect of the active substance.
Effects on inflammation and immune processes – methylprednisolone has anti-inflammatory, immunosuppressive and anti-allergic action with a minimal mineralocorticoid effect. It leads to reduction in the number of the immunoactive cells in the region of inflammation, reduction in the vasodilation, stabilisation of lysosomal membranes, inhibition of the process of phagocytosis, reduced formation of prostaglandins and related substances.
Effects on carbohydrate and protein metabolism – methylprednisolone has a catabolic effect on the proteins, as in the liver, the released amino acids are converted to glucose and glycogen as a result of gluconeogenesis. The absorption of glucose in the periphery decreases, which may lead to hyperglycaemia and glycosuria, particularly in patients with predisposition or latent diabetes.
Effects on fat metabolism – methylprednisolone has a lipolytic action affecting mainly the limbs and a lipogenic effect on the chest, neck and head, causing the effect of redistribution of fat depots.
Pharmacokinetic properties
Absorption and distribution: Corticosteroids are absorbed mainly in the proximal portion of the small intestine, and about 50% of the amount of the active substance, absorbed in the proximal segments, is absorbed in the distal segments.
Between 40 and 90% of methylprednisolone binds the plasma albumin and transcortin via a weak, dissociable bond.
Metabolism and excretion: The metabolism takes place mainly in the liver. The main metabolites are 20 -hydroxy-methyl-prednisolone and 20 -hydroxy-6-α-methylprednisolone. The metabolites are excreted mainly in the urine as glucuronides, sulphates and unconjugated compounds. These processes take place mainly in the liver and to a lesser extent in the kidneys.
5. Indication
The product is used as a substitution therapy in endocrine disorders, such as primary and secondary adrenal insufficiency, and congenital adrenal hyperplasia.
It is used as a symptomatic agent in the following groups of diseases:
- In adjunction to the maintenance treatment and for short-term use for the management of an acute episode or exacerbation in rheumatic diseases: psoriatic arthritis, rheumatoid arthritis, including juvenile rheumatoid arthritis, ankylosing spondylitis, acute and subacute bursitis and tenosynovitis, acute podagrous arthritis, post-traumatic osteoarthritis, synovitis in osteoarthritis, epicondylitis;
- During an exacerbation or for the maintenance treatment of systemic lupus erythematosus, systemic dermatomyositis, acute rheumatic carditis and giant cell arteritis;
- Skin diseases – pemphigus, bullous herpetiform dermatitis, Steven-Johnson's syndrome, exfoliative dermatitis, fungoid mycosis, severe psoriasis, severe seborrheic dermatitis;
- Management of severe allergic conditions, refractory to conventional treatment – seasonal or non-seasonal allergic rhinitis, serum disease, bronchial asthma, drug hypersensitivity reactions, contact and atopic dermatitis;
- Acute and chronic allergic and inflammatory processes with severe course, involving the eye and ocular appendages – allergic ulcers of the corneal margin, ophthalmic herpes zoster, inflammation of the anterior eye segment, diffuse posterior uveitis and choroiditis, sympathetic ophthalmia, allergic conjunctivitis, keratitis, chorioretinitis, iridocyclitis, optic neuritis;
- In pulmology and phtysiatrics, in sarcoidosis with pulmonary localisation, refractory Loeffler's syndrome, berylliosis, fulminant or disseminated pulmonary tuberculosis, in the complex therapy with anti-tuberculous agents, aspiration pneumonitis;
- Haematological diseases, such as idiopathic thrombocytopenic purpura in adults, secondary thrombocytopenia in adults, acquired (autoimmune) haemolytic anaemia, erythrocytic anaemia, congenital hypoplastic anaemia;
- For palliative management in oncology – leukosis and lymphomas in adults and acute blastic leukosis in children;
- Severe exacerbation in ulcerative colitis and Crohn's disease;
- Acute exacerbation of multiple sclerosis and brain tumour-associated oedema;
- Tuberculous meningitis with subarachnoid block or impending block, in the complex therapy with anti-tuberculous agents;
- Trichinellosis affecting the brain or myocardium;
- Organ transplantation;
- Nephrotic syndrome (without uremia, idiopathic or associated with lupus erythematosus) - for inducing diuresis or remission of proteinuria.

6. Recommended Dose
Adults: The amount of the initial dose may vary, depending on the type and severity of disease/condition and the response to the treatment performed. The treatment should continue at this dosage regimen to achieving the desired clinical response. Very high doses are required in multiple sclerosis (200 mg daily), brain oedema (200 – 1000 mg daily) and organ transplantation (up to 7 mg/kg daily). If no adequate clinical response has been achieved after a sufficient period of administration, re-evaluation is needed with regard to verifying the initial diagnosis or switching to another clinically adequate therapy.
Once the desired therapeutic response has been achieved, the daily dose should be gradually reduced, as soon as possible, to complete cessation of the treatment in acute conditions (seasonal asthma, exfoliative dermatitis, acute eye inflammation) or to achieving the minimal effective maintenance dose in chronic diseases/conditions (rheumatoid arthritis, systemic lupus erythematosus, bronchial asthma, atopic dermatitis).
In chronic diseases/conditions, it is important to take into consideration that the dose reduction (from the initial to the maintenance dose) should be done in a suitable way, depending on the clinical status, and to levels, where the risk of an eventual relapse of the disease is not high.
Children: The dosage in children is determined by the physician's evaluation and is based on the clinical response. The treatment should be performed by administering the minimal effective dose for the shortest period of time. If possible, the daily dose should be administered as a single dose, every other day.
Elderly: The treatment in the elderly, especially the continuous one, should be carefully performed with regard to more serious complications resultant from the undesirable effects in this age group, particularly, osteoporosis, diabetes, hypertension, higher susceptibility to infections and skin atrophy, etc.
Alternative dose regimen: In the alternative dose regimen, the daily dose is doubled and administered as a single daily dose, received at 08:00 in the morning, every other day.
With this type of therapy is meant, on one side, to ensure the positive therapeutic effects in patients with chronic diseases, and on the other, to diminish some of the severe undesirable effects, such as pituitary-adrenal suppression, Cushing's syndrome, withdrawal symptoms and growth retardation in children.
7. Route Of Administration: Orally
8. Contraindication
- Hypersensitivity to the active substance and/or to any of the excipients in the composition of the product and Systemic fungal infections.

9. Warnings and Precautions
Adrenal suppression and secondary adrenal insufficiency
Adrenocortical suppression and secondary adrenal insufficiency may develop during a long-term treatment and may persist for months following treatment discontinuation. The severity and duration of adrenocortical insufficiency are determined, to a significant degree, by the amount of the dose received, the frequency and time of administration and the duration of treatment.
The amount of dose reduction depends also on whether a relapse of the disease can be avoided on the background of the physiological glucocorticosteroid levels. During the period of treatment discontinuation, periodic control on disease activity is required with regard to avoiding an eventual relapse.
It should be also taken into consideration, that abrupt cessation of glucocorticoids may lead to acute adrenal insufficiency, which may result in a fatal outcome.
Adrenal insufficiency can be avoided or the risk can be minimised by using an alternative therapy and by gradually reducing the received daily dose.
Adrenal insufficiency may persist for varying periods, for which, in any intercurrent disease, surgical intervention or stress situation, the need of resuming corticosteroid therapy should be considered.
Due to the possibility of disturbances in mineral-corticoid secretion, sufficient simultaneous intake of mineral-corticoid preparations and/or salt should be ensured.
Patients receiving systemic corticosteroids should be informed in details, prior to treatment, as well as during its course, about the method of administration of the product, instructions on recommended treatment duration and, particularly, instructions on treatment cessation.
Immunosuppressive effects and increased susceptibility to infections
Corticosteroids may mask some of the symptoms of infection; in the course of corticosteroid treatment, a new infection may develop or susceptibility to infections may increase. Suppression of the inflammatory response and immune function increases the likelihood of developing fungal, viral and bacterial infections. In many cases, clinical manifestations can be atypical and may progress to advanced forms prior to their verification.
Varicella may have a fatal course in immunocompromised patients, for which, patients with uncertain anamnestic data for varicella, should avoid close contacts with varicella- or herpes zoster-infected or contact individuals.
In a case of verified varicella, close, regular monitoring by a specialist and adequate treatment are required. Corticosteroid therapy should not be discontinued and even a dose increase may be required.
Exposure to and contacts with morbilli-diseased individuals should be avoided. Prophylaxis with a common intramuscular immunoglobulin, as well as regular medical supervision by a specialist may be required.
In immunocompromised patients, the administration of live or live-attenuated vaccines should be avoided. The antibody-response to other vaccines (e.g. killed or inactivated vaccines) may be diminished.
The product administration should be limited in patients with active tuberculosis, except for the cases of fulminant or disseminated tuberculosis; in such cases, corticosteroids are used for the treatment of the main disease in combination with an appropriate anti-tuberculous therapy.
If corticosteroid therapy is indicated in patients with latent tuberculosis or positive tuberculin test results, strict control is required to prevent re-activation of the disease. During a long-term treatment with corticosteroids, these patients should receive adequate chemoprophylaxis.
There are reports of Kaposi's syndrome in patients receiving corticosteroids. Clinical remission may occur upon discontinuation of the treatment.
In patients with septic shock presented with symptoms of adrenal failure, the possibility of corticosteroid administering as a substitution therapy should be considered.
Corticosteroids should be administered with caution to patients with overt or suspected parasitic infections (e.g., enterobiosis), since in these cases, hyperinfection and disease dissemination with related complications may be provoked.
Psychiatric disorders: Patients and caregivers should be informed that during the treatment with systemic corticosteroids, there is a potential risk of psychiatric disorders, as a manifestation of undesirable effect.
Symptoms typically emerge within a few days or weeks after treatment initiation. The risk is higher after a high-dose treatment or a long-term systemic exposure, although there is no definite correlation between the amount of the administered dose and the rate, type, severity or duration of these reactions. Most of them resolve completely after dose reduction or treatment discontinuation, but this does not cancel the necessity of specific treatment administering.
Patients and caregivers should be informed that they should consult a medical specialist if depressive feeling or suicidal thoughts appear. They should also be alert to possible psychiatric disturbances that may occur either during or immediately after treatment cessation, although such reactions and manifestations have been reported infrequently.
This particularly applies to patients with existing or previous history of severe affective disorders, as well as familial history for such diseases (especially depressive or maniac-depressive disorders or preceding steroid psychosis).
Hepatobiliary effects: Rarely hepatobiliary disorders were reported, in the majority of cases reversible after withdrawal of therapy. Therefore appropriate monitoring is required.
Other precautions: Caution with corticosteroid treatment is required in patients with:
- *Cardiovascular diseases*: arterial hypertension or congestive heart failure, recent myocardial infarction (there are reports of myocardial rupture), predisposition to thrombophlebitis;
- *Musculoskeletal diseases*: osteoporosis (there is an increased risk in postmenopausal women), preceding corticosteroid-induced myopathy;
- *Endocrine diseases*: diabetes mellitus (including familial aggravation), hypothyroidism;
- *Eye diseases*: herpes simplex ophthalmicus (there is a risk of corneal perforation), glaucoma (including familial history), subcapsular cataract and nuclear cataract;
- *Gastrointestinal diseases*: peptic ulcer, recent intestinal anastomose, ulcerative colitis, diverticulitis;
- *Infections*: anamnestic data of tuberculosis, abscess or other suppurative infections;
- *Neurological diseases*: epilepsy, myasthenia gravis;
- *Other*: hepatic insufficiency or cirrhosis, renal failure.

Thrombosis including venous thromboembolism has been reported to occur with corticosteroids. As a result corticosteroids should be used with caution in patients who have or may be predisposed to thromboembolic disorders.
Undesirable effects can be limited by using the lowest effective dose for the shortest period possible and by administering the required daily dose as a single daily dose in the mornings or a single daily dose received every other morning.
Periodic control on the patient's status is required with regard to determination of the minimal effective dose, leading to adequate suppression of the disease activity.
Control and periodic following-up are required in patients receiving digoxin, since corticosteroids may induce electrolytic disturbances and loss of potassium.
Acetylsalicylic acid-containing products and non-steroidal anti-inflammatory drugs should be administered with caution in patients with hypoprothrombinaemia, receiving corticosteroid preparations.
Lactose is included as an excipient in the composition of this medicinal product. Therefore, it is not suitable for patients with lactase insufficiency, Lapp lactase deficiency, galactosaemia or glucose-galactose malabsorption syndrome.
Use in children: Corticosteroids may induce growth retardation in children and adolescents. The treatment should be limited to the lowest effective dose for the shortest administration period possible. To minimise the suppression of the hypothalamic-pituitary-adrenal system and growth, the treatment should be performed (where possible), as an alternative dose regimen.
Use in the elderly: The common undesirable effects of systemic corticosteroids may manifest more seriously in the elderly. This particularly applies to osteoporosis, hypertension, hypokalaemia, diabetes mellitus, predisposition to infections and skin atrophy.
In patients of this age group, intensified clinical control is recommended in order to avoid life-threatening undesirable effects.
Effects on ability to drive and use machines: No unfavourable effects have been established.
10. Interaction With Other Medicaments
Cyclosporine: Seizures have been reported during co-administration of methylprednisolone and cyclosporine. Since co-administration of the two products results in reciprocal inhibition of their metabolisms, it is possible to avoid the occurrence of seizures and other undesirable effects by administering separately both products.
Liver enzyme inducers: Rifampicin, rifabutin, carbamazepine, phenobarbitone, phenytoin, etc. intensify the metabolism of methylprednisolone and may lower its therapeutic effect.
Grapefruit and other citrus fruits may lead to induction of liver metabolism, thus lowering the effects of corticosteroids, including methylprednisolone.
CYP3A4 inhibitors: Cimetidine, erythromycin, ketoconazole, itraconazole, etc. may lower the rate of liver metabolism of methylprednisolone and thus, increase its serum concentrations.
Other: Corticosteroids may reduce the effects of anticholinesterases in myasthenia gravis.
The desired effects of hypoglycaemic agents (including insulin), antihypertensives and diuretics are antagonised by corticosteroids, and the hypokalaemic effects of acetazolamide, loop and thiazide diuretics and carbenoxolone are increased.
The efficacy of coumarin anticoagulants may increase, when concomitantly administered with corticosteroids, which requires intensified monitoring of the INR and prothrombin time, in order to avoid spontaneous bleeding.
The renal clearance of salicylates increases with corticosteroid and steroid discontinuation, which may lead to salicylic intoxication.
Salicylates and NSAIDs should be administered with caution to patients with hypoprothrombinaemia.
There are reports of steroid interactions with neuromuscular blockers, such as pancuronium, due to partial reversal of the neuromuscular blockade.
11. Pregnancy and Lactation
Pregnancy: The ability to pass through the placenta varies among the different representatives of the group. It is known that methylprednisolone crosses the placental barrier.
Administration of corticosteroids to pregnant animals may cause abnormalities in the foetal development, including hard palate clefts, delayed intrauterine development, unfavourable effects on cerebral growth and development.
There is no evidence that corticosteroids may lead to increased incidences of congenital abnormalities in humans, but their long-term or repeated administration during pregnancy may increase the risk of intrauterine retardation of the foetal development.
Theoretically, hypo-adrenalism can be observed in newborns with prenatal exposure to corticosteroids, but usually, this condition restores spontaneously after birth; this, however, does not exclude the need of careful monitoring and evaluation of the status.
Like other medicines, corticosteroids should be administered during pregnancy only when the benefits for the mother overweigh the risk for the foetus.
Breast-feeding: Corticosteroids are excreted in human breast milk.
Like other medicines, methylprednisolone should be administered during the period of breast-feeding only when the benefits for the mother overweigh the risk for the breast-fed child. If treatment is required by the mother, the possibility of breast-feeding discontinuation for the period of treatment with the product should be discussed.
12. Undesirable Effects
The frequency of anticipated undesirable effects related with the use of corticosteroids, including hypothalamic-pituitary-adrenal suppression, correlates with the relative potency of the medicine, the dosage, the method of administration and duration of treatment.
Infections and infestations: Increased susceptibility and severity of the course of infections, masking of clinical signs and symptoms, secondary infections, suppression of reactions to skin tests, activation of latent tuberculosis.
Immune system disorders: Hypersensitivity reactions, including anaphylactic and anaphylactoid reactions, suppression of reactions to skin tests.
Endocrine disorders: Suppression of the hypothalamic-pituitary-adrenal system, growth retardation in newborns, children and adolescents, Cushingoid face, hirsutism , weight gain.
Metabolism and nutrition disorders: Sodium and water retention, hypokalaemic alkalosis, potassium loss, impaired glucose tolerance with increased demand for anti-diabetic therapy, negative nitrogen and calcium balance, epidural lipomatosis.
Psychiatric disorders: Affective disorders (irritability, euphoria, depression and mood lability, suicidal thoughts), psychotic reactions (including mania, delusion, hallucinations and aggravation of schizophrenia), behavioural disorders, agitation, anxiety.
Nervous system disorders: Cognitive dysfunction, including confusion and amnesia, sleep disorders, seizures, dizziness, headache, vertigo, increased intracranial pressure with papilloedema (pseudotumour cerebri).
Eye disorders: Increased intraocular pressure, glaucoma, papilloedema with possible damage of the optic nerve, cataract, thinning and rupture of the cornea and sclera, exacerbation of ophthalmic viral or fungal infections, exophthalmos, chorioretinopathy.
Cardiovascular disorders: Congestive heart failure, arterial hypertension, hypotension, thrombotic events.**Gastrointestinal disorders:** Dyspepsia, nausea, flatulence, peptic ulcer with perforation and haemorrhage, oesophageal ulceration, oesophageal candidiasis, acute pancreatitis, intestinal perforation, gastric haemorrhage.
Hepatobiliary disorders: Increase of liver enzymes
Skin and subcutaneous tissue disorders: Impaired, delayed wound healing, skin atrophy, predisposition to injury, formation of striae, telangiectasias, acne, petechiae and ecchymoses.
Kaposi's sarcoma has been reported in patients receiving corticosteroids.
Reproductive system and breast disorders: Menstrual irregularities and amenorrhoea.
Musculoskeletal disorders: Osteoporosis, fractures of vertebrae and diaphyses, avascular osteonecrosis, tendon ruptures, muscle weakness, proximal myopathy.
Withdrawal symptoms: Rapid dose tapering in long-term treatment may lead to acute adrenal insufficiency, hypotension and death. In "withdrawal syndrome", fever, myalgia, arthralgia, rhinitis, conjunctivitis, sore, itchy skin nodules and weight loss can also be observed.
General disorders: Rare: malaise, fatigue.
Investigations: Increases in ALT, AST, ALP, hypokalaemia, hypercalcaemia.
13. Overdose and Treatment
Symptoms: No specific syndrome is known in acute overdose with methylprednisolone. Cushingoid symptoms have been observed in chronic overdose.
Treatment: In acute overdose, agents and methods with regard to rapid emptying of the stomach and lowering the rate of absorption of the active substance, as well as appropriate symptomatic agents are applied. Methylprednisolone is dialyzable. No specific antidote is known.
14. Dosage Forms and packaging available
Slideron Methylprednisolone 4 mg, tablets: 10 (ten) tablets in PVC/PVdC foil/Aluminium foil blister pack; 2 (two) blister packs in a cardboard box.
15. Name and Address of Manufacturer/Marketing Authorisation Holder
Manufacturer
BALKANPHARMA-RAZGRAD AD
68, Aprilsko Vastanie Blvd.
7200 Razgrad, BULGARIA
Marketing Authorisation Holder
SPEY MEDICAL LTD.
Lynton House 7-12, Tavistock Square, London, England, WC1H 9LT, United Kingdom
16. Date of Revision of Package Insert
12/2015

SPEY