**PATIENT INFORMATION LEAFLET**

**STARTUM**

**TRADE NAME**
Startum

**INTERNATIONAL NONPROPRIETARY NAME**
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**PHARMACEUTICAL FORM**
Lyophilized powder for injections. 
*Description:* pink, lyophilized powder. 
*solvent:* clear colourless solution.

**COMPOSITION**
1 vial of the drug product contains
*Active substances:*  
- cocarboxylase chloride 50 mg  
- nicotinamide 20 mg  
- adenosine triphosphate disodium trihydrate 10 mg  
- cyanocobalamin 0.5 mg  
*Excipients:* glycine, methyl parahydroxybenzoate, propyl parahydroxybenzoate.

*Solvent:* 0.5% lidocaine hydrochloride solution, 2 ml.

**ATC CODE OF THE DRUG** A11AB

**PHARMACOTHERAPEUTIC GROUP**
Vitamins. Polyvitamins in combination with other preparations.

**PHARMACOLOGICAL PROPERTIES**

**PHARMACODYNAMICS**
The drug is a balanced complex of metabolic substances and vitamins.  
*Cocarboxylase* is a coenzyme formed in the body from exogenous thiamine (vitamin B<sub>1</sub>). It plays an essential part in carbohydrate metabolism and is part of the enzyme carboxylase which catalyzes carboxylation and decarboxylation of α-ketoacids. It indirectly facilitates synthesis of nucleic acids, proteins and lipids. It reduces the levels of lactic and pyruvic acids in the body, promotes glucose intake and improves trophism of nerve tissue.  
*Nicotinamide* is one of the forms of vitamin PP. It participates in oxidation-reduction processes in the cell and improves carbohydrate and nitrogen metabolism.  
*Adenosine triphosphate disodium trihydrate* is an adenosine derivative. It stimulates metabolic processes, performs hypotensive and antiarrhythmic action and has a vasodilating effect, including on coronary arteries.  
*Cyanocobalamin* (vitamin B<sub>12</sub>) is converted into the active form (adenosylcobalamin or cobamamide) with high biological activity in the body. It increases protein synthesis and promotes its accumulation in the body. It activates carbohydrate and lipid metabolism, reduces blood cholesterol level and prevents adipose infiltration of liver. Cyanocobalamin is essential for normal functioning of hematopoietic organs, it facilitates erythrocyte accumulation of compounds containing sulfhydryl groups, thus increasing their resistance to hemolysis. It increases tissue regeneration property and has a favourable effect on the function of liver and nervous system.

**PHARMACOKINETICS**
*Cocarboxylase*
Cocarboxylase is rapidly absorbed after intramuscular injection. It penetrates into the majority of the body tissues and is metabolically degraded. Metabolic products are excreted mainly via kidneys.

**Nicotinamide**
Absorption from the gastrointestinal tract (mainly in the pyloric part of the stomach and the antral part of the duodenum) is rapid and is significantly reduced and slowed in malabsorption syndrome. It is rapidly distributed in all tissues, penetrates through placenta and into breast milk. It is metabolized in liver with formation of N-methylnicotinamide, methylpyridon carboxamides, ether with glucuronic acid and a complex compound with glycine. Elimination half-life is 45 minutes.
Nicotinamide is excreted via kidneys in the form of metabolites; after administration of high doses – mainly in the unchanged form.

**Adenosine triphosphate disodium trihydrate**
Tracing of the kinetics of parenterally administered ATP preparation is impossible due to a large number of various reactions performed with participation of endogenous ATP. It is known that sodium adenosine triphosphate is rapidly decomposed in the injection site to adenosine and phosphate residuals which are further used for synthesis of new ATP molecules.

**Cyanocobalamin**
Vitamin B_{12} binds in blood with transcobalamins I and II which perform its transport to tissues. It is deposited mainly in liver. Plasma protein binding is 90%. The peak concentration after intramuscular injection is achieved within 1 hour. Cyanocobalamin is eliminated in bile to the intestine and is reabsorbed in blood. Elimination half-life is 500 days. In normal renal function it is excreted by 7-10% via kidneys and by about 50% with faeces; in reduced renal function it is excreted by 0-7% via kidneys and by 70-100% with faeces. The substance penetrates through the placental barrier and into breast milk.

**THERAPEUTIC INDICATIONS**
- neuritis, neuropathy (in diabetes mellitus, pernicious anemia, etc.);
- neuralgias of various origin;
- myalgia, ischialgia;
- lumbago, radiculitis;
- bursitis, tendinitis;
- ischemic heart disease, myocarditis, myocardiopathy.

**DOSAGE AND ADMINISTRATION**
**Startum** is administered intramuscularly, 1-2 vials once daily.
Duration of treatment and the need for repeated courses depend on the character and severity of the disease.
No dose adjustment is required in patients with hepatic and renal failure.
No dose adjustment is required in patients over 65 years old.

**CONTRAINDICATIONS**
- hypersensitivity to any component of the drug;
- acute period of myocardial infarction;
- hypercoagulation (including in acute thrombosis), erythremia, erythrocytosis, severe forms of arterial hypertony, arterial hypotony, inflammatory pulmonary diseases, severe heart failure, psoriasis, severe conductivity disorders, acute heart failure.

**SIDE EFFECTS**
**Immune system disorders:** hypersensitivity reactions (skin reactions, anaphylactic shock, Quincke’s edema). It is recommended to perform an intracutaneous test before administration of **Startum** in patients with suspected hypersensitivity to the components of the drug.
Cardiovascular system disorders: pulmonary edema and congestive heart failure at the beginning of treatment; thrombosis of peripheral vessels.

Hematopoietic organs disorders: polycythemia vera.

Gastrointestinal tract disorders: mild temporary diarrhea.

Skin disorders: itching, transitory exanthema.

General symptoms: sudden sweating, weakness sensation, dizziness.

In case of appearance of these or other side effects consult the doctor.

SPECIAL INDICATIONS
The prepared solution should be reddish-pink coloured.
Do not use the solution if its colour has changed.

Startum should be administered with caution in patients with history of ulcerative disease, gastritis, gout, hemorrhages, damages of liver and bile duct.

Long-term administration of the drug requires control of erythrocyte count in the general blood analysis, coagulation time, prothrombin index in the coagulogram, serum levels of transaminases, alkaline phosphatase, gamma-glutamyl transpeptidase, bilirubin, uric acid, and blood thrombocyte count.
The solution should be used immediately after preparation!

PREGNANCY AND LACTATION
Startum should be used in pregnancy only in case if expected benefit for the mother outweighs potential risk for the fetus.
Breast feeding should be terminated for the period of treatment with the drug.

PEDIATRIC USE
No data on administration of the drug in children are available.

DRUG INTERACTIONS
Cocarboxylase potentiates the cardiotonic effect of cardiac glycosides.
In concomitant administration of nicotinamide with antiepileptic agents, especially such as carbamazepine, diazepam and sodium valproate, the anticonvulsive effect of the latter may be potentiated.

OVERDOSE
Long-term administration of nicotinamide may also result in methyl group deficiency in the setting of participation of methylation reactions in elimination.
Clinical cases of hepatic dysfunction in long-term administration of high doses of nicotinamide (3000-9000 mg = 150-450 vials of Startum) were observed.

Treatment: symptomatic.
Toxicity may develop in accidental ingestion or intravenous administration.

PACKAGING
Lyophilized powder for injections in an amber glass vial with bromobutyl rubber stopper and combined aluminum cap Flip off type.
3 vials with lyophilized powder together with solvent (3 ampoules of 0.5% lidocaine hydrochloride solution, 2 ml) in a contour tray.
Contour tray together with a leaflet in a carton box.

STORAGE CONDITIONS
Store in a protected from light place at temperature not exceeding 25°C.
Keep out of reach of children!
**SHELF LIFE**
3 years from the date of manufacture.
Do not apply after the shelf-life expiration.

**SALES TERMS**
Sold under prescription.

**MANUFACTURER**
The holder of trade mark and Marketing Authorization is
"DR SERTUS İLAÇ SANAYİ VE TİCARET LİMİTED ŞİRKETİ", TURKEY.
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