APPROVED
Order of the Ministry of Health of Ukraine
13.02.10 **No.** ***125***
Marketing Authorisation
No. UA/13453/01/01

INSTRUCTIONS
for medical use of the drug

AQUAVIT-D_3

Composition:
active ingredient: cholecalciferol (vitamin D_3);
1 ml of solution contains cholecalciferol (vitamin D_3) 375 μg (15,000 IU);
Excipients: castor oil, polyethoxylated; white crystalline sugar; sodium hydrophosphate, dodecahydrate; citric acid monohydrate; benzyl alcohol; anise aroma; purified water.

Dosage form. Oral solution.

Pharmacotherapeutic group. Vitamins. Preparations of vitamin D and its analogues. Cholecalciferol.
ATC code: A11CC05.

Clinical particulars.

Indications.
Prophylaxis of rickets in children.
Prophylaxis of vitamin D deficiency in high-risk groups, in malabsorption (chronic diseases of the small intestine, biliary cirrhosis, condition after resection of the stomach and/or small intestine).
Treatment of rickets and osteomalacia.
Maintenance treatment of osteoporosis.

Contraindications.
Hypersensitivity to the components of the drug.
Hypervitaminosis D, elevated levels of calcium in the blood and urine, urolithiasis, sarcoidosis, renal failure, nephrolithiasis.
Do not use to treat children aged below 4 weeks due to the possible occurrence of hypersensitivity to benzyl alcohol.

Posology and method of administration.
The drug is administered orally.
1 ml of the solution contains about 30 drops. 1 drop contains about 500 IU of cholecalciferol (vitamin D_3). To accurately measure the dose of the drug, you should keep the vial at an angle of 45° during dropping.
The usual dose for the prophylaxis of rickets in term new-born infants aged 4 weeks to 1 year with proper care and sufficient exposure to sunlight is 1 drop (about 500 IU of vitamin D_3) per day, in preterm new born infants - 2 drops (about 1,000 IU vitamin $_3$) per day. During a sunny summer, you can limit the dose to 1 drop (about 500 IU of vitamin D_3) per day. During the second and third years of life, there may be a need for further administration of vitamin D_3, especially in winter.
Infants receive drops in a spoonful of milk or cereal. It is not recommended to add drops to the bottle

or into a dish, because it is not possible to guarantee the administration of the whole dose.
Older children and adults take the drug with a spoonful of liquid.
Duration of administration is determined by the doctor.
In the treatment of rickets and osteomalacia the dose is 2-10 drops (about 1,000 - 5,000 IU of vitamin D_3) per day. Duration of treatment - 1 year.
In the maintenance treatment of osteoporosis, the dose is 2-6 drops (about 1,000 - 3,000 IU of vitamin D_3) per day.
Prophylaxis of vitamin D deficiency in high-risk groups – 1-2 drops (about 500 - 1,000 IU of vitamin D_3) per day.
Prophylaxis of malabsorption – 6-10 drops (about 3,000 - 5,000 IU of vitamin D_3) per day.
When using doses over 1,000 IU vitamin D_3 per day, as well as with prolonged administration of the drug, the level of calcium in the blood serum should be monitored.

Adverse effects.
Adverse reactions are generally not observed when the drug is used in recommended doses.
In the case of individual hypersensitivity to vitamin D_3, which is rare, or if too high doses are used for a long period, vitamin D hypervitaminosis may develop.
Gastrointestinal system disorders: loss of appetite, nausea, vomiting, constipation, dry mouth.
Nervous system disorders: headache, mental disorders, depression.
Urinary system disorders: increased levels of calcium in blood and/or urine, urolithiasis and calcification of tissues, polyuria.
Skin disorders: allergic reactions, including hives, rash, itching.
Musculoskeletal disorders: muscular and joint pain.
Other effects: loss of body weight.

Overdose.
Symptoms: toxic symptoms due to acute poisoning are rare, a bowl in new-borns and in children after administration of 100,000 IU or more of vitamin D per day.
Weakness, lack of appetite, nausea, vomiting, constipation, anxiety, thirst, polyuria, gastric hyperacidity, diarrhoea, intestinal colic develop in overdose. Sweating, dizziness, heart arrhythmia may develop.
Common symptoms are: pain in the muscles and joints, headache, depression. mental disorders, ataxia, stupor and loss of body weight. Renal function impairment develops with albuminuria, erythrocyturia and polyuria, increased loss of potassium, hypostenuria, nicturia and moderate increased blood pressure. In severe cases, corneal opacity may occur, less common – papilloedema, inflammation of the iris up to cataract development.
There may be calculi in the kidneys, calcification in the kidneys, soft tissues, such as blood vessels, heart, lungs and skin.
Rarely develops cholestatic jaundice.
Treatment: withdrawal of the drug, bed rest, low calcium diet, consumption of large amounts of fluid, use of laxatives, in significant hypercalcemia - intravenous injection of a large amount of isotonic sodium chloride solution, administration of furosemide or ethacrynic acid derivatives, glucocorticosteroids, calcitonin preparations, haemodialysis. There is no specific antidote.

Administration during pregnancy and breastfeeding.
Chronic overdose (hypercalcemia, transplacental penetration of vitamin D_3 metabolites into the foetus), which occurs with prolonged administration of vitamin D_3 at doses exceeding the recommended levels, may cause defects in the physical development of the foetus, aortic stenosis.
Vitamin D_3 penetrates breast milk, therefore the drug should be used during breastfeeding only on prescription of the doctor.

Children.
The drug is applied to children older than 4 weeks.

Special warnings and precautions for use.
When determining the need for vitamin D_3, you should consider all possible sources of intake of this vitamin.

Too high doses of vitamin D_3, which are used for a long time, or loading doses can be the cause of chronic hypervitaminosis D_3.
The daily requirement of the child in vitamin D_3 and the method of administration should be determined individually, each time revising during periodic studies, especially in the first months of life.
The drug should be carefully applied in the treatment of immobilized patients taking thiazide diuretics, digitalis glycosides, as well as patients with nephrolithiasis, heart diseases.
Do not use large doses of calcium concomitantly.
During treatment with the drug it is recommended to control the level of calcium, phosphate and sugar in blood serum and in urine.

Effects on ability to drive and use other machines.
Currently, there are no reports on the harmful effect of the drug on the ability to drive a car or work with other mechanisms. However, when driving or working with other mechanisms, it is recommended that special care should be taken, considering possible adverse reactions from the nervous system.

Interaction with other drugs and other forms of interaction.
Antiepileptic drugs, especially phenytoin and phenobarbital, as well as rifampicin, neomycin, cholestyramine, liquid paraffin reduce the effect of vitamin D_3.
Simultaneous use with thiazides increases the risk of hypercalcemia.
Administration simultaneously with cardiac glycosides can enhance their toxic effects (increases the risk of heart rhythm disorder).
Ketoconazole may decrease the biosynthesis and catabolism of 1,25 $(OH)_2$cholecalciferol.
Simultaneous administration of vitamin D_3 with metabolites or analogues of vitamin D is possible only as an exception and only under control of the calcium level in the blood serum.

Pharmacological properties.
Pharmacodynamics. Vitamin D_3 is an active antirachitic factor. The most important function of vitamin D_3 is the regulation of the metabolism of calcium and phosphate, which contributes to the proper mineralization and growth of the skeleton.
Vitamin D_3 is a natural form of vitamin D, which is formed in animals and humans. Compared to vitamin D_2 it is characterized by a higher activity (by 25%). It is necessary for the functioning of parathyroid glands, intestine, kidneys and bone system. It plays an important role in the absorption of calcium and phosphate from the intestine, in the transport of mineral salts and in the process of calcification of bones, regulates the excretion of calcium and phosphate by the kidneys. The concentration of calcium ions affects several important biochemical processes that support the maintenance of muscle tone of the skeletal muscles involved in conducting nervous excitement and affecting blood clotting. Vitamin D_3 also participates in the functioning of the immune system, which affects the production of lymphokines.
The lack of vitamin D_3 in food, its reduced absorption, calcium deficiency, as well as the lack of exposure to sunlight during the rapid growth of the child lead to rickets,
and in adults – to osteomalacia, in pregnant women – to the appearance of symptoms of tetania and further to the non-formation of tooth enamel in children.
Women in menopause with osteoporosis, due to hormonal disorders, require the increase of the dose of vitamin D_3.
Pharmacokinetics.
Absorption. An aqueous solution of vitamin D_3 is better absorbed than an oil solution. In premature infants, there is insufficient formation and bile flow into the intestine, which disrupts the absorption of vitamins in the form of oily solutions.
Following oral administration, cholecalciferol is absorbed in the small intestine.
Distribution. It crosses the placental barrier and is excreted in breast milk.
Metabolism. It is metabolised in the liver and kidneys, transforming into an active metabolite – calcitriol, which binds to a carrier protein and is transported to target organs (intestine, bones, kidneys). The half-life in the blood is several days and can be prolonged in the case of kidney disease.
Elimination. It is excreted in the urine and faeces.

Vitamin D_3 takes part in the regulation of phosphorus and calcium metabolism in the body 6 hours after administration of the drug.
Following administration of vitamin D_3 in 48 hours there is a significant increase in the level of cholecalciferol in the blood serum.

Pharmaceutical characteristics.

Basic physical and chemical properties: transparent colourless liquid with a characteristic anise odour. Opalescence is allowed.

Shelf life. 2 years.

Storage conditions.
Store at temperatures below +25°C in the original packaging. *Keep out of reach of the children.*
After opening, store the vial with a tightly closed cap in the refrigerator (at a temperature of +2°C to +8°C) for no more than 6 months.

Packaging.
10 ml in a vial of dark glass. 1 bottle with a stopper-dropper in a pack of cardboard.

Dispensing conditions.
On prescription.

Manufacturer.
PJSC "Technologist".

Location.
8, Manuilskogo Str., Uman, Cherkassy region, 20300, Ukraine.

Date of last revision.

Stamp: /Agreed with materials of the registration dossier and well-known data on the use of the medicinal product/