Hydroxychloroquine instructions

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Brand Names: Plaquenil (Плаквенил) , Immard (Иммард), Hydroxychloroquine (Гидроксихлорохин)

Active substance: Hydroxychloroquine.

Pharmachologic effect: antiprotozoal, antimalarial, anti-inflammatory, immunosuppressive

Pharmacodynamics:
Hydroxychloroquine has antimalarial properties and also has anti-inflammatory and immunosuppressive effects in chronic discoid or systemic lupus erythematosus (SLE) and acute and chronic rheumatoid arthritis (RA). Its mechanism of action in malaria, SLE, and RA is not fully known.
Hydroxychloroquine has the properties of a moderate immunosuppressant, inhibiting the synthesis of rheumatoid factor and components of the acute phase reaction. It also accumulates in leukocytes, stabilizing lysosomal membranes, and inhibits the activity of many enzymes, incl. collagenases and proteases that cause cartilage breakdown.
The drug actively suppresses the asexual erythrocyte forms, as well as the gametes of Plasmodium vivax and Plasmodium malariae, which disappear from the blood almost simultaneously with the asexual forms. Hydroxychloroquine has no effect on Plasmodium falciparum gametes. Hydroxychloroquine is ineffective against chloroquine-resistant strains of Plasmodium falciparum, and is also inactive against extra-erythrocyte forms of Plasmodium vivax, Plasmodium malariae and Plasmodium ovale, and therefore cannot prevent infection with these microorganisms when administered prophylactically, and cannot prevent recurrence of the disease caused by these pathogens.

Pharmacokinetics:
After oral administration, hydroxychloroquine is rapidly and almost completely absorbed. After a single dose of 400 mg Cmax of hydroxychloroquine in plasma is achieved through 1.83. Plasma protein binding - 45%. In the liver, it is partially converted into active ethylated metabolites. The unchanged drug and its metabolites are well distributed in the body. Hydroxychloroquine accumulates in tissues with a high level of metabolism (in the liver, kidneys, lungs, spleen - in these organs the concentration exceeds the plasma concentration by 200-700 times; CNS, erythrocytes, leukocytes), as well as in the retina and tissues rich in melanin. Hydroxychloroquine and its metabolites are excreted primarily in the urine and, to a lesser extent, in the bile. The release of the drug is slow, the terminal T1 / 2 is about 50 days (from whole blood) and 32 days (from plasma). For 24 hours, 3% of the administered dose of the drug is excreted in the urine. Hydroxychloroquine crosses the placental barrier and is found in small amounts in breast milk.

Indications:
rheumatoid arthritis;
juvenile rheumatoid arthritis;
lupus erythematosus (systemic and discoid);
malaria (with the exception of those caused by chloroquine-resistant Plasmodium falciparum):
- for the prevention and treatment of acute attacks of malaria caused by Plasmodium vivax, Plasmodium ovale and Plasmodium malariae, as well as susceptible strains of Plasmodium falciparum;
- for the radical treatment of malaria caused by susceptible strains of Plasmodium falciparum.

Contraindications:
hypersensitivity to 4-aminoquinoline derivatives;
retinopathy;
pregnancy;
hereditary lactose intolerance, lactase deficiency, galactosemia or glucose / galactose malabsorption syndrome (due to the presence of lactose in the preparation).

children's age if long-term therapy is necessary (children have an increased risk of developing toxic effects);
children under 6 years of age (200 mg tablets are not intended for children with an "ideal" body weight of less than 31 kg).

Use with caution:
visual disorders (decreased visual acuity, impaired color vision, narrowing of the visual fields), simultaneous administration of drugs that can cause adverse ophthalmic reactions (risk of progression of retinopathy and visual disorders);
hematological diseases (including history);
severe neurological diseases, psychosis (including history);
tardive cutaneous porphyria (risk of exacerbation), psoriasis (risk of increased skin manifestations of the disease), concomitant use of drugs that can cause skin reactions;
renal failure and / or liver failure, hepatitis, concomitant use of drugs that can adversely affect the function of the liver and / or kidneys (in case of severe impairment of kidney or liver function, the dose should be selected under the control of plasma concentrations of hydroxychloroquine);
deficiency of glucose-6-phosphate dehydrogenase;
severe gastrointestinal diseases;
hypersensitivity to quinine (possibility of cross-allergic reactions).

Pregnancy and breast-feeding:
Hydroxychloroquine crosses the placenta. It should be noted that 4-aminoquinolines in therapeutic doses can cause intrauterine damage to the central nervous system, incl. auditory nerve (hearing and vestibular disorders, congenital deafness), retinal hemorrhages and abnormal retinal pigmentation. Therefore, the use of hydroxychloroquine during pregnancy should be avoided unless the potential benefit to the mother outweighs the risk to the fetus.
The need to use the drug during breastfeeding should be carefully weighed, because. it has been shown to be excreted in small amounts into breast milk, and young children are especially sensitive to the toxic effects of 4-aminoquinolines.

Side effects:
Organ of vision:
retinopathy may develop, although rarely, with changes in pigmentation and defects in the visual fields. In the early form, these effects are usually reversible upon discontinuation of hydroxychloroquine. If the condition remains undiagnosed and retinal lesions continue to develop further, then there may be a risk of their progression even after discontinuation of the drug.
Retinal changes may initially be asymptomatic, or manifest as paracentral or pericentral scotomas, transient scotomas, and color vision disturbances.
Corneal changes are possible, including swelling and opacity. They may be asymptomatic or cause visual disturbances such as halos, blurred vision, or photophobia. When treatment is stopped, these changes may be reversed.
There may also be visual disturbances associated with disturbances of accommodation, which are dose-dependent and reversible.
Skin:
sometimes there are skin rashes; itching, changes in the pigmentation of the skin and mucous membranes, discoloration of the hair and alopecia are also described. These changes usually disappear quickly after treatment is stopped. A bullous rash has been reported, including very rare cases of erythema multiforme and Stevens-Johnson syndrome, photosensitivity, and isolated cases of exfoliative dermatitis.

Very rare cases of acute generalized exanthematous pustulosis (AGEP) must be distinguished from psoriasis, although hydroxychloroquine can also exacerbate psoriasis. AHEP may be accompanied by fever and hyperleukocytosis. After discontinuation of the drug, the outcome is usually favorable.

Gastrointestinal tract: nausea, diarrhea, anorexia, abdominal pain and rarely vomiting. These symptoms usually resolve immediately after dose reduction or discontinuation of the drug.

Hepatobiliary system: with prolonged use in large doses, the development of a hepatotoxic effect is possible. There are reports of isolated cases of abnormal liver function and a few cases of sudden onset liver failure.

Central nervous system: infrequently - dizziness, tinnitus, hearing loss, headache, irritability, emotional instability, psychosis, convulsions, muscle weakness, ataxia.

Peripheral nervous system and muscles: there have been cases of skeletal muscle myopathy or neuromyopathy, leading to progressive weakness and atrophy of the proximal muscle groups. Myopathy may be reversible after discontinuation of the drug, but full recovery may take several months. At the same time, weak sensory changes, suppression of tendon reflexes and a decrease in nerve conduction can be observed.

Cardiovascular system: there are rare reports of the development of cardiomyopathy.
Chronic cardiac toxicity may be suspected in the presence of conduction abnormalities (His bundle branch block/AV conduction abnormalities) or biventricular hypertrophy. With the abolition of the drug, the reverse development of these changes is possible.

Hematopoietic organs: cases of oppression of bone marrow hematopoiesis were rarely observed. Rare cases of anemia have been reported, incl. aplastic, agranulocytosis, leukopenia and thrombocytopenia.

Hydroxychloroquine may provoke or exacerbate porphyria.

Immune system: urticaria, angioedema, bronchospasm.

Interaction:

Digoxin. It has been reported that hydroxychloroquine is able to increase plasma concentrations of digoxin, therefore, in order to avoid the development of glycoside intoxication while taking these drugs, it is necessary to reduce the dose of digoxin under the control of its plasma concentrations.

Drugs used to treat diabetes. Since hydroxychloroquine may enhance the effects of insulin and oral hypoglycemic agents, it may be necessary to reduce the dose of these hypoglycemic agents when starting hydroxychloroquine.

Antacids. May reduce the absorption of hydroxychloroquine. Therefore, with the simultaneous use of antacids and hydroxychloroquine, the interval between their intake should be at least 4 hours.

With hydroxychloroquine, the following interactions with other drugs cannot be excluded, which have been described for chloroquine, but have not yet been observed with hydroxychloroquine.

Aminoglycosides. Potentiation of their direct blocking action on neuromuscular transmission.

Cimetidine. Suppresses the metabolism of antimalarial drugs, which can lead to an increase in their plasma concentrations and increase the risk of developing their side effects, especially toxic ones.

Neostigmine and pyridostigmine. Action antagonism.

Any intradermal human diploid cell rabies vaccine. Decreased antibody production in response to primary immunization with intradermal human diploid cell rabies vaccine.

Dosing and Administration:
Hydroxychloroquine tablets should be taken during meals or with a glass of milk.

RA treatment. Hydroxychloroquine has cumulative activity. For the manifestation of its therapeutic effect, several

weeks of taking the drug are necessary, while side effects can appear relatively early. The necessary therapeutic effect develops after several months of taking the drug. If there is no objective improvement in the patient's condition within 6 months of taking hydroxychloroquine, the drug should be discontinued.

Adults (including the elderly) should take the minimum effective dose. They should not exceed 6.5 mg/kg/day (calculated from "ideal" body weight, not actual body weight) and can be either 200 or 400 mg/day.
In patients able to take 400 mg daily:
Initially - 400 mg daily, in divided doses. When an obvious improvement in the condition is achieved, the dose can be reduced to 200 mg. If the effect decreases, the maintenance dose may be increased to 400 mg.

Children. The lowest effective dose should be used. The dose should not exceed 6.5 mg/kg (based on "ideal" body weight). Therefore, 200 mg tablets are not suitable for children with an "ideal" body weight of less than 31 kg.

The use of Hydroxychloroquine in combination therapy for RA. Hydroxychloroquine can be safely used in combination with corticosteroids, salicylates, NSAIDs, methotrexate, and other second-line therapies. After several weeks of using Hydroxychloroquine, the doses of corticosteroids and salicylates may be reduced or these drugs may be discontinued. Doses of corticosteroids should be reduced gradually every 4-5 days: the dose of cortisone - no more than 5-15 mg, the dose of hydrocortisone - no more than 5-10 mg, the dose of prednisolone and prednisone - no more than 1-2.5 mg , the dose of methylprednisolone and triamcinolone - no more than 1-2 mg and dexamethasone - no more than 0.25-0.5 mg.

SLE treatment. The initial average dose in adults is 400 mg 1 or 2 times a day. It should be administered over several weeks or months, depending on the response of the patient. For long-term maintenance therapy, it is sufficient to use the drug at a lower dose - from 200 to 400 mg.

Malaria treatment
Prevention of acute attacks of malaria due to P. malariae and susceptible strains of Plasmodium falciparum
Adults: 400 mg weekly on the same day of the week.
For children, the weekly dose is 6.5 mg / kg (the “ideal” body weight is taken for calculation), however, regardless of body weight, it should not exceed the adult dose.
If conditions permit, prophylactic therapy should be initiated 2 weeks prior to entry into an endemic area. If this is not possible, then you can prescribe an initial double (loading) dose: adults - 800 mg, children - 12.9 mg / kg of "ideal" body weight (but not more than 800 mg), divided into two doses with a 6-hour interval. Prophylactic treatment should be continued for 8 weeks after leaving the endemic area.

Treatment of acute attacks of malaria:
For adults, an initial dose of 800 mg is followed by a dose of 400 mg every 6 or 8 hours, followed by 400 mg on 2 consecutive days (for a total of 2 g of hydroxychloroquine sulfate).
Alternative treatment: The effectiveness of a single dose of 800 mg has also been proven.
Doses for adults can also be calculated according to the "ideal" body weight, similar to the calculation of doses in children (see below).
For children, a total dose of 32 mg/kg "ideal" body weight (but not more than 2 g) is prescribed for 3 days as follows: the first dose - 12.9 mg / kg (single dose not more than 800 mg); the second dose - 6.5 mg / kg (not more than 400 mg) 6 hours after the first; third dose - 6.5 mg / kg (not more than 400 mg) 18 hours after the second dose; fourth dose - 6.5 mg / kg (not more than 400 mg) 24 hours after the third dose.

Radical treatment of malaria caused by Plasmodium malariae and Plasmodium vivax:
For the radical treatment of malaria caused by Plasmodium malariae and Plasmodium vivax, simultaneous administration of 8-aminoquinolone derivatives is necessary.

Overdose:
An overdose of 4-aminoquinolines is especially dangerous in children, even 1-2 g of the drug can be fatal.
Symptoms: headache, visual disturbances, collapse, convulsions, hypokalemia, rhythm and conduction disturbances,

followed by cardiac and respiratory arrest.
Treatment: because these effects can develop very quickly after taking a large dose of the drug, in these cases, appropriate measures should be started immediately. Induction of vomiting or gastric lavage through a tube should be carried out immediately. To slow absorption - the appointment of activated charcoal at a dose of at least 5 times the accepted dose of the drug. It is advisable to parenteral administration of diazepam (a decrease in the cardiotoxicity of chloroquine against its background is described).
If necessary, artificial ventilation of the lungs and antishock therapy should be carried out.
After relief of overdose symptoms, continued medical supervision is required for at least 6 hours.

Special instructions:
The toxic effect on the retina is largely dose-dependent. The incidence of retinopathy at doses up to 6.5 mg/kg "ideal" body weight is small. Exceeding the recommended daily dose dramatically increases the risk of developing retinopathy and accelerates its appearance.
Before starting a long course of treatment with the drug, a thorough examination of both eyes should be carried out. The examination should include determination of visual acuity, examination of the fundus, assessment of color vision and visual fields. During therapy, such an examination should be carried out at least 1 time in 6 months.

Examination should be more frequent in the following situations:
- at a daily dose exceeding 6.5 mg / kg of "ideal" body weight (in obese patients, the use of absolute body weight to calculate the dose may lead to overdose);
- with renal failure;
- with a total dose of more than 200 g;
- in the elderly;
- with reduced visual acuity.

If any visual disturbances occur (decreased visual acuity, change in color vision), the drug should be immediately discontinued and the patient's state of vision should be carefully monitored, because. retinal changes (and visual disturbances) may progress even after discontinuation of the drug.

Caution is advised when prescribing hydroxychloroquine to patients with liver and kidney disease, who may need to reduce the dose of the drug, and also due to the possibility of the drug affecting the function of these organs (in case of severe impairment of kidney or liver function, the dose should be selected under the control of plasma concentrations of hydroxychloroquine) .

In patients receiving long-term treatment, a complete blood count should be performed periodically; if hematological disorders occur, hydroxychloroquine should be discontinued.

Children are especially sensitive to the toxic effects of 4-aminoquinolines, so care should be taken to keep hydroxychloroquine out of the reach of children.

All patients receiving the drug for a long time should be periodically examined by a neurologist regarding skeletal muscle function and the severity of tendon reflexes. If muscle weakness occurs, the drug should be discontinued.

Manufacturer:
Plaquenil : Sanofi (Great Britain)
Immard : Ipca Laboratories (India)
Hydroxychloroquine : Biocom (Russia)

Storage:
The temperature is not above 25 °C (77 °F) . Keep out of the reach of children.