

**PACKAGE LEAFLET**  
**for medical use of a medicinal product**

**DROTADAR-DARNITSA**

***Qualitative and quantitative composition:***

*Active substance:* drotaverine;

1 tablet contains drotaverine hydrochloride 40 mg;

*Excipients:* lactose monohydrate, maize starch, cellulose microcrystalline, silica colloidal anhydrous, magnesium stearate.

**Pharmaceutical form** Tablets.

*Basic physical and chemical properties:* light yellow or dark yellow with inclusion, flat bevel-edged tablets with a score line on one side.

**Pharmacotherapeutic group**

Drugs for functional gastrointestinal disorders. Papaverine and derivatives. ATC code A03AD02.

***Pharmacological properties***

*Pharmacodynamic properties*

Drotadar-Darnitsa, is a isoquinoline derivative that has a spasmolytic effect on smooth muscles by inhibiting the action of the enzyme phosphodiesterase IV (PDE IV), which leads to an increased concentration of cAMP and, due to the inactivation of myosin kinase light chain (MLCK), to the relaxation of smooth muscles.

*In vitro*, drotaverine inhibits the action of the PDE IV enzyme and the phosphodiesterase III (PDE III) and phosphodiesterase V (PDE V) isoenzymes. PDE IV is functionally very important for reducing the contractility of smooth muscles, therefore selective the enzyme inhibitors can be effective fin the treatment of hyperkinetic diseases and different diseases associated with spastic conditions of the gastrointestinal tract.

In the smooth muscle cells of the myocardium and vessels, cAMP is hydrolyzed to a greater extent by the PDE III isoenzyme, therefore, drotaverine is an effective antispasmodic in the absence of a significant adverse effects on the cardiovascular system and a strong therapeutic effect on the system. Drotadar-Darnitsa is effective in spasms of smooth muscles of both nervous and muscular etiology. Regardless of the type of autonomous innervation, Drotadar-Darnitsa acts on the smooth muscles of the gastrointestinal, biliary, urogenital and vascular systems. The medicinal product enhances blood supply to the tissues due to its ability to expand the vessels.

Action of drotaverine is stronger than papaverine. Absorption is faster and more complete. It is less associated with plasma proteins. The advantage of drotaverine is that, unlike papaverine, there is no such adverse effect as stimulation of breathing after its parenteral administration.

*Pharmacokinetic properties*

Drotadar-Darnitsa is rapidly and completely absorbed after oral administration. It binds highly (95-98 %) to plasma proteins, especially albumin, gamma and beta globulins. The maximum concentration in the blood after oral administration is reached within 45–60 minutes. 65 % of the administrated dose is released into the bloodstream in unchanged form after the primary metabolism. It is metabolized in the liver. The half-life of drotaverine is 8–10 hours. In 72 hours drotaverine is almost completely excreted from the body, more than 50 % is excreted in the urine and about 30 % with the feces. Basically, drotaverine is excreted in the form of metabolites and it is not found unchanged in the urine.

**Clinical particulars**

*Therapeutic indications*

For therapeutic purposes with:

- spasms of smooth muscles associated with diseases of the biliary tract: cholecystolithiasis,

cholangiolithiasis, cholecystitis, pericholecystitis, cholangitis, papillitis;  
- spasms of smooth muscles in diseases of the urinary tract: nephrolithiasis, urethrolithiasis, pyelitis, cystitis, tenesmus of the bladder.

As an adjunct treatment for:

- spasms of the smooth muscles of the gastrointestinal tract: gastric ulcer and duodenal ulcer, gastritis, cardio and/or pylorospasm, enteritis, colitis, spastic colitis with constipation and irritable bowel syndrome, accompanied by flatulence;
- tension headache;
- gynecological diseases (dysmenorrhea).

### ***Contraindications***

Hypersensitivity to drotaverine or to any excipient of the medicinal product; severe hepatic, renal or heart failure (low cardiac output syndrome).

### ***Interaction with other medicinal products and other forms of interaction***

With the simultaneous use of the drug with levodopa it may decrease antiparkinsonic effect of the latter. This combination should be used with caution, since the antiparkinsonian effect of levodopa is reduced, and the rigidity and the tremor are intensified.

### ***Special warnings and precautions for use***

The drug is used with caution in case of arterial hypotension.

#### ***Excipients***

Drotadar-Darnitsa contains 64.0 mg of lactose monohydrate, therefore, the medicinal product is not prescribed to patients with rare hereditary forms of intolerance to galactose, lactase deficiency or glucose-galactose malabsorption syndrome.

#### ***Hypersensitivity reactions***

Drotaverine is a histamine liberator and it can cause non-allergic (false allergic) reactions that have no immunological mechanisms, but mimic allergic symptoms (mimicry). They are usually associated with non-immune release of histamine, bradykinin, activation of the complement, induction of the synthesis of leukotrienes, which in turn induces bronchospasm and skin manifestations. The medicinal product should be carefully prescribed to patients with a history of allergic reactions or asthma. If you experience symptoms of hypersensitivity after taking drotaverine (rash, itching, swelling of the tissues of the upper respiratory tract), you should immediately cancel the medicinal product and prescribe therapy. In case of symptoms of angioedema or urticaria, oral antihistamines should be used.

If it is known about asthma in a patient, use an inhaled beta-2-agonist. It is necessary to monitor the patient for the next 4 hours. If there is continuous vomiting and/or abdominal pain, the possibility of administering epinephrine intramuscularly should be considered.

### ***Fertility, pregnancy and lactation***

#### ***Pregnancy***

Results of animal studies have shown that oral administration of drotaverine did not rise to any direct or indirect effect on pregnancy, embryonic development, childbirth, or postpartum development. However, it is necessary to use the drug with caution during pregnancy.

#### ***Breastfeeding***

Due to the lack of necessary clinical data, it is not recommended to administer medicinal product during breastfeeding.

#### ***Effects on ability to drive and use machines***

If dizziness is observed in patients after using the medicinal product, they should refrain from potentially hazardous activities, such as driving and doing work that requires increased attention.

***Posology and method of administration***

Drotadar-Darnitsa is intended for oral administration.

*Adults:* the average daily dose is 120–240 mg (3–6 tablets), divided into 2–3 doses.

*Children 6–12 years old:* the maximum daily dose is 80 mg, divided into 2 doses.

*Children over 12 years old:* the maximum daily dose is 160 mg, divided into 2–4 doses.

The duration of treatment is determined individually.

***Children***

Administration of the medicinal product is contraindicated for children under 6 years old. Use of drotaverine for children has not been evaluated in clinical trials.

***Overdose***

*Symptoms:* with a significant overdose of drotaverine, cardiac rhythm and conduction disorders were observed, including a complete blockade of the His bundle and cardiac arrest, which can be lethal.

*Treatment:* in case of overdose, the patient should be under the close medical supervision and receive symptomatic and supportive treatment, including induction of vomiting and/or gastric lavage.

***Undesirable effects***

The undesirable effects observed during clinical trials and may have been caused by drotaverine distributed to organs and the frequency of occurrence: very often ( $>1/10$ ), common ( $>1/100 < 1/10$ ), uncommon ( $>1/1000, <1/100$ ), rare ( $>1/10000, <1/1000$ ), very rare ( $<1/10000$ ).

*Gastrointestinal disorders.* Rarely: nausea, vomiting, constipation.

*Nervous system disorders.* Rarely: headache, dizziness, insomnia.

*Cardiac disorders.* Rarely: rapid heartbeat, hypotension.

*Immune system disorders.* Rarely: allergic reactions, including angioedema, urticaria, skin rash, itching, skin flushing, fever, chills, weakness.

***Shelf life***

3 years.

***Special precaution for storage***

Store in the original package at temperature not above 25 °C. Keep out of reach of children.

***Nature and contents of container***

10 tablets in a blister; 3 blisters in a pack.

***Category of release***

Non-prescription medicine.

***Manufacture***

PrJSC “Pharmaceutical firm “Darnitsa”.

***The manufacturer's location and address of the place of business***

13, Boryspilska Street, Kyiv, 02093, Ukraine.

***Date of revision of the text***

13.10.2017.