METAPHARMACEUTICAL IND SL
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TECHNICAL DATA SHEET

0113-TDS-ENG-2023

NADOLOL (PH. EUR)		
DESCRIPTION DCI: NADOLOL	DESCRIPTION DOE: NADOLOL	
CAS Nº: 42200-33-9	EC Nº: 255-706-3	AEMPS CODE: 548A
MOL. WEIGHT: 309.401	MOL. FORMULA: C17H27NO4	ARTICLE CODE: 0113

ATTRIBUTES	SHOULD BE
Appearance	White or almost white, crystalline powder.
Solubility	Slightly soluble in water, freely soluble in ethanol (96%), practically insoluble in acetone.
Identification	Complies
Racemate Content	Complies
Related substances	
Impurity A	<= 0,2 %
Impurity C	<= 0,2 %
Impurity D	<= 0,2 %
Unspecified impurities	<= 0,10 %
Total impurities	<= 0,5 %
Loss on drying	<= 2,0 %
Sulfated ash	<= 0,1 %
Assay	98,5 - 101,0 %

COMPLIES WITH

European Pharmacopeia 11.0

STORAGE

Store in a cool and well-ventilated place; keep the container closed when not used;

REMARKS

El Nadolol está sujeto a lo dispuesto en la guía ICH Q3D "Elemental Impurities" y cumple con lo indicado en las guías EMA/CHMP/ICH/82260/2006 - ICH Q3C (R6) "Residual solvents".

La ausencia de impurezas de N-nitrosaminas se ha asegurado después de un análisis de riesgos de acuerdo con la guía ICH Q9, ICH M7 y de acuerdo con las directrices EMA/428592/2019 Rev 2 y EMA/189634/2019.

Se dispone bajo petición de los certificados de solventes residuales, alérgenos, no-OMG y BSE-TSE, entre otros.

Todos los métodos de análisis están validados por las farmacopeas oficiales o son métodos internos validados del fabricante, que se pueden obtener a petición expresa. La información anterior no exime de la obligación de identificar el producto antes de su uso.

Properties and uses
NADOLOL is a non-cardioselective beta-blocker with no intrinsic sympathomimetic activity or membrane stabilizing activity, and little lipid-soluble. It is very similar to propranolol, but differs in its longer action. It is incompletely absorbed in the digestive tract. The maximum plasma concentrations are reached at 3 - 4 h. It distributes widely, joining 30% to plasma proteins. It does not seem to be metabolized. The plasma half-life is 12-24 hours. It is excreted in the urine. It has been used in the treatment of high blood pressure, angina pectoris, cardiac arrhythmias, hyperthyroidism, and migraine prophylaxis. Dosage: Orally, usually at a dose of 40 - 160 mg / day (sometimes up to 240 mg / day) depending on the pathology.

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Side effects
The most serious side effects of beta-blockers are heart failure, heart block, and bronchospasm. The cardiovascular effects are bradycardia and hypotension. The reduction of the peripheral circulation causes cooling of the extremities and can exacerbate peripheral vascular diseases. The effects on the CNS are depression, dizziness, hallucinations, confusion and sleep disorders, including nightmares. Fatigue is a frequent effect. Paresthesias, peripheral neuropathy, and myopathies, including muscle cramps, have been described. Gastrointestinal side effects are nausea, vomiting, diarrhea, constipation, and abdominal cramps. Beta-blockers interfere with the metabolism of carbohydrates and lipids, and can cause hypoglycaemia, hyperglycaemia and alterations in blood levels of triglycerides and cholesterol. Ocular use can cause decreased production of tears, blurred vision, and pain, as well as systemic effects. The blood reactions are non-thrombocytopenic purpura, thrombocytopenia, agranulocytosis, and transient eosinophilia. A case of hypersensitivity pneumonitis has been described.

Contraindications
Patients with bronchospasm, asthma, or with a history of obstructive respiratory diseases. Also patients with uncontrolled heart failure, metabolic acidosis, severe peripheral artery disease, sinus bradycardia, and 2nd or 3rd degree atrioventricular block.

Precautions
Abrupt withdrawal of beta-blockers could trigger angina, stroke, ventricular arrhythmias, and even cause death. Caution also before 1st degree blocks. Patients with pheochromocytoma should not receive beta-blockers unless they are being treated concomitantly with alpha-blockers. Beta-blockers can mask hyperthyroidism and hypoglycemia, and can unmask myasthenia gravis. The taking of beta-blockers by pregnant women before delivery has resulted in bradycardia, hypoglycemia, and hypotension in the newborn.

Interactions
NSAIDs antagonize the antihypertensive effects of beta-blockers. The use of beta-blockers with other cardiac depressants such as antiarrhythmics and limited-speed calcium antagonists can trigger bradycardia and heart block. Beta-blockers can potentiate bradycardia due to digoxin. In diabetic patients reduce the response to insulin and oral hypoglycaemic agents Patients treated with beta-blockers may develop hypertension when adrenaline is administered, and may stop responding to this drug in situations of anaphylaxis. Aluminum salts and cholestyramine reduce the absorption of beta-blockers. The metabolism of β-blockers may be increased due to the concomitant treatment with drugs such as barbiturates and rifampin and decreases with drugs such as cimetidine, erythromycin, fluvoxamine and hydralazine. Cimetidine and hydralazine reduce hepatic clearance of beta-blockers. Avoid using anesthetics such as ether, cyclopropane, and trichlorethylene in patients taking beta-blockers.

Formulation examples

NADOLOL capsules

NADOLOL - **40 mg**
Excipient c.p.s. - **1 capsule**