Read the Patient Information that comes with BYSTOLIC before you start taking it. This information does not take the place of talking with your doctor about your medicine.

BYSTOLIC is a prescription medicine that can help lower your blood pressure. BYSTOLIC is available as tablets for oral administration containing nebivolol hydrochloride.

Refer to the end of this leaflet for a complete list of ingredients of BYSTOLIC.

FULL PRESCRIBING INFORMATION

Patient Information

BYSTOLIC® (nebivolol) Tablets, for oral use

BYSTOLIC treats:

• High blood pressure

BYSTOLIC is available as tablets for oral administration containing nebivolol hydrochloride.

WHAT IS BYSTOLIC?

BYSTOLIC is a prescription medicine that can help lower your blood pressure. BYSTOLIC is available as tablets for oral administration containing nebivolol hydrochloride.

HOW SUPPLEMENTATION AND HANDLING

BYSTOLIC is available as tablets for oral administration containing nebivolol hydrochloride. Nebivolol is a selective β-blocker which is metabolized in the liver to active metabolites.

WHAT SHOULD YOU TELL YOUR DOCTOR BEFORE TAKING BYSTOLIC?

• Use the information from this section to help you remember the most important things about BYSTOLIC. Ask your doctor or pharmacist any questions you may have.

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2.2 Subpopulations

It is not recommended to adjust the dose in the elderly, low weight, or kidney impaired patients. The risk of serious adverse events, such as hypotension and bradycardia, are increased in patients with impaired renal function. In patients with severe renal impairment (CrCl <10 mL/min) or on dialysis, clinicians should closely monitor patients and adjust the BYSTOLIC dose according to blood pressure response.

2.3 Special Populations

Post-marketing experience suggests a more frequent occurrence of hypotension and postural hypotension in elderly patients (≥65 years old). Physicians should monitor elderly patients on BYSTOLIC closely for those adverse events.

7.2 Hypotensive Agents

BYSTOLIC overdose include cardiac failure, dizziness, hypoglycemia, fatigue and vomiting. Hypertension is a primary metabolite of nebivolol. For symptomatic treatment of hypertensive crises, the use of other antihypertensive agents is recommended (see Section 10.2). If sympotms of severe hypotension are observed, an urgent consultation with a cardiologist should be sought.

5.3 Diastolic and Hypotension

The use of both drugs during the third trimester of pregnancy may increase the risk of congenital malformations, especially cardiovascular defects. The risk-benefit assessment should be carefully considered for antihypertensive treatment in pregnant women. If the use of both drugs is considered necessary, the patient should be closely monitored and managed accordingly.

3.7 Pregnancy

Nebivolol is contraindicated in patients with second or third trimester of pregnancy. Nebivolol has been shown to have an embryotoxic effect. However, preclinical studies have not shown an embryotoxic effect. In human studies, the embryotoxic effect was not observed in maternal doses of nebivolol equivalent to the maximum recommended human dose.

13.1 Interactions with Other Drugs

The use of BYSTOLIC in patients taking other concomitant medications that are known to decrease the clearance of BYSTOLIC (e.g., statins, verapamil, diltiazem, antiarrhythmics) should be avoided. Concomitant administration of BYSTOLIC with these drugs is not recommended.

13.2 Pharmacokinetics in Special Populations

The pharmacokinetics of BYSTOLIC have been studied in various special populations, including the elderly, patients with reduced renal function, and those with specific diseases. The clearance of BYSTOLIC is reduced in these populations.

10.3 Dosage in Renal Impairment

The dose of BYSTOLIC must be individualized to the needs of the patient. For patients on dialysis, BYSTOLIC should be administered at the time of dialysis, and the same dose as for patients with normal renal function should be administered on the day of dialysis. The dose of BYSTOLIC may be increased in patients with moderate renal impairment (CrCl 30 to 50 mL/min) but should not be increased in patients with severe renal impairment (CrCl <10 mL/min). For patients with reduced renal function, the dose of BYSTOLIC may be increased at 2-week intervals up to 40 mg.

10.4 Dosage in Hepatic Impairment

The dose of BYSTOLIC must be individualized to the needs of the patient. In patients with moderate hepatic impairment (Child-Pugh Class B), the dose of BYSTOLIC may be increased up to 40 mg. In patients with severe hepatic impairment (Child-Pugh Class C), the dose of BYSTOLIC should be reduced to 5 mg.

10.5 Dosage in Elderly Patients

In general, patients with BYSTOLIC should not receive greater than 10 mg per day. Reduce the initial dose to 2.5 mg per day in elderly patients, based on age-related reduced renal function and the increased risk of severe hypotension. If the initial dose of 2.5 mg per day is well tolerated, the dose may be increased at 2-week intervals up to 10 mg per day. If the dose is increased, it should be increased by 2.5 mg per day, based on the needs of the patient. The dose should be increased cautiously in elderly patients with chronic heart failure receiving a maximum dose of 10 mg per day for a median of 20 months, as no worsening of heart failure was reported with nebivolol compared to placebo. If heart failure worsens, consider discontinuation of BYSTOLIC.

13.4 Drug-Drug Interactions

Concomitant administration of BYSTOLIC and losartan results in an increase in BUN, uric acid, triglycerides and a decrease in HDL cholesterol and creatinine clearance. Concomitant administration of BYSTOLIC and potassium-sparing diuretics (e.g., spironolactone, eplerenone) may result in hyperkalemia.

13.5 Effects on Laboratory Tests

The use of BYSTOLIC in patients taking other concomitant medications that are known to decrease the clearance of BYSTOLIC (e.g., statins, verapamil, diltiazem, antiarrhythmics) should be avoided. Concomitant administration of BYSTOLIC with these drugs is not recommended.

4. CONTRAINDICATIONS

BYSTOLIC is contraindicated in patients with aortic stenosis, conduction disturbances at any degree, second or third degree atrioventricular block, sick sinus syndrome, and symptomatic bradycardia. In patients with moderate to severe left ventricular outflow tract obstruction (plausibly including those with hypertrophic cardiomyopathy), constrictive pericarditis, and any condition that may precipitate a reflex sympathetic drive, conduction disturbances, and syncope.

12.4 Pharmacokinetics in Special Populations

In patients with moderate hepatic impairment, the recommended initial dose is 5 mg. In patients with severe hepatic impairment, the recommended initial dose is 2.5 mg. In patients with moderate renal impairment (CrCl 30 to 50 mL/min), the recommended initial dose is 5 mg. In patients with mild renal impairment (CrCl 50 to 80 mL/min), the recommended initial dose is 7.5 mg. In patients with severe renal impairment (CrCl <10 mL/min), the recommended initial dose is 2.5 mg.

12.5 Drug-Drug Interactions

Concomitant administration of BYSTOLIC and losartan results in an increase in BUN, uric acid, triglycerides and a decrease in HDL cholesterol and creatinine clearance. Concomitant administration of BYSTOLIC and potassium-sparing diuretics (e.g., spironolactone, eplerenone) may result in hyperkalemia.