NEW

Bystolic™

(nebivolol)

Next generation beta blocker

New BYSTOLIC.

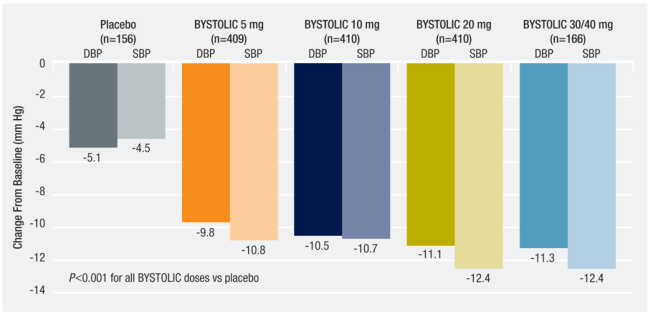
Significant blood pressure reductions with a favorable tolerability profile.

- Unique mechanism of action includes cardioselective beta blockade and vasodilation[1]*
- Significant BP reductions as monotherapy and in combination[1-3]
- Effective across a broad range of patients[1-3]
- Favorable tolerability profile with a low incidence of beta blocker-related side effects[1,2]
- Once-daily antihypertensive, with efficacy maintained over 24 hours[1]

In 3-month studies

BYSTOLIC monotherapy achieves significant BP reductions[1,2]

Reductions From Baseline in Mean Sitting DBP and SBP at Trough at 3 Months[2]

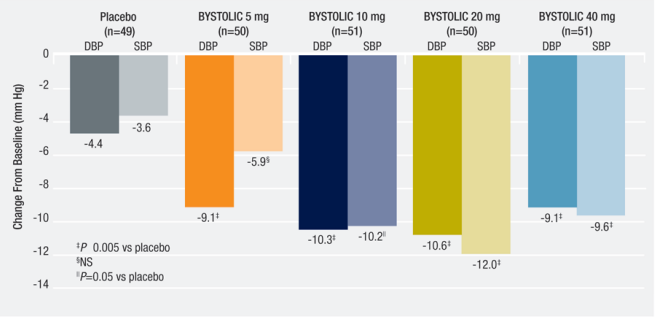


Pooled results from two U.S. phase III, 3-month, placebo-controlled studies of BYSTOLIC monotherapy for the treatment of mild to moderate hypertension. Primary endpoint was sitting DBP at trough. Mean values at baseline: sitting DBP at trough, 99.3 mm Hg; sitting SBP at trough, 152.4 mm Hg (N=1716; n=1551). The 30/40 mg treatment arm (n=166) was included in one of the two studies. Treatment with BYSTOLIC was initiated with 30 mg and then titrated to 40 mg if the 30 mg dose was tolerated (ie, heart rate >55 beats per minute).

In a separate 3-month study

BYSTOLIC provides significant BP reductions in Black patients[3†]

Reductions From Baseline in Mean DBP and SBP at Trough[3]



Results from a U.S. phase III, 3-month, multicenter, placebo-controlled, randomized, double-blind, parallel-group study of BYSTOLIC monotherapy for the treatment of mild to moderate hypertension in Black patients (N=300). Mean values at baseline: sitting DBP at trough, 100.4 mm Hg; sitting SBP at trough, 152.9 mm Hg.

*In extensive metabolizers (most of the population) and at doses ≤10 mg, BYSTOLIC is preferentially β_1 selective. The mechanism of action of the antihypertensive response of BYSTOLIC has not been definitively established. Possible factors that may be involved include: (1) decreased heart rate, (2) decreased myocardial contractility, (3) diminution of tonic sympathetic outflow to the periphery from cerebral vasomotor centers, (4) suppression of renin activity, and (5) vasodilation and decreased peripheral vascular resistance.

†As monotherapy the magnitude of effect was somewhat less than in Caucasians.

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Overall low incidence of side effects[1]

Percentage of Adverse Events by Dose, Occurring in ≥1% of Patients Taking BYSTOLIC and More Frequently Than in Patients Taking Placebo[1]

Adverse Event	Placebo (n=205) %	BYSTOLIC 5 mg (n=459) %	BYSTOLIC 10 mg (n=461) %	BYSTOLIC 20-40 mg (n=677) %
Headache	6	9	6	7
Fatigue	1	2	2	5
Dizziness	2	2	3	4
Diarrhea	2	2	2	3
Nausea	0	1	3	2
Insomnia	0	1	1	1
Chest pain	0	0	1	1
Bradycardia	0	0	0	1
Dyspnea	0	0	1	1
Rash	0	0	1	1
Peripheral edema	0	1	1	1

Pooled results from three U.S. phase III, 3-month, placebo-controlled studies of BYSTOLIC monotherapy for the treatment of mild to moderate hypertension (N=2016; n=1802).

Low incidence of beta blocker-related side effects[2]

Beta Blocker-Related Adverse Events and Discontinuations[2]

Adverse Event	Placebo Adverse Events (n=205) %	BYSTOLIC 5-40 mg Adverse Events (n=1597) %	BYSTOLIC 5-40 mg Discontinuation Rate (n=1597) %
Fatigue	1	4	NONE
Dyspnea	0	1	0.13
Symptomatic bradycardia	0	1	0.19
Sexual dysfunction	0	0	NONE
Depression	0	0	NONE

Pooled results from three U.S. phase III, 3-month, placebo-controlled studies of BYSTOLIC monotherapy for the treatment of mild to moderate hypertension (N=2016; n=1802).

Important Safety Information

Patients being treated with BYSTOLIC should be advised against abrupt discontinuation of therapy. Severe exacerbation of angina and the occurrence of myocardial infarction and ventricular arrhythmias have been reported following the abrupt cessation of therapy with beta blockers. When discontinuation is planned, the dosage should be reduced gradually over a 1- to 2-week period and the patient carefully monitored.

BYSTOLIC is contraindicated in severe bradycardia, heart block greater than first degree, cardiogenic shock, decompensated cardiac failure, sick sinus syndrome (unless a permanent pacemaker is in place), severe hepatic impairment (Child-Pugh >B), and in patients who are hypersensitive to any component of this product.

BYSTOLIC should be used with caution in patients with peripheral vascular disease, thyrotoxicosis, in patients treated concomitantly with beta blockers and calcium channel blockers of the verapamil and diltiazem type (ECG and blood pressure should be monitored), severe renal impairment, and any degree of hepatic impairment or in patients undergoing major surgery. Caution should also be used in diabetic patients as beta blockers may mask some of the manifestations of hypoglycemia, particularly tachycardia.

In general, patients with bronchospastic disease should not receive beta blockers.

BYSTOLIC should not be combined with other beta blockers.

The most common adverse events with BYSTOLIC versus placebo (approximately 1% and greater than placebo) were headache, fatigue, dizziness, diarrhea, nausea, insomnia, chest pain, bradycardia, dyspnea, rash, and peripheral edema.

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2.5 mg **5 mg** **10 mg**

Tablets are not actual size

Flexible dosing and administration[1]

- For most patients, the recommended starting dose of BYSTOLIC is 5 mg once daily[1]
  - Dose should be individualized to the needs of the patient
  - For patients requiring further reduction in blood pressure, the dose can be increased at 2-week intervals up to 40 mg
- Once-daily dosing, as demonstrated by a trough-to-peak ratio >90%[2]
- Can be taken with or without food, as monotherapy or in combination with other agents[1]
- Available in 2.5 mg, 5 mg, and 10 mg tablets[1]
- Patients with severe renal impairment or moderate hepatic impairment should begin with an initial dose of 2.5 mg once daily; upward titration, if needed, should be performed cautiously[1†]

References: **1**. BYSTOLIC [package insert]. St. Louis, MO: Forest Pharmaceuticals, Inc.; 2007. **2**. Data on file. Forest Laboratories, Inc. **3**. Saunders E, Smith WB, DeSalvo KB, Sullivan WA. The efficacy and tolerability of nebivolol in hypertensive African American patients. J Clin Hypertens. 2007;9:866-875.

†BYSTOLIC has not been studied in patients undergoing dialysis.
See the complete Prescribing Information.

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