Byvalson

(nebivolol, valsartan)

New Product Slideshow

MPR

Introduction

- **Brand name:** Byvalson
- **Generic name:** Nebivolol, valsartan
- **Pharmacological class:** Beta-blocker + angiotensin II receptor blocker (ARB)
- **Strength and Formulation:** 5mg/80mg; tablets
- **Manufacturer:** Allergan
- **How supplied:** Bottles—30, 90
- **Legal Classification:** Rx

Indications

- Hypertension

Dosage & Administration

- Initial therapy or if inadequately controlled on valsartan 80mg or nebivolol doses ≤10mg: 1 tab once daily

Considerations for Special Populations

- **Pregnancy:** Discontinue as soon as pregnancy detected
- **Nursing mothers:** Not recommended
- **Pediatric:** Not established
- **Geriatric:** No overall differences in safety or efficacy observed
- **Hepatic impairment:** Moderate: initial therapy not recommended; Severe: not recommended
- **Renal impairment:** Severe: initial therapy not recommended

Contraindications

- Severe bradycardia
- Heart block >1st-degree
- Cardiogenic shock
- Decompensated cardiac failure
- Sick sinus syndrome (unless paced)
- Severe hepatic impairment (Child-Pugh >B)
- Concomitant aliskiren in patients with diabetes

Warnings/Precautions

- **Fetal toxicity may develop; discontinue if pregnancy is detected**
- Hypotension: correct salt/volume depletion prior to initiation
- Coronary artery disease, angina, post-MI, arrhythmias: avoid abrupt cessation (taper over 1–2 weeks)
- Worsening HF or fluid retention; consider diuretics and treat appropriately
- Bronchospastic disease
- Surgery

Warnings/Precautions

- Diabetes
- Hyperthyroidism
- Peripheral vascular disease
- Monitor renal function in renal artery stenosis, chronic kidney disease, severe CHF, or volume depletion
- Risk of hyperkalemia; discontinue if necessary
- Risk of anaphylactic reactions
- Pheochromocytoma
- Neonates

Adverse Reactions

- Hypotension
- Hyperkalemia
- Others (see full labeling)

Interactions

- See **Contraindications**
- Avoid concomitant CYP2D6 inhibitors (eg, quinidine, propafenone, fluoxetine, paroxetine), other beta-blockers
- If concomitant with clonidine, discontinue nebivolol for several days before tapering clonidine
- Increased risk of bradycardia with concomitant digitalis glycosides; monitor
- Concomitant anesthetics (eg, ether, cyclopropane, trichloroethylene), reserpine, guanethidine; monitor closely

Interactions

- Beta-blockers may mask hypoglycemia; caution with concomitant insulin or antihyperglycemics
- Concomitant verapamil or diltiazem (monitor HR, BP), disopyramide (monitor HR, cardiac conduction)
- Concomitant K^+ supplements, K^+-sparing diuretics, K^+-containing salt substitutes may cause hyperkalemia; monitor
- May be antagonized by, and renal toxicity potentiated by, NSAIDs, including selective COX-2 inhibitors (monitor renal function periodically in elderly and/or volume-depleted)

Interactions

- Dual inhibition of the renin-angiotensin system with ACEIs, or aliskiren may increase risk of hypotension, hyperkalemia, renal function changes; monitor closely, in general, avoid combined use of RAS inhibitors
- Concomitant aliskiren in renal impairment (GFR <60mL/min): not recommended
- May increase lithium levels; monitor
- May be potentiated by inhibitors of OATP1B1 (eg, rifampin, cyclosporine) or MRP2 (eg, ritonavir)

Mechanism of Action

- The antihypertensive response of **nebivolol** may be due to: decreased heart rate, decreased myocardial contractility, decreased sympathetic activity, suppression of renin activity, and vasodilation and decreased peripheral vascular resistance
- **Valsartan** blocks the vasoconstrictor and aldosterone-secreting effects of angiotensin II by selectively blocking the binding of angiotensin II to the AT1 receptor in many tissues, such as vascular smooth muscle and the adrenal gland

Clinical Trials

- Byvalson was studied in a Phase 3, double-blind, placebo-controlled, dose-escalating, 8-week study (n=4,161) in patients with Stage 1 or 2 hypertension

Clinical Trials

- Patients were initially randomized to 1 of the following treatment groups:
  - Nebivolol/valsartan 5mg/80mg
  - Nebivolol/valsartan 5mg/160mg
  - Nebivolol/valsartan 10mg/160mg
  - Nebivolol 5mg
  - Nebivolol 20mg
  - Valsartan 80mg
  - Valsartan 160mg
- After 4 weeks, all doses were doubled

Clinical Trials

- Treatment with Byvalson 5mg/80mg for 4 weeks led to placebo-adjusted reductions from baseline in systolic (SBP) and diastolic (DBP) blood pressure of -8.3mmHg and -7.2mmHg, respectively
- There were also **greater reductions in SBP and DBP** vs. treatment with nebivolol 5mg alone ($P<0.0001$ for both SBP and DBP) or valsartan 80mg alone ($P=0.0007$ [SBP] and $P<0.0001$ [DBP])

Clinical Trials

- The antihypertensive effect of valsartan and nebivolol was independent of age and gender in studies evaluating the effect of nebivolol and valsartan given as monotherapies

- The BP lowering effect of Byvalson was maintained over the 24-hour dosing interval based on Ambulatory Blood Pressure Monitoring (ABPM) assessments

Clinical Trials

- Mean heart rate was reduced in patient groups treated with Byvalson
- For more clinical trial data, see full labeling

New Product Monograph

- For more information view the product monograph available at:

  http://www.empr.com/byvalson/drug/34577/