

# STEPS

## New Drug Reviews

# Nebivolol/Valsartan (Byvalson) for Hypertension

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Nebivolol/valsartan (Byvalson) is a combination of a beta<sub>1</sub> adrenergic blocker/nitric oxide producer and an angiotensin receptor blocker (ARB) labeled for the treatment of patients with hypertension.<sup>1-5</sup>

| Drug                           | Dosage             | Dose form          | Cost* |
|--------------------------------|--------------------|--------------------|-------|
| Nebivolol/valsartan (Byvalson) | 5/80 mg once daily | 5-mg/80-mg tablets | \$123 |

\*—Estimated retail price of one month's treatment based on information obtained at <http://www.drugs.com> (accessed October 26, 2017).

## Safety

Adverse effects of nebivolol/valsartan therapy comprise those of the individual drug components. Valsartan may induce changes in renal function, including acute renal failure, especially when combined with other medications that have been shown to affect renal function. Valsartan rarely causes angioedema or hypersensitivity reactions.<sup>6</sup> Nebivolol may cause or worsen bradycardia, heart block, and heart failure. Use of combination nebivolol/valsartan should be avoided in patients with a history of hypersensitivity reaction to either component.<sup>1,3-5</sup>

No dosage adjustment is required for patients with mild hepatic impairment; however, nebivolol/valsartan is not recommended as an initial therapy in patients with moderate hepatic impairment. It is contraindicated in patients with severe hepatic impairment.<sup>1,3-5</sup>

Nebivolol/valsartan inhibits the cytochrome P450 (CYP450) 2D6 enzyme and should be avoided in combination with other CYP2D6

inhibitors. Use of nebivolol/valsartan with other antihypertensive medications such as beta blockers, angiotensin-converting enzyme (ACE) inhibitors, and ARBs can increase the risk of hypotension, bradycardia, hyperkalemia, and changes in renal function. Concomitant medications affected by changes in renal function such as oral or intravenous antibiotics, lithium, and immunosuppressants should be monitored. Nebivolol/valsartan should not be used with aliskiren (Tekturna) because of the increased risk of hyperkalemia, renal impairment, and hypotension.<sup>1,3-5</sup>

The safety and effectiveness of the valsartan component have not been established in patients with severe renal impairment.<sup>1-5</sup> The nebivolol component has been shown to cause severe exacerbation of angina, myocardial infarction, and ventricular arrhythmias in patients following the abrupt discontinuation of beta-blocker therapy.<sup>1,3-5</sup> Nebivolol/valsartan should be discontinued

in women who become pregnant because risk to the fetus is unknown, and it should not be used by breastfeeding women.<sup>1,3-5</sup>

## Tolerability

In clinical trials of carefully selected patients, nebivolol/valsartan was generally

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well-tolerated at the starting dosage, with about 2% of patients discontinuing treatment because of adverse effects. Bradycardia was the most common adverse effect (3.1%) of nebivolol/valsartan therapy and occurred more often when it was used at higher doses or combined with other rate-controlling agents.<sup>1,3,5</sup>

### Effectiveness

In clinical trials of patients with untreated hypertension and an average blood pressure of 155/100 mm Hg, treatment with 5 mg/80 mg per day of nebivolol/valsartan for four weeks resulted in an average reduction in systolic and diastolic blood pressures of 8.3 mm Hg and 7.2 mm Hg, respectively. Higher doses did not typically improve blood pressure control.<sup>1,3-5,7</sup> The individual components of nebivolol/valsartan have been evaluated separately in trials, but the combination has not been studied in comparison with other treatments, as a substitute for other treatments, or as an additional therapy in patients already receiving treatment. Patient-oriented outcomes such as the risk of cardiovascular events have not been evaluated, and these reductions in blood pressure cannot be assumed to confer reduced risk.

### Price

A one-month supply of nebivolol/valsartan costs approximately \$123. No other U.S. Food and Drug Administration–approved combination medications for the treatment of hypertension include a beta blocker and ACE inhibitor/ARB for cost comparison.<sup>1</sup> However, other generic single and combination antihypertensive agents (e.g., lisinopril/hydrochlorothiazide, bisoprolol/hydrochlorothiazide) are available and cost approximately \$10 for a 30-day supply.

### Simplicity

Nebivolol/valsartan is taken once daily with or without food. Before patients start treatment, renal function and serum potassium levels should be evaluated. Periodic monitoring of renal function may be necessary in certain patients. In those at risk of developing acute renal failure, consider withholding or discontinuing combination nebivolol/valsartan and treat with

nebivolol alone. No recommendations for dosage adjustment are available for patients with mild (creatinine clearance = 60 to 90 mL per minute per 1.73 m<sup>2</sup> [1.00 to 1.50 mL per second per m<sup>2</sup>]) or moderate (creatinine clearance = 30 to 60 mL per minute per 1.73 m<sup>2</sup> [0.50 to 1.00 mL per second per m<sup>2</sup>]) renal impairment.

### Bottom Line

Nebivolol/valsartan is an option for the treatment of patients with newly diagnosed or poorly controlled hypertension. Although it offers a new beta-blocker option, no research has demonstrated its benefit over existing treatments. Less expensive individual and combination medication options are available; therefore, until more information is available that demonstrates superiority of nebivolol/valsartan, other options are preferred for initial treatment.

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