

Daiichi Sankyo, Inc.
2 Hilton Court
Parsippany, NJ 07054 • USA
Phone +1 973 944 2600
Fax +1 973 944 2645
www.dsi.com

BENICAR® (olmesartan medoxomil) & BENICAR HCT® (olmesartan medoxomil/hydrochlorothiazide) Fact Sheet

- **BENICAR®** and **BENICAR HCT®** are indicated for the treatment of hypertension. **BENICAR** is a monotherapy while **BENICAR HCT** is a two-in-one combination product. Both **BENICAR** and **BENICAR HCT** may be used alone or in combination with other antihypertensive agents.
 - **BENICAR** can be used as initial therapy in adult patients and pediatric patients (aged six to 16).
 - **BENICAR HCT** is not indicated for initial therapy. Safety and effectiveness in pediatric patients has not been established.
- The U.S. Food and Drug Administration (FDA) granted marketing approval for **BENICAR** in April 2002 and for **BENICAR HCT** in June 2003. **BENICAR** and **BENICAR HCT** are marketed by Daiichi Sankyo, Inc.

Importance of Hypertension Control

- Lowering blood pressure reduces the risk of fatal and nonfatal cardiovascular events, primarily strokes and myocardial infarctions (heart attacks). These benefits have been seen in controlled trials of antihypertensive drugs from a wide variety of pharmacologic classes including the class to which **BENICAR** principally belongs. There are no controlled trials demonstrating risk reduction with **BENICAR** or **BENICAR HCT**.
- Control of high blood pressure should be part of comprehensive cardiovascular risk management, including, as appropriate, lipid control, diabetes management, antithrombotic therapy, smoking cessation, exercise, and limited sodium intake. Many patients will require more than one drug to achieve blood pressure goals.

Mechanism of Action

- **BENICAR** belongs to the angiotensin receptor blocker (ARB) class of antihypertensive agents. Angiotensin II is a substance found in the body that causes vasoconstriction of blood vessels leading to an increase in blood pressure. **BENICAR** blocks the vasoconstrictor effects of angiotensin II by selectively blocking the binding of angiotensin II to the AT₁ receptor in the vascular smooth muscle.
- **BENICAR HCT** is one tablet that combines the ARB power of **BENICAR** with the diuretic hydrochlorothiazide (HCTZ), which works to increase water excretion from the body. The two different classes of drugs have a complementary effect in reducing blood pressure.

Clinical Data

- Studies in patients with mild-to-moderate hypertension (mean baseline 159–162/104 mm Hg) show that **BENICAR** at the usual recommended starting dose of 20 mg resulted in significant blood pressure reductions, lowering systolic blood pressure by a mean of 15 mm Hg and diastolic blood pressure by a mean of 12 mm Hg versus baseline. At the maximum recommended dose of 40 mg, patients experienced mean reductions of systolic blood pressure of 18 mm Hg and diastolic blood pressure of 13 mm Hg versus baseline. In these studies, patients taking placebo had average reductions in systolic blood pressure of 5.6 mm Hg and diastolic of 6.2 mm Hg versus baseline. Onset of action occurred within one week of starting therapy.¹
- In a placebo-controlled, factorial trial (N=502) in mild-moderate hypertension, **BENICAR HCT** given once a day in dose of 40 mg olmesartan medoxomil/25 mg HCTZ produced significant mean blood pressure reductions versus baseline at trough in systolic and diastolic blood pressure of 27/22 mm Hg (mean placebo reductions of 3/8 mm Hg). Onset of action occurred within one week of starting therapy.²
- In clinical studies, adverse events generally were mild and transient and had no relationship to the dose of **BENICAR** / **BENICAR HCT**. The withdrawal rates due to adverse reactions for **BENICAR** / **BENICAR HCT** were similar to placebo: **BENICAR** (2.4 percent vs. 2.7 percent, respectively); **BENICAR HCT** (2.0 percent vs. 2.0 percent, respectively).
 - In placebo-controlled trials, the only adverse reaction that occurred in more than one (1) percent of patients treated with **BENICAR** and at a higher incidence than placebo was dizziness (3 percent vs. 1 percent). The following adverse reactions occurred in placebo-controlled clinical trials at an incidence of more than one (1) percent of patients treated with **BENICAR**, but also occurred at about the same or greater incidence in patients receiving placebo: back pain, bronchitis, creatine phosphokinase increased, diarrhea, headache, hematuria, hyperglycemia, hypertriglyceridemia, influenza-like symptoms, pharyngitis, rhinitis, and sinusitis.
 - Adverse reactions reported in greater than two (2) percent of patients taking **BENICAR HCT** and more frequently than placebo included nausea, hyperuricemia, dizziness and upper respiratory tract infection.

Dose Strengths

- **BENICAR** is available in three dose strengths: 5 mg, 20 mg and 40 mg.
- **BENICAR HCT** is available in three dose strengths:
 - 20 mg olmesartan medoxomil / 12.5 mg hydrochlorothiazide (HCTZ)
 - 40 mg olmesartan medoxomil / 12.5 mg HCTZ
 - 40 mg olmesartan medoxomil / 25 mg HCTZ

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Important Safety Information for BENICAR® and BENICAR HCT®

WARNING: FETAL TOXICITY

- When pregnancy is detected, discontinue BENICAR or BENICAR HCT as soon as possible
- Drugs that act directly on the renin-angiotensin system can cause injury and death to the developing fetus. See **WARNINGS AND PRECAUTIONS: Fetal Toxicity**

CONTRAINDICATIONS

Do not co-administer aliskiren with BENICAR or BENICAR HCT in patients with diabetes. BENICAR HCT is contraindicated in patients with anuria or hypersensitivity to other sulfonamide-derived drugs.

WARNINGS AND PRECAUTIONS

Morbidity in Infants: Children <1 year of age must not receive BENICAR for hypertension.

Fetal Toxicity: BENICAR and BENICAR HCT are **Pregnancy Category D**.

Hypotension in Volume- or Salt-Depleted Patients: In patients with an activated renin-angiotensin system, such as volume- and/or salt-depleted patients (eg, those being treated with high doses of diuretics), symptomatic hypotension may occur after initiation of treatment with BENICAR or BENICAR HCT.

Impaired Renal Function: Monitor for worsening renal function in patients with renal impairment while on BENICAR or BENICAR HCT.

In patients whose renal function may depend upon the activity of the renin-angiotensin-aldosterone system (eg, patients with severe congestive heart failure), treatment with angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor antagonists has been associated with oliguria and/or progressive azotemia and rarely with acute renal failure and/or death. Similar results may be anticipated in patients treated with BENICAR and BENICAR HCT.

In studies of ACE inhibitors in patients with unilateral or bilateral renal artery stenosis, increases in serum creatinine or blood urea nitrogen (BUN) have been reported, and similar results may be expected with BENICAR or BENICAR HCT.

BENICAR HCT is not recommended in patients with severe renal impairment.

Sprue-like Enteropathy: Severe, chronic diarrhea with substantial weight loss has been reported in patients taking olmesartan months to years after drug initiation. Intestinal biopsies of patients often demonstrated villous atrophy. If a patient develops these symptoms during treatment with olmesartan, exclude other etiologies. Consider discontinuation of BENICAR or BENICAR HCT in cases where no other etiology is identified.

Hepatic Impairment: Thiazides (a component in BENICAR HCT) should be used with caution in patients with impaired hepatic function or progressive liver disease, since minor alterations of fluid and electrolyte balance may precipitate hepatic coma.

Electrolyte and Metabolic Imbalances: Due to the hydrochlorothiazide (HCTZ) component in BENICAR HCT, observe patients for clinical signs of metabolic, fluid, or electrolyte imbalance.

Hypersensitivity Reaction: Hypersensitivity reactions to HCTZ (a component in BENICAR HCT) may occur in patients with or without a history of allergy or bronchial asthma.

Systemic Lupus Erythematosus: Thiazides (a component in BENICAR HCT) have been reported to cause exacerbation or activation of systemic lupus erythematosus.

Acute Myopia and Secondary Angle-Closure Glaucoma: Thiazides can cause an idiosyncratic reaction, resulting in acute transient myopia and acute angle-closure glaucoma. Discontinue HCTZ (a component in BENICAR HCT) as rapidly as possible in these patients.

Laboratory Tests: Lab abnormalities may include increased blood creatinine levels and hyperkalemia (olmesartan medoxomil) and increased cholesterol and triglyceride levels (HCTZ).

DRUG INTERACTIONS

Non-Steroidal Anti-Inflammatory Agents: Concurrent administration of non-steroidal anti-inflammatory drugs (NSAIDs) may lead to increased risk of renal impairment (including possible acute renal failure) and loss of antihypertensive effect of BENICAR and BENICAR HCT.

Dual Blockade of the Renin-Angiotensin System (RAS): Dual blockade of the RAS with angiotensin receptor blockers, ACE inhibitors, or aliskiren is associated with increased risks of hypotension, hyperkalemia, and changes in renal function (including acute renal failure) compared to monotherapy. Most patients receiving the combination of two RAS inhibitors do not obtain any additional benefit compared to monotherapy. In general, avoid combined use of RAS inhibitors. Closely monitor blood pressure, renal function, and electrolytes in patients on BENICAR or BENICAR HCT and other agents that affect the RAS.

Avoid use of aliskiren with BENICAR or BENICAR HCT in patients with renal impairment (GFR <60 mL/min).

Concurrent Use with Colesevelam Hydrochloride: Concurrent administration of colesevelam hydrochloride with BENICAR or BENICAR HCT reduces the systemic exposure and peak plasma concentration of olmesartan. Consider administering olmesartan at least 4 hours before the colesevelam hydrochloride dose.

Lithium: Increases in serum lithium concentrations and lithium toxicity have been reported with concomitant use of olmesartan or thiazide diuretics. Monitor lithium levels in patients receiving BENICAR or BENICAR HCT and lithium.

ADVERSE REACTIONS

BENICAR: The only adverse reaction that occurred in >1% of patients treated with BENICAR and more frequently than placebo was dizziness (3% vs 1%).

BENICAR HCT: Adverse reactions reported in >2% of patients taking BENICAR HCT and more frequently than placebo included nausea (3% vs 0%), hyperuricemia (4% vs 2%), dizziness (9% vs 2%), and upper respiratory tract infection (7% vs 0%).

USE IN SPECIFIC PATIENT POPULATIONS

Nursing Mothers: Avoid use while nursing; discontinue either nursing or the drug.

Please see Full Prescribing Information for [BENICAR](#) and [BENICAR HCT](#).

References:

¹ Neutel, JM. Clinical Studies of CS-866, the Newest Angiotensin II Receptor Antagonist. *Am J Cardiol*. 2001;87:37C-43C.

² Chrysant, SG, Weber MA, Wang AC, Hinman, DJ. Evaluation of Antihypertensive Therapy With the Combination of Olmesartan Medoxomil and Hydrochlorothiazide. *Am J Hypertens*. 2004; 17:252-259.