NOW APPROVED

DIOVAN HCT First-Line

For patients who may need more than one agent to get to BP goal

WHAT'S POWER WITHOUT PROTECTION?

DIOVAN and DIOVAN HCT are indicated for the treatment of hypertension. DIOVAN HCT may be used in patients whose blood pressure is not adequately controlled on monotherapy and as initial therapy in patients who are likely to need multiple drugs to achieve blood pressure goals.

IMPORTANT CONSIDERATIONS

WARNING: AVOID USE IN PREGNANCY

When pregnancy is detected, discontinue DIOVAN or DIOVAN HCT as soon as possible. Drugs that act directly on the renin-angiotensin system can cause injury and even death to the developing fetus.
[See Warnings and Precautions [5.1]]

Please see additional Important Considerations on following pages.
Please see accompanying full Prescribing Information.

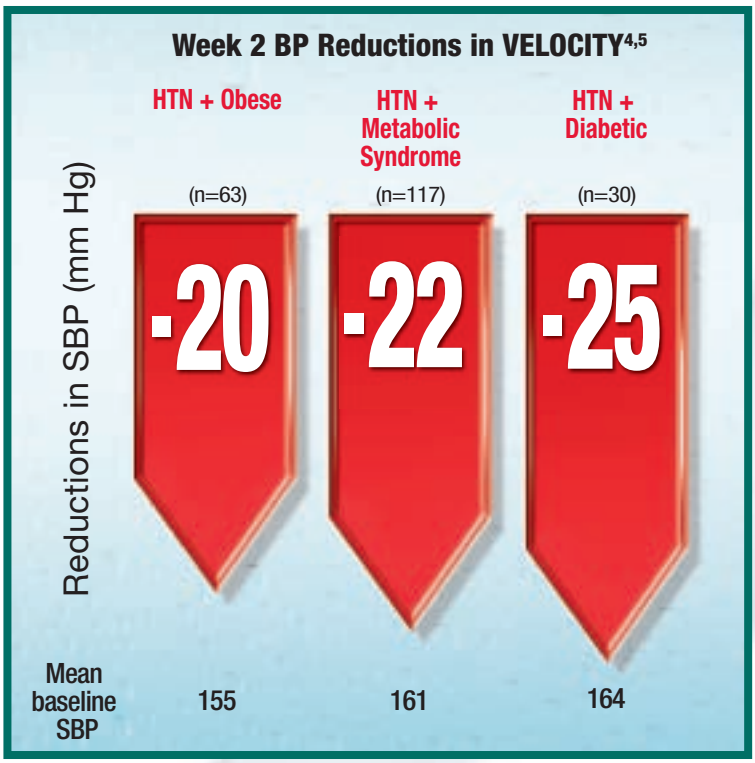
Diovan HCT® valsartan/hydrochlorothiazide tablets

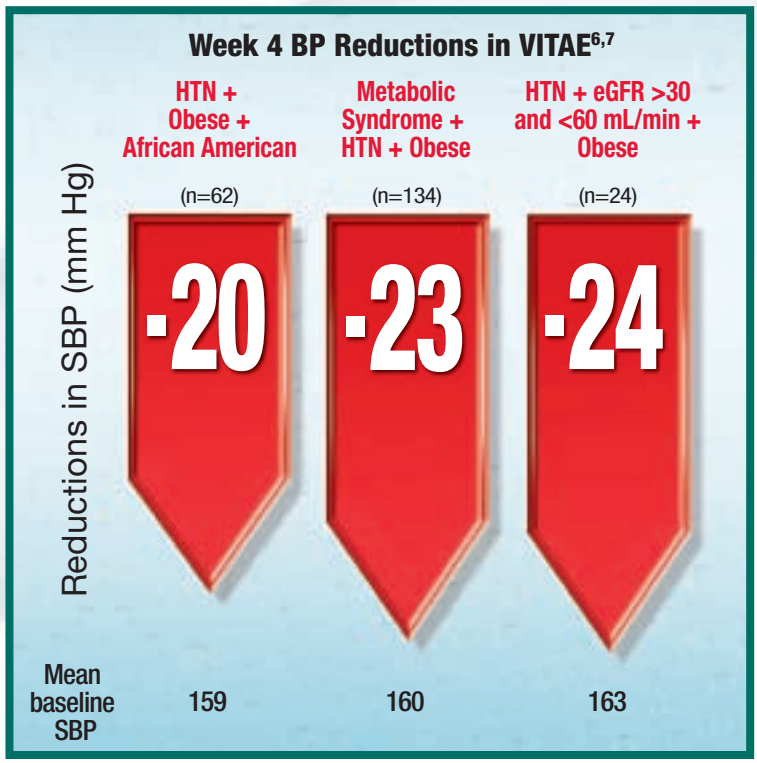
Diovan® valsartan tablets

More than effective. Protective.

FIRST-LINE POWER CHALLENGING PATIENTS

For patients who may need more than one agent, start with DIOVAN HCT and protect your hypertension patients from rises in BP





In the DIOVAN HCT Prescribing Information, placebo-subtracted reductions in SBP with 80/12.5 mg to 320/25 mg are 14 mm Hg to 21 mm Hg; mean baseline SBP (mm Hg): 150-156. No placebo arm was included in the study from which the above data are derived.

DIOVAN HCT is not recommended for patients with severe renal impairment (creatinine clearance ≤30 mL/min).

- **Low incidence of hypotension (0% and 0.49%) in VELOCITY or VITAE, respectively[4,6]**

DIOVAN HCT is indicated for the treatment of hypertension. DIOVAN HCT may be used in patients whose blood pressure is not adequately controlled on monotherapy and as initial therapy in patients who are likely to need multiple drugs to achieve blood pressure goals.

IMPORTANT CONSIDERATIONS

WARNING: AVOID USE IN PREGNANCY
When pregnancy is detected, discontinue DIOVAN HCT as soon as possible. Drugs that act directly on the renin-angiotensin system can cause injury and even death to the developing fetus. ***[See Warnings and Precautions [5.1]]***

DIOVAN HCT is contraindicated in patients who are hypersensitive to any component of this product. Because of the thiazide component, DIOVAN HCT is contraindicated in patients with anuria or hypersensitivity to sulfonamide-derived drugs.

Volume and/or salt depletion should be corrected in patients prior to administering DIOVAN HCT because symptomatic hypotension may occur.

Important considerations due to the hydrochlorothiazide component: Thiazide diuretics should be used with caution in patients with impaired hepatic function or progressive liver disease; lithium generally should not be given with thiazides. Thiazides have been reported to cause exacerbation or activation of systemic lupus erythematosus. Patients taking DIOVAN HCT should be observed for clinical signs of fluid or electrolyte imbalance.

The choice of Diovan HCT as initial therapy for hypertension should be based on an assessment of potential benefits and risks.

In hypertension, the most common adverse events with DIOVAN HCT are headache and dizziness.

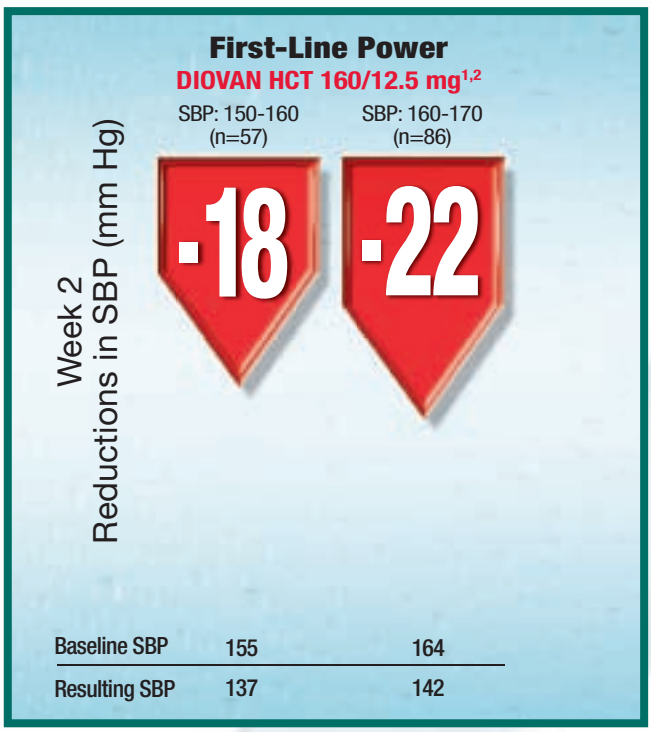
Please see accompanying full Prescribing Information.
Please see adjoining page for study descriptions.

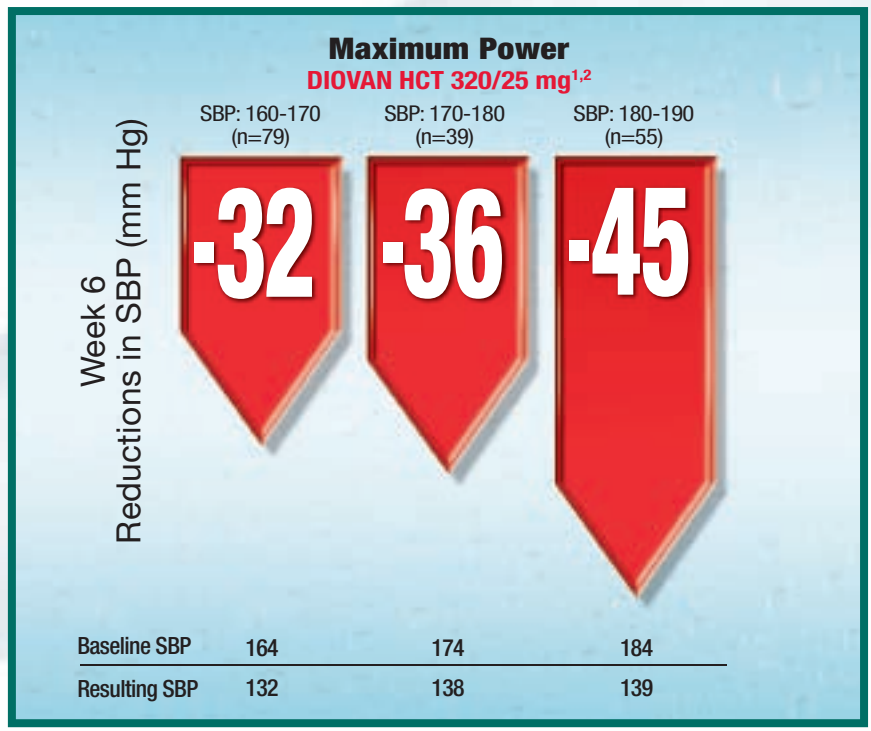
BP DiovanHCT® valsartan/hydrochlorothiazide tablets

More than effective. Protective.

FIRST-LINE POWER
MILD-TO-SEVERE HYPERTENSION

For patients who may need more than one agent, start with DIOVAN HCT and protect your hypertension patients from rises in BP





In the DIOVAN HCT Prescribing Information, placebo-subtracted reductions in SBP with 80/12.5 mg to 320/25 mg are 14 mm Hg to 21 mm Hg; mean baseline SBP (mm Hg): 150-156. No placebo arm was included in the study from which the above data are derived.

- **Overall incidence of AEs was comparable with placebo[3]**
- **No dosage adjustment is required for elderly patients[3]**

DIOVAN HCT is indicated for the treatment of hypertension. DIOVAN HCT may be used in patients whose blood pressure is not adequately controlled on monotherapy and as initial therapy in patients who are likely to need multiple drugs to achieve blood pressure goals.

IMPORTANT CONSIDERATIONS

WARNING: AVOID USE IN PREGNANCY
When pregnancy is detected, discontinue DIOVAN HCT as soon as possible. Drugs that act directly on the renin-angiotensin system can cause injury and even death to the developing fetus. ***[See Warnings and Precautions [5.1]]***

DIOVAN HCT is contraindicated in patients who are hypersensitive to any component of this product. Because of the thiazide component, DIOVAN HCT is contraindicated in patients with anuria or hypersensitivity to sulfonamide-derived drugs.

Volume and/or salt depletion should be corrected in patients prior to administering DIOVAN HCT because symptomatic hypotension may occur.

Important considerations due to the hydrochlorothiazide component: Thiazide diuretics should be used with caution in patients with impaired hepatic function or progressive liver disease; lithium generally should not be given with thiazides. Thiazides have been reported to cause exacerbation or activation of systemic lupus erythematosus. Patients taking DIOVAN HCT should be observed for clinical signs of fluid or electrolyte imbalance.

The choice of DIOVAN HCT as initial therapy for hypertension should be based on an assessment of potential benefits and risks.

No significant differences between the adverse events (AEs) of DIOVAN HCT and placebo. AEs more frequent with DIOVAN HCT than placebo: nasopharyngitis (2.4% vs 1.9%). In individual studies, a dose-related increase in the incidence of dizziness was observed in DIOVAN HCT-treated patients.

Please see accompanying full Prescribing Information.
Please flip up to see study descriptions.

BP
Diovan HCT®
valsartan/hydrochlorothiazide tablets

More than effective. Protective.

PROVEN PROTECTION
HF AND POST-MI

The class doesn't, only DIOVAN does

- **Only ARB indicated for both HF and post-MI**

Val-HeFT: Protection in HF[8-10]
(from a subanalysis of patients not on ACEIs [n=366])

- All-cause mortality: **41%*** risk reduction (*P*=0.017 vs placebo)
- HF morbidity: **49%*** risk reduction (*P*=0.0002 vs placebo)
- HF hospitalizations: **57%*** risk reduction (*P*=0.0006 vs placebo)

VALIANT: Protection Post-MI[11]

- **Reduced** CV mortality

*Relative risk reduction = (1 – hazard ratio) X 100%.

	Placebo (n=181)	DIOVAN (n=185)	*P*
Sudden death with resuscitation	2 (1.1%)	1 (0.5%)	ns
HF therapy†	1 (0.6%)	0 (0.0%)	ns

†Treatment with IV inotropes or vasodilators for ≥4 hours without hospital admission.

- **Improved cardiac structure and output in HF and post-MI patients[9,12]**
- **Definitive dosing: titrating patients to a maximum total daily dose of 160 mg, as tolerated, has proven benefits in HF and post-MI[8,12]**

DIOVAN is indicated for the treatment of hypertension.

In heart failure (HF), DIOVAN is indicated in NYHA class II-IV patients. In a controlled clinical trial, DIOVAN significantly reduced hospitalizations for HF. There is no evidence that DIOVAN provides additional benefits when given with an adequate dose of an ACEI. In clinically stable patients with left ventricular failure or left ventricular dysfunction following myocardial infarction, DIOVAN is indicated to reduce cardiovascular mortality.

DIOVAN HCT is not indicated for the treatment of HF or post-MI.

IMPORTANT CONSIDERATIONS

Care should be exercised with dosing of DIOVAN in patients with severe renal impairment. As a consequence of inhibiting the renin-angiotensin system, changes in renal function may be observed in susceptible individuals (e.g. patients with renal artery stenosis or severe heart failure).

Because of the risk of hypotension, caution should be observed when initiating therapy with DIOVAN in HF and post-MI patients. Evaluation of these patients should always include assessment of renal function. If symptomatic hypotension or renal dysfunction occurs, consideration should be given to a dosage reduction.

The most common AEs in HF: dizziness, hypotension, and diarrhea. In post-MI, the most common AEs resulting in drug discontinuation: hypotension, cough, increased serum creatinine, and rash.

Antihypertensive drugs that affect the renin-angiotensin system have generally been found to be less effective in low-renin hypertensives (frequently blacks) than in high-renin hypertensives (frequently whites).

Please see accompanying full Prescribing Information.

BP/ HF/ Post-MI

Diovan®
valsartan tablets

More than effective. Protective.

MORE THAN EFFECTIVE. PROTECTIVE.

FIRST-LINE

POWER in mild-to-severe HTN: DIOVAN HCT

POWER in challenging patients: DIOVAN HCT

ONLY ARB with proven protection in both HF and post-MI: DIOVAN

ONLY comprehensive HTN management support service: BP Success Zone Program[14]

For patients who may need more than one agent to reach BP goal:

PRESCRIBE

The starting dose for initial therapy for DIOVAN HCT is 160/12.5 mg.

160/12.5 mg

320/25 mg

BP SUCCESS 140/90 ZONE ≥20/80

Individual results may vary

PROVIDE a BP Success Zone kit or have patients enroll online at **www.BPSuccesszone.com** or by phone at 866-630-0350

Superior formulary coverage vs other ARBs at HMOs for fewer callbacks[15]

DIOVAN and DIOVAN HCT are indicated for the treatment of hypertension. DIOVAN HCT may be used in patients whose blood pressure is not adequately controlled on monotherapy and as initial therapy in patients who are likely to need multiple drugs to achieve blood pressure goals.

In heart failure (HF), DIOVAN is indicated in NYHA class II-IV patients. In a controlled clinical trial, DIOVAN significantly reduced hospitalizations for HF. There is no evidence that DIOVAN provides additional benefits when given with an adequate dose of an ACEI. In clinically stable patients with left ventricular failure or left ventricular dysfunction following myocardial infarction, DIOVAN is indicated to reduce cardiovascular mortality.

DIOVAN HCT is not indicated for the treatment of HF or post-MI.

IMPORTANT CONSIDERATIONS

WARNING: AVOID USE IN PREGNANCY

When pregnancy is detected, discontinue DIOVAN or DIOVAN HCT as soon as possible. Drugs that act directly on the renin-angiotensin system can cause injury and even death to the developing fetus. *[See Warnings and Precautions [5.1]]*

Important considerations due to the hydrochlorothiazide component: Thiazide diuretics should be used with caution in patients with impaired hepatic function or progressive liver disease; lithium generally should not be given with thiazides. Thiazides have been reported to cause exacerbation or activation of systemic lupus erythematosus. Patients taking DIOVAN HCT should be observed for clinical signs of fluid or electrolyte imbalance.

The choice of DIOVAN HCT as initial therapy for hypertension should be based on an assessment of potential benefits and risks.

In hypertension, the most common adverse events with DIOVAN and DIOVAN HCT are headache and dizziness.

Please see accompanying full Prescribing Information.

BP
Diovan HCT®
valsartan/hydrochlorothiazide tablets

BP/ HF/ Post-MI
Diovan®
valsartan tablets

More than effective. Protective.

NOVARTIS

Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936

Printed in U.S.A.

8/08

DIO-100409

Printed on Recycled Paper

Study Descriptions

MILD-TO-SEVERE HYPERTENSION[1,2]

Double-blind, randomized study in patients with severe hypertension (MSDBP ≥110 mm Hg and <120 mm Hg with MSSBP ≥140 mm Hg and <200 mm Hg; N=608) randomized to DIOVAN 160 mg once daily or DIOVAN HCT 160/12.5 mg once daily. At 2 weeks, dosages were titrated to DIOVAN 320 mg once daily or DIOVAN HCT 160/25 mg once daily, respectively. After an additional 2 weeks, patients in the DIOVAN HCT group were titrated to DIOVAN HCT 320/25 mg once daily. Patients in the DIOVAN group continued to receive DIOVAN 320 mg once daily for the remainder of the study. Patients were treated for a total of 6 weeks.

CHALLENGING PATIENTS

VELOCITY[4,5]

Post hoc, subgroup analysis of a double-blind, randomized, active-controlled, parallel group study. Patients randomized to treatment with DIOVAN 80 mg, DIOVAN 160 mg or DIOVAN HCT 160/12.5 mg once daily, were then titrated after weeks 2 and 4 to the next dosage level if BP >140/90 mm Hg. Maximum dose was DIOVAN 160/25 mg. Patients were treated for a total of 6 weeks.

VITAE[6,7]

Post hoc, subgroup analysis of a 16-week, double-blind, randomized, multicenter, forced-titration study comparing the antihypertensive efficacy, safety, and tolerability of valsartan/HCTZ therapy to HCTZ-based therapy in obese, hypertensive patients with MSSBP ≥150 mm Hg. The HCTZ-based therapy consisted of HCTZ alone from baseline to week 8. After 8 weeks patients were force titrated to HCTZ plus amlodipine for weeks 8 through 16. Primary efficacy variable was the change in MSSBP; an analysis was performed at weeks 4, 8,12, and 16. Renal function can be determined by calculating eGFR, which stands for estimated glomerular filtration rate. The mean eGFR at baseline for this patient population was 73.2 mL/min. The eGFR in this analysis was calculated using the MDRD equation.

HEART FAILURE

Val-HeFT[8-10]

A double-blind, randomized study of 5,010 patients with HF (NYHA class II-IV), designed to assess if DIOVAN would have an additive benefit to standard therapy for HF. DIOVAN was initiated at 40 mg BID, and was doubled every 2 weeks until the target dose of 160 mg BID (320 mg total daily dose) was reached. Placebo doses were similarly adjusted. The primary end points were mortality and the combination of morbidity plus mortality. The mean follow-up was 23 months. Subgroup analysis performed to evaluate the effects of DIOVAN in patients with chronic heart failure in the 366 patients not receiving ACE inhibitors at baseline (185 receiving DIOVAN and 181 receiving placebo). The mean follow-up was 23 months.

POST-MI

VALIANT[11]

Double-blind, randomized study of 14,703 patients with acute MI and either HF or LV systolic dysfunction. Left ventricular failure was diagnosed by signs, symptoms, or radiological evidence; left ventricular dysfunction was defined as ejection fraction ≤40% by radionuclide ventriculography or ≤35% by echocardiography or ventricular contrast angiography. Patients were randomized within 12 hours to 10 days after the onset of MI symptoms to either DIOVAN, captopril, or DIOVAN plus captopril in addition to baseline therapy. Baseline therapy included aspirin (91% of patients), beta-blockers (70%), ACEIs (40%), thrombolytics (35%), and statins (34%). Study treatment was titrated to maximum tolerated dosage by 3 months. The median treatment duration was 2 years.

References

1. Calhoun DA, Glazer RD, Pettyjohn FS, Coenen PD, Zhao Y, Grosso A. Efficacy and tolerability of combination therapy with valsartan/hydrochlorothiazide in the initial treatment of severe hypertension. *Curr Med Res Opin.* 2008;24(8):2303-2311.
2. Data on file. Study CVAH631D2301—Post hoc analysis of change in MSSBP/MSDBP ranges from baseline. Novartis Pharmaceuticals Corp.
3. DIOVAN HCT [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corp; 2008.
4. Data on file. Study CVAH631BUS05. Novartis Pharmaceuticals Corp.
5. Data on file. Study CVAH631BUS05—Post hoc analysis of MSSBP/MSDBP change from baseline in patient subgroups. Novartis Pharmaceuticals Corp.
6. Data on file. Study CVAH631BUS06. Novartis Pharmaceuticals Corp.
7. Data on file. Study CVAH631BUS06—Post hoc analysis of MSSBP/MSDBP change from baseline in patient subgroups. Novartis Pharmaceuticals Corp.
8. Maggioni AP, Anand I, Gottlieb SO, Latini R, Tognoni G, Cohn JN; Val-HeFT Investigators. Effects of valsartan on morbidity and mortality in patients with heart failure not receiving angiotensin-converting enzyme inhibitors. *J Am Coll Cardiol.* 2002;40(8):1414-1421.
9. DIOVAN [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corp; 2007.
10. Cohn JN, Tognoni G; Valsartan Heart Failure Investigators. A randomized trial of the angiotensin-receptor blocker valsartan in chronic heart failure. *N Engl J Med.* 2001;345(23):1667-1675.
11. Pfeffer MA, McMurray JJV, Velazquez EJ, et al; Valsartan in Acute Myocardial Infarction Trial Investigators. Valsartan, captopril, or both in myocardial infarction complicated by heart failure, left ventricular dysfunction, or both. *N Engl J Med.* 2003;349(20):1893-1906.
12. Solomon SD, Skali H, Anavekar NS, et al. Changes in ventricular size and function in patients treated with valsartan, captopril, or both after myocardial infarction. *Circulation.* 2005;111(25):3411-3419.
13. IMS PADDS. October 2007 to March 2008.
14. Data on file. Patient Program Competitive Analysis. May 2007. Novartis Pharmaceuticals Corp.
15. Verispan Managed Care Formulary Drug Audit. Spring 2007.