Every heartbeat is a step closer to the peak

Indication

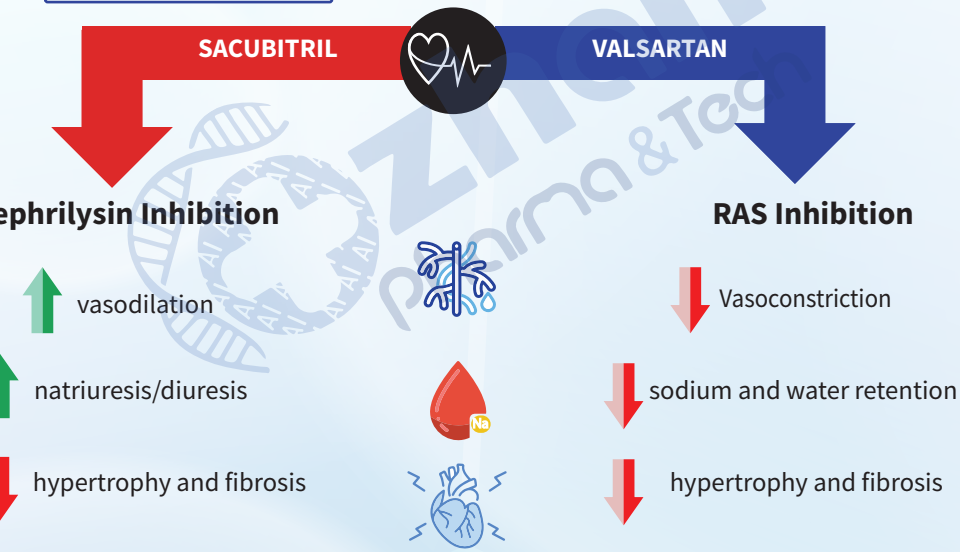
Reduces the risk of cardiovascular death and hospitalization for heart failure in adult patients with chronic heart failure.

Valsartan in Sacubitril/Valsartan is more bioavailable than in other single-agent Valsartan tablets.

Therapeutic equivalency

- 26 mg of Valsartan in Sacubitril/Valsartan (24 mg/26 mg) = 40 mg of Valsartan in single-agent tablets.
- 51 mg of Valsartan in Sacubitril/Valsartan (49 mg/51 mg) = 80 mg of Valsartan in single-agent tablets.
- 103 mg of Valsartan in Sacubitril/Valsartan (97 mg/103 mg) = 160 mg of Valsartan in single-agent tablets.

Mechanism of action



Parameters to Monitor

- Blood pressure
- Serum potassium
- Renal function (creatinine, eGFR)

Special Patient Monitoring

- Systolic BP < 80 mmHg
- Low serum sodium
- Diabetes mellitus
- Renal dysfunction

Monitoring Schedule

- Baseline
- 1-2 weeks after starting treatment
- After any dose change

Dosing and Transition Guidance

Patient's Scenario	Transition Steps	Starting Dose	Titration Plan	Target Dose
Low-Dose ACEi	STOP ACEi Wait 36 hours Switch to Sacubitril/Valsartan	24/26 mg BID, as tolerated. Follow up in 2-4 weeks.	Titrate to 49/51 mg BID, then titrate to target dose. Follow up in 2-4 weeks for each step.	97/103 mg BID
High-Dose ACEi		49/51 mg BID, as tolerated. Follow up in 2-4 weeks.	Titrate to target dose.	
Low-Dose ARB Or No ACEi/ARB	Stop ARB GO Switch to Sacubitril/Valsartan	24/26 mg BID, as tolerated. Follow up in 2-4 weeks.	Titrate to 49/51 mg BID, then titrate to target dose. Follow up in 2-4 weeks for each step.	
High-Dose ARB		49/51 mg BID, as tolerated. Follow up in 2-4 weeks.	Titrate to target dose.	

- Low Dose ACE Inhibitor: For example, ≤10 mg/day of Enalapril or an equivalent dose of another ACE inhibitor.
- Moderate to High Dose ACE Inhibitor: For example, >10 mg/day of Enalapril or an equivalent dose.
- Low Dose ARB: For example, ≤160 mg/day of Valsartan or an equivalent dose of another ARB.
- Moderate to High Dose ARB: For example, >160 mg/day of Valsartan or an equivalent dose.

Comprehensive Clinical Evidence

Reference: www.entrestohcp.com
Uptodate, Sacubitril and valsartan:Drug information

PARADIGM-HF Study in Patients with HFrEF

multinational, randomized, double-blind trial comparing **ENTRESTO to Enalapril** in 8442 symptomatic (NYHA Class II–IV) adult **HFrEF patients (LVEF ≤40%).**

CV death or HF hospitalization

ENTRESTO showed a **20% relative risk reduction (Hazard Ratio [HR] 0.80; 95% CI: 0.73–0.87)** for the composite endpoint of CV death or HF hospitalization as a first event.

Biomarkers

ENTRESTO **lowered NT-proBNP by 32% compared to a 7% reduction with Enalapril** at 4 weeks after randomization.

Quality of Life

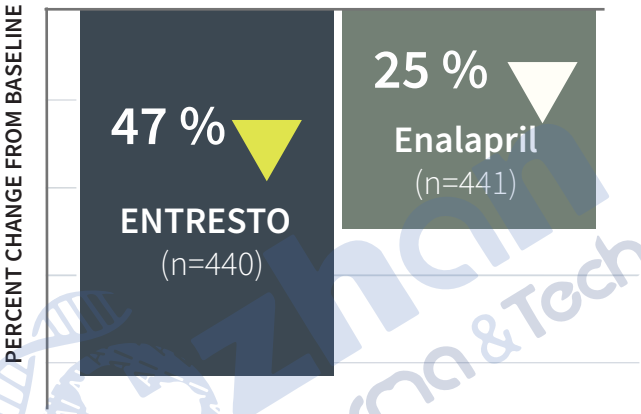
35% less decline in health-related QoL vs an ACEi2

ENTRESTO Improves Patients' Quality of Life (KCCQ-23)

Patients on ENTRESTO® experienced **35% less decline in health-related QoL vs an ACEi2.**

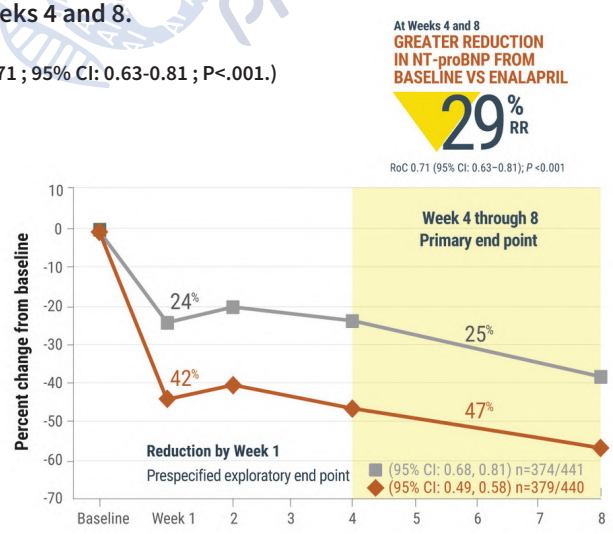
PIONEER-HF: ENTRESTO's early start: beginning treatment in the hospital improves outcomes and lowers heart failure biomarkers in stabilized patients.

randomized, double-blind trial on 881 hospitalized adult patients with **acute decompensated heart failure** and **LVEF ≤40%.** The primary goal : short-term effects of in-hospital initiation of **ENTRESTO vs Enalapril** on **NT-proBNP reduction.**



29% greater reduction in NT-proBNP from baseline vs Enalapril at Weeks 4 and 8.

(RR: 0.71 ; 95% CI: 0.63-0.81 ; P<.001.)



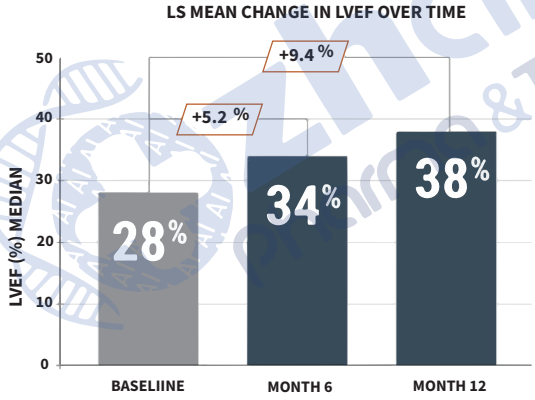
PROVE-HF Study in Patients with HFrEF

52-week, single-arm trial of 794 HFrEF patients (NYHA Class II-IV, LVEF ≤40%), with the primary endpoint of correlating **changes in NT-proBNP with changes in cardiac remodeling.**

In the PROVE-HF trial, reduction in NT-proBNP with ENTRESTO® significantly correlated with improvement across measures of cardiac structure and function

Functional Measures
— E/e': r=0.269
— LVEF: r=-0.381
Structural Measures
— LAVI: r=0.263
— LVEDVI: r=0.320
— LVESVI: r=0.405

ENTRESTO **improved key echocardiographic measures of cardiac remodeling**, including **increased LVEF**, and **reduced NT-proBNP1**



Remodeling measure	LS mean change 6 months	LS mean change 12 months
LVESVI (mL/m²)	-8.7	-15.3
LVEDVI (mL/m²)	-6.7	-12.3
LAVI (mL/m²)	-4.4	-7.6
E/e'	-1.2	-1.3

Reduction in NT-proBNP was demonstrated at 6 months (35%) and 12 months (37%)

PARAGON-HF Study in Patients with HFpEF

a randomized, double-blind, active-controlled trial comparing **ENTRESTO to Valsartan** in 4796 adult patients with symptomatic **HFpEF (LVEF ≥45%)**. Patients were followed for a median duration of 35 months.

No statistical significance was achieved for the primary endpoint (a composite of total HF hospitalizations and CV death)

(RR: 0.87 ; 95% CI: 0.75–1.01 ; P=.06)

Prespecified Subgroup (LVEF ≤57%):

RELATIVE RATE REDUCTION IN TOTAL HF HOSPITALIZATIONS AND CV DEATH VS VALSARTAN

(RR 0.78 ; 95% CI: 0.64–0.95);
ARR 3.6 Driven by reduction in HF hospitalizations

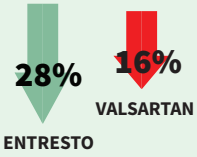
PARAGLIDE-HF Study

a randomized, double-blind, head-to-head trial comparing **ENTRESTO to Valsartan** in **stabilized HFmrEF and HFpEF patients** following a worsening heart failure event.

reduction in NT-proBNP

ENTRESTO demonstrating a **significant reduction in NT-proBNP compared to Valsartan.**

(RR: 0.85 ; 95% CI: 0.73–0.999 ; P=.049)



Win-ratio analysis

Win-ratio analysis consisted of:

Priority

1) Time to CV death
2) Number and timing of HF hospitalizations
3) Number and timing of urgent HF visits
4) Time-averaged proportional change in NT-proBNP from baseline to Weeks 4 and 8

In Total Population

NUMERICALLY FAVORED ENTRESTO vs Valsartan (NS)
Win ratio: 1.19
(95% CI: 0.93–1.52)

In patients with LVEF ≤60%

NUMERICALLY FAVORED ENTRESTO vs Valsartan
Win ratio: 1.46
(95% CI: 1.09–1.95)

Safety

No new safety signals were identified.
The rates of serious adverse events and deaths were **similar between the two groups.**

Adverse events:
- Symptomatic hypotension
- Hyperkalemia
- Worsening renal function
- Angioedema

Sacubitril / Valsartan

50 mg - 100 mg - 200 mg

Film-Coated Tablets

Therapeutic Class:
Cardiovascular

Therapeutic Indication:
- Treatment of Chronic Heart Failure

Keep this leaflet. You may need to read it again

➢ **For further information, please contact**:

Phone: +98-21-88020579 or +98-21-40882675
Website: www.ozhanpharm.com
Email: info@ozhanpharm.com

General Information For The patient:
This medicine has been prescribed specifically for the treatment of your current illness; therefore, Do not pass it on to others.

talk to your physician or pharmacist if any of the following applies to you:

1. A history of allergy or angioedema reaction (symptoms include swelling of the face, lips, tongue, arms, legs, or throat, which can be life-threatening if throat swelling blocks air way).
2. Pregnancy or breastfeeding.
3. Underlying conditions such as diabetes, liver disease, kidney disorders, or significant hypotension caused by factors like diarrhea or vomiting, especially in individuals over 65 years of age.
4. Concurrent use of other medicines, supplements, or dietary salts.

Contraindications:
Do not take Sacubitril/Valsartan under the following conditions, and talk to your physician or pharmacist:

- If you are allergic to sacubitril, valsartan or any of the other ingredients of this medicine.
- If you are taking another type of medicine called an angiotensin converting enzyme (ACE) inhibitor (for example, enalapril, lisinopril, or ramipril), as the concomitant use may increases the risk of angioedema.
- If you have ever had history of angioedema reaction (symptoms include swelling of the face, lips, tongue, arms, legs, or throat, which can be life threatening if throat swelling blocks air way) during treatment with ACE inhibitors (e.g., Enalapril, Lisinopril, Ramipril) or angiotensin receptor blockers (ARBs) such as Losartan, Valsartan, or Telmisartan.
- If you have diabetes or impaired kidney function and you are being treated with a blood pressure-lowering medicine containing aliskiren.
- If you have severe liver impairment (e.g., biliary cirrhosis or cholestasis).
- If you have very severe kidney impairment (eGFR < 15 mL/min/1.73 m²) or, in some cases, (eGFR < 30 mL/min/1.73 m²) due to the risk of severe hypotension.
- If you have end-stage renal disease, as diagnosed by your physician.
- If you have Systolic blood pressure below 100 mmHg.

Pregnancy and Breastfeeding:
This medicine is not recommended during pregnancy and must not be taken when more than 3 months pregnant, ask your doctor for advice before taking this medicine.

Warnings:
Talk to your physician or pharmacist before taking Sacubitril/Valsartan. Dose adjustment or temporary discontinuation of Sacubitril/Valsartan may be necessary under the following conditions:

- If you have Low blood pressure (systolic <112 mmHg) or are taking any other medicines that reduce your blood pressure (e.g., diuretics that increase urine production) or are suffering from vomiting or diarrhoea leading to severe dehydration, especially in individuals over 65 years of age, or if you have kidney disease. All of these factors lead to a significant reduction in blood pressure.
- If you have moderate or chronic kidney impairment (eGFR< 30–60 mL/min/1.73 m²).
- If you have moderate or chronic liver impairment.
- If you have renal artery stenosis (blood tests may be required to monitor kidney function).
- If you have hyperkalemia (elevated potassium levels in the blood).
- If you experience symptoms such as hallucinations or changes in sleeping patterns while taking this Sacubitril/Valsartan.

Precautions:
- This medicine may cause dizziness, If this happens, do not drive or use tools or machines.
- If you have been taking an ACE inhibitor, wait 36 hours after taking the last dose of the ACE inhibitor before starting to take Sacubitril/Valsartan. If you stop taking Sacubitril/Valsartan, wait 36 hours after taking your last dose of Sacubitril/Valsartan before starting an ACE inhibitor.
- Caution is advised when consuming potassium-rich supplements, foods, or salt substitutes containing potassium to avoid hyperkalemia.
- In cases of moderate or chronic liver or kidney dysfunction, use of Sacubitril/Valsartan is recommended with caution

Drug Interactions:
Talk to your physician or pharmacist if you are taking any other medicines. Key interactions include:

- Concomitant use of Sacubitril/Valsartan with ACE inhibitors (e.g. enalapril, lisinopril or ramipril) are contraindicated.
- Concomitant use of Sacubitril/Valsartan with Losartan, Valsartan, or Telmisartan is not recommended.
- Concomitant use of Sacubitril/Valsartan with aliskiren-containing medicinal product is contraindicated in diabetic or renal-impaired patients (eGFR < 60 mL/min/1.73 m). [2]
- Caution should be taken when concomitant use Sacubitril/Valsartan with medicines such as Spironolactone, Eplerenone, Triamterene, Amiloride, Heparin, and supplements and foods or dietary salts containing potassium, due to the possibility of increased blood potassium and serum creatinine levels.
  - Caution should be taken when using sacubitril/valsartan concurrently with NSAIDs (such as Ibuprofen, Diclofenac, Celecoxib, etc.), lithium, furosemide, atorvastatin, sildenafil, tadalafil, metformin, nitrates (nitroglycerin), and trimethoprim.
  - Caution should be taken when concomitant use of sacubitril/valsartan with Rifampin (rifamycin group), Cyclosporine, and Ritonavir due to these medicines increase the concentration of sacubitril/valsartan.

Dosage and Administration:
Adults:

- Initial dose is 50–100 mg twice daily (one tablet in the morning and one in the evening).
- Your doctor will then adjust the dose every 2–4 weeks depending on how you respond to the treatment.
- Maximum recommended dose is 200mg twice daily (one tablet in the morning and one in the evening).
- In moderate to severe kidney impairment (eGFR 30-60 mL/min/1.73 m² or eGFR < 30 mL/min/1.73 m²) and moderate liver impairment and systolic blood pressure 100–110 mmHg, the starting dose is 50 mg twice daily.
- Not recommended this medicine for patients with severe liver impairment (biliary cirrhosis or cholestasis) or severe kidney impairment.
- Swallow the tablets with a glass of water. you can take tablets with or without food. Splitting or crushing of the tablets is not recommended.

Side Effects:
Like all medicines, this medicine can cause side effects, although not everybody gets them. if any of the side effects listed below become severe, tell your physician or pharmacist.

Serious: Stop taking sacubitril/valsartan and seek immediate medical attention if you notice any swelling of the face, lips, tongue and/or throat, which may cause difficulties in breathing or swallowing. These may be signs of angioedema

Very common: low blood pressure, which can cause symptoms of dizziness and light-headedness (hypotension) • high level of potassium in the blood, shown in a blood test (hyperkaliemia) • decreased kidney function (renal impairment)

Common: cough • dizziness • diarrhea • low level of red blood cells, shown in a blood test (anemia) • tiredness (fatigue) • (acute) inability of the kidney to work properly (renal failure) • headache • fainting (syncope) • weakness (asthenia) • feeling sick (nausea) • low blood pressure (dizziness, light-headedness) when switching from sitting or lying to standing position • gastritis (stomach pain, nausea) • spinning sensation (vertigo) • low level of sugar in the blood, shown in a blood test (hypoglycemia)

Uncommon: allergic reaction with rash and itching (hypersensitivity) • dizziness when switching from sitting to standing position (dizziness postural) • low level of sodium in the blood, shown in a blood test (hyponatremia)

Rare: seeing, hearing or feeling things that are not there (hallucinations) • changes in sleeping pattern (sleep disorder)

Very rare: paranoia

Overdose:
In case of accidental overdose, immediately seek medical attention or contact a healthcare provider.

Storage Instructions:
- Store the medicine at temperatures below 30°C, away from light and moisture.
- Keep this medicine out of the sight and reach of children.

Packaging and Available Strengths:
- **50 mg film-coated tablets :**

Each film-coated tablet contains 24.3 mg sacubitril and 25.7 mg valsartan (as sacubitril valsartan sodium salt complex). 30 tablets per bottle or 3 blister in carton box with leaflet.

- **100 mg film-coated tablets**:

Each film-coated tablet contains 48.6 mg sacubitril and 51.4 mg valsartan (as sacubitril valsartan sodium salt complex). 30 tablets per bottle or 3 blister in carton box with leaflet.

- **200 mg film-coated tablets**:

Each film-coated tablet contains 97.2 mg sacubitril and 102.8 mg valsartan (as sacubitril valsartan sodium salt complex). 30 tablets per bottle or 3 blister in carton box with leaflet.

References :

1. https://www.medicines.org.uk/emc(Medicines Compendium) (abpi)
2. BNF-85-2023

Last Revised: August 2025

شرکت داروفناوران اوژن

خیابان کارگر شمالی، جنب کوی دانشگاه، مرکز رشد واحدهای فناوری فرآورده های دارویی دانشگاه علوم پزشکی تهران، پلاک 1462

www.ozhanpharm.com 021-88020579, 021-40882675 Info@ozhanpharm.com