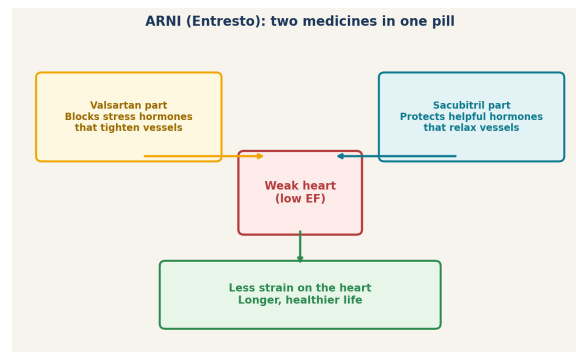


Understanding ARNI (Entresto)

Sacubitril/valsartan — a core medicine for a weak heart pump (HFrEF)

Two medicines in one pill that help people with heart failure live longer and stay out of the hospital.



Online: <https://go.riasalimd.com/arni-guide>

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Names & Terms You Will Hear

Term	Meaning
ARNI	Angiotensin receptor-neprilysin inhibitor. The medicine class name. ARNI is the short form your care team will use.
Sacubitril/valsartan	The two drug names inside the pill. Sacubitril protects helpful hormones. Valsartan blocks stress hormones.
Entresto	The most common brand name for sacubitril/valsartan in the United States.
HFrEF	Heart failure with reduced ejection fraction. A weak heart pump. This is the main reason ARNI is prescribed.
Ejection fraction (EF)	The share of blood the heart pumps out with each beat. A low EF (40% or less) means a weak pump.
Neprilysin	A body enzyme that breaks down helpful hormones. The sacubitril part blocks it so those hormones last longer.
GDMT (guideline-directed medical therapy)	The set of proven heart failure medicines your care team builds up together. ARNI is one of them.
Four pillars	The four core heart failure medicines used together: ARNI, a beta-blocker, an MRA, and an SGLT2 inhibitor.

ARNI is a team player. It is one of four core heart failure medicines used together: ARNI, a beta-blocker, an MRA, and an SGLT2 inhibitor. Each adds its own benefit, so your care team builds them up side by side.



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What Is ARNI (Entresto)?

- ARNI is two medicines combined in one pill: sacubitril and valsartan. It is sold most often under the brand name Entresto.
- It treats heart failure with a weak pump, called HFrEF. This is when the heart muscle cannot squeeze out enough blood with each beat.
- The valsartan part blocks stress hormones that tighten blood vessels and make the heart work harder.
- The sacubitril part protects the heart's own helpful hormones. These hormones relax blood vessels and help the body shed extra salt and water.
- Together, the two parts lower the strain on a weak heart. The heart can pump against less resistance.
- ARNI is one of the four core heart failure medicines. Your care team usually builds it up alongside the other three.



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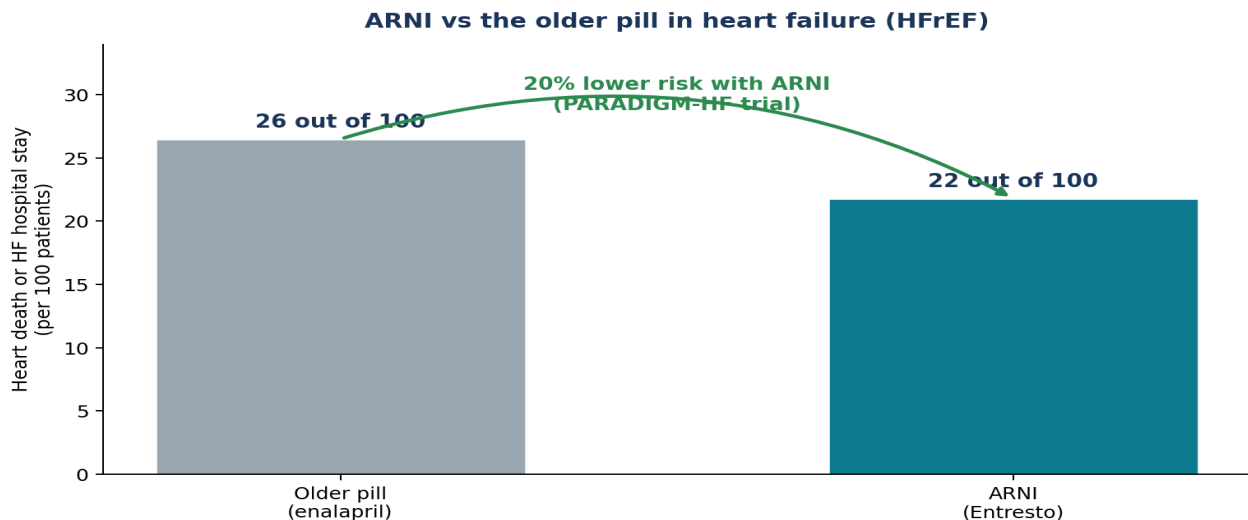
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Why It Matters

- In the large PARADIGM-HF trial, ARNI lowered the risk of heart death or a heart failure hospital stay by 20% compared with an older pill (enalapril).
- That benefit is why heart failure guidelines now prefer ARNI over the older ACE-inhibitor or ARB pills for most people with HFrEF.
- People on ARNI tend to feel better day to day. Many have less shortness of breath and more energy.
- The chart below shows the difference ARNI made in the trial. Fewer patients on ARNI had a heart death or a hospital stay.
- ARNI works best as part of a team of medicines. The other three core medicines add their own benefit on top.



In the PARADIGM-HF trial, fewer people on ARNI had a heart death or a heart failure hospital stay than people on the older pill — a 20% lower risk.



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Risk Factors

Some patients are more likely to develop this condition. Knowing your risk helps your care team take extra precautions.

Risk Factor	Why It Increases Risk
Very low blood pressure	ARNI lowers blood pressure. If your pressure is already low (top number under 100), your care team may wait or start at a low dose.
Past swelling (angioedema)	If you ever had deep swelling of the face, lips, or throat from an ACE inhibitor or ARB, ARNI is not safe for you.
Pregnancy	ARNI can harm an unborn baby. It must not be used in pregnancy. Tell your care team right away if you could be pregnant.
Severe kidney or liver disease	These change how the body handles the medicine. Your care team may adjust the dose or choose another plan.
High potassium	ARNI can raise blood potassium. Your care team checks this with a blood test, especially when starting or raising the dose.



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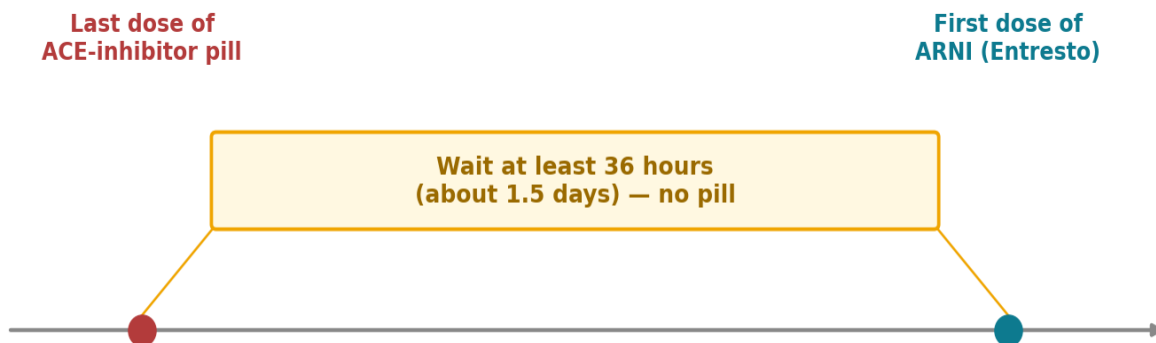
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Treatment Options

- ARNI is a pill taken by mouth two times a day, about 12 hours apart. Take it the same way each day, with or without food.
- If you are switching from an ACE-inhibitor pill, you must wait at least 36 hours after your last dose before your first ARNI dose. The timeline below shows why.
- Your care team usually starts at a low or middle dose. They raise it step by step every 2 to 4 weeks, as your body allows.
- The goal (target) dose is 97/103 mg two times a day. Some people stay on a lower dose if a higher one causes side effects. A lower dose still helps.
- Expect blood tests for kidney function and potassium, plus blood pressure checks, when starting and after each dose increase.
- ARNI works alongside the other three core heart failure medicines. See our guides on heart failure, beta-blockers, and the other pillars below.
- Learn more in our [heart failure \(HFrEF\) guide](#), our [beta-blocker guide](#), our [SGLT2 inhibitor guide](#), and our [MRA \(finerenone\) guide](#).



The gap prevents dangerous swelling (angioedema) from the two medicines overlapping.

Switching from an ACE-inhibitor pill? Wait at least 36 hours after the last dose before your first ARNI dose to avoid dangerous swelling.



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Why the 36-Hour Gap Matters

- ACE-inhibitor pills (like lisinopril) and ARNI both act on the same body pathway.
- Taking them too close together raises the risk of deep swelling, called angioedema.
- So you stop the ACE inhibitor and wait at least 36 hours — about a day and a half — before the first ARNI dose.
- This gap does not apply if you are coming from an ARB pill (like losartan). Ask your care team about your exact plan.



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How the dose builds up over time

Start	Build up	Target
• 24/26 mg or 49/51 mg • Two times a day • A gentle starting dose • Lets your body adjust	• Dose is doubled • Every 2 to 4 weeks • Only as your body allows • Blood pressure and labs checked	• 97/103 mg • Two times a day • The full proven dose • A lower dose still helps if needed



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Comfort Measures at Home (No Medication Needed)

These simple steps support healing and ease symptoms. Use them alongside any medication your doctor prescribes.

- Take your dose at the same two times every day. A phone alarm or a weekly pill box makes this easier.
- Stand up slowly from sitting or lying down. ARNI lowers blood pressure, so rising slowly helps you avoid dizziness.
- Weigh yourself each morning after you use the bathroom. Quick weight gain (3 pounds in a day or 5 in a week) can mean fluid is building up.
- Follow your low-salt eating plan. Less salt helps the medicine work and keeps fluid down.
- Do not add salt substitutes or potassium pills unless your care team says so. Many salt substitutes are high in potassium.
- Keep your blood test and clinic visits. They let your team raise the dose safely.



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Risks, Benefits, and Alternatives

Every choice has trade-offs. Use this table to start the shared decision conversation.

Option	Risks	Benefits	Alternatives
Start ARNI (sacubitril/valsartan)	Low blood pressure, dizziness. Higher potassium. Rare deep swelling (angioedema). Kidney changes. Not safe in pregnancy.	20% lower risk of heart death or hospital stay vs the older pill. Often less shortness of breath. A proven core medicine.	Stay on an ACE inhibitor or ARB. These help but less than ARNI for most people with HFrEF.
Stay on an ACE inhibitor (such as lisinopril)	Cough is common. Can raise potassium. Less benefit than ARNI in HFrEF.	Long track record. Low cost. Still a proven heart failure medicine.	Switch to ARNI (after a 36-hour gap). Use an ARB if cough is the problem.
Raise to the target dose (97/103 mg twice a day)	More chance of low blood pressure or dizziness as the dose climbs.	The full proven dose gives the strongest benefit when your body can take it.	Stay on a lower dose. A lower dose still helps if a higher one is not tolerated.
No ARNI (other heart failure medicines only)	Misses the added benefit ARNI brings on top of the other medicines.	Avoids ARNI side effects. May fit people with very low pressure or past swelling.	Use the other three core medicines. Revisit ARNI later if your pressure improves.



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Common Misconceptions

Myth	Reality
Entresto is just a stronger blood pressure pill.	ARNI does lower blood pressure, but its main job is treating a weak heart pump. It was proven to help people with heart failure live longer, not just to lower numbers.
I can switch straight from my ACE-inhibitor pill to ARNI.	No. You must wait at least 36 hours after your last ACE-inhibitor dose. Taking both too close together raises the risk of dangerous swelling.
If a low dose helps, I should jump to the full dose fast.	The dose is raised slowly, every 2 to 4 weeks, so your body can adjust. A slow climb lowers the chance of dizziness and low blood pressure.
ARNI replaces all my other heart failure medicines.	No. ARNI is one of four core medicines. It works best alongside a beta-blocker, an MRA, and an SGLT2 inhibitor.
Feeling fine means I can stop ARNI.	Feeling well usually means the medicine is working. Stopping it can let heart failure come back. Never stop without talking to your care team.
A little face or lip swelling is no big deal.	Swelling of the face, lips, tongue, or throat can be a serious reaction. Stop the pill and get emergency help right away.



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Possible Complications

Knowing what can go wrong helps you spot problems early. Most complications are uncommon, especially with treatment.

Where / What	What Can Happen
Blood pressure	Low blood pressure is the most common effect. It can cause dizziness or lightheadedness, especially when standing up.
Potassium (blood salts)	Potassium can rise too high. Very high potassium can affect the heart rhythm. Blood tests catch this early.
Kidneys	Kidney numbers can shift, especially early on or with water pills. Your care team watches them with blood tests.
Allergic swelling (angioedema)	Rare but serious deep swelling of the face, lips, tongue, or throat. It can block breathing and needs emergency care.
Pregnancy	ARNI can seriously harm an unborn baby. It must be stopped before or as soon as pregnancy is known.
Cough or dizziness	Some people feel dizzy. Cough is less common than with the older ACE-inhibitor pills.

What your care team watches — and what you can do

What to watch	Why it matters	What you can do
Low blood pressure	Most common effect. Can cause dizziness.	Stand up slowly. Report bad dizziness.
High potassium	Can affect the heart rhythm if very high.	Avoid salt substitutes. Keep blood tests.
Kidney changes	Numbers can shift when starting or with water pills.	Stay hydrated as advised. Keep blood tests.
Swelling (angioedema)	Rare but can block breathing.	Stop the pill. Call 911 right away.



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Points to Know

If you remember nothing else, remember these key points.

- ARNI (Entresto) is two medicines in one pill — sacubitril and valsartan — for a weak heart pump (HFrEF).
- It lowered the risk of heart death or a hospital stay by 20% versus the older pill in a large trial.
- Wait at least 36 hours after your last ACE-inhibitor dose before your first ARNI dose.
- Take it two times a day, about 12 hours apart, the same way each day.
- Watch for dizziness from low blood pressure. Rise slowly and tell your care team if it is bad.
- Get blood tests for potassium and kidney function when starting and after each dose increase.
- ARNI is one of four core heart failure medicines. It works best with the other three.
- Never stop ARNI on your own, even if you feel well.



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When to Call Us - and When to Call 911

If you are not sure, call. We would rather hear from you twice than miss a real problem.

- Call 911 now if you have swelling of the face, lips, tongue, or throat, or any trouble breathing or swallowing.
- Call 911 for fainting, chest pain, or a fast or pounding heartbeat with dizziness.
- Call us if you feel very dizzy or lightheaded, or you nearly pass out when standing.
- Call us if you gain more than 3 pounds in a day or 5 pounds in a week, or your swelling gets worse.
- Call us for muscle weakness, numb or tingling feelings, or a slow or odd heartbeat — these can be signs of high potassium.
- Call us if you make much less urine than usual, or you feel very tired and weak.
- Call us right away if you are pregnant or think you might be — ARNI must be stopped.

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Trusted Resources

The links below are the trusted resources Dr. Ali used to write this guide and that he recommends you visit for more information. Each is a clickable link in the digital version and a Short.io tracked URL on the printed version.

- [American Heart Association — Heart Failure Medicines](#) - Patient-friendly overview of the medicines used to treat heart failure, including ARNI.
- [Cleveland Clinic — Sacubitril/Valsartan \(Entresto\)](#) - Plain-language drug page on how ARNI works, how to take it, and key cautions.
- [MedlinePlus — Sacubitril and Valsartan](#) - NIH/NLM drug page on side effects, the swelling warning, and pregnancy safety.
- [Heart Failure Society of America — Patient Resources](#) - Tools and tips for living well with heart failure and managing your medicines.



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Sources Used to Build This Guide

Every recommendation in this guide is grounded in one or more of the studies, guidelines, or trusted resources below. Short links are tracked so Dr. Ali can see which references patients are reading; nothing personally identifying is captured.

- [PARADIGM-HF — Sacubitril/Valsartan vs Enalapril in HF \(NEJM 2014\)](#) [Clinical Trial]
Landmark RCT (8,442 patients): 20% lower risk of cardiovascular death or heart failure hospitalization vs enalapril (HR 0.80). The trial that made ARNI a first-line heart failure medicine.
- [2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure](#) [Guideline]
Class 1 recommendation: ARNI is preferred over an ACE inhibitor or ARB in HFrEF. Names ARNI as one of the four core (pillar) heart failure medicines.
- [2023 ESC Focused Update — Heart Failure Guidelines](#) [Guideline]
European guideline confirming ARNI as a foundational HFrEF therapy alongside beta-blockers, MRA, and SGLT2 inhibitors.
- [ENTRESTO \(sacubitril/valsartan\) FDA Prescribing Information \(2024\)](#) [Drug Label]
Official FDA label: dosing (24/26, 49/51, 97/103 mg twice daily), 36-hour ACE-inhibitor washout, angioedema and pregnancy warnings, potassium and kidney monitoring.
- [Cleveland Clinic — Sacubitril/Valsartan \(Entresto\)](#) [Clinical]
Plain-language drug overview — how ARNI works, how to take it, and the ACE-inhibitor switch caution.
- [MedlinePlus — Sacubitril and Valsartan](#) [Clinical]
NIH/NLM patient drug page on side effects, the angioedema warning, and pregnancy safety.
- [American Heart Association — Medications Used to Treat Heart Failure](#) [Patient Education]
AHA patient-facing overview placing ARNI among the standard heart failure medicines.



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About This Guide

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Reviewer note: Reviewed: Cleveland Clinic, Mayo Clinic, AHA, MedlinePlus drug pages. This guide adds a how-it-works diagram, a PARADIGM-HF benefit chart, a 36-hour washout timeline, a side-effect monitoring table, and dose step-up cards — tied to the four-pillar heart failure plan.

Disclaimer

This guide is for educational purposes only and does not replace medical advice from your physician. Recommendations may not apply to every patient. Always follow the specific instructions of Dr. Ali and your care team. In an emergency call 911 or go to the nearest emergency department.



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