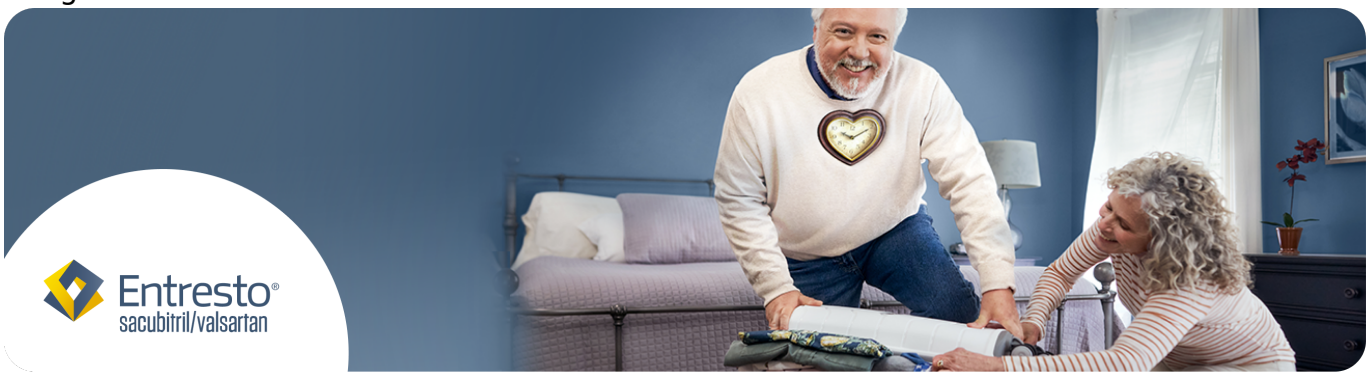
NOVARTIS

Entresto - Dosing & Administration - HCP

Prescribing information

Image



Image

ENTRESTO (sacubitril/valsartan) dosing and administration

ENTRESTO (sacubitril/valsartan) dosing

ENTRESTO is indicated in adult patients for the treatment of symptomatic chronic heart failure with reduced ejection fraction (HFrEF).

ENTRESTO is a film-coated tablet and combines two active ingredients:

- Sacubitril, a neprilysin inhibitor
- Valsartan, an angiotensin II receptor blocker (ARB)

Please refer to the Summary of Product Characteristics (SmPC) before prescribing ENTRESTO (sacubitril/valsartan).

Recommended dosing schedule for ENTRESTO (sacubitril/valsartan)

Flexible starting doses tailored to your patients' needs, with titration similar to ACEi (enalapril).[1-3]

Image

Low dose: 24/26 mg

Image

Mid dose: 49/51 mg

Image

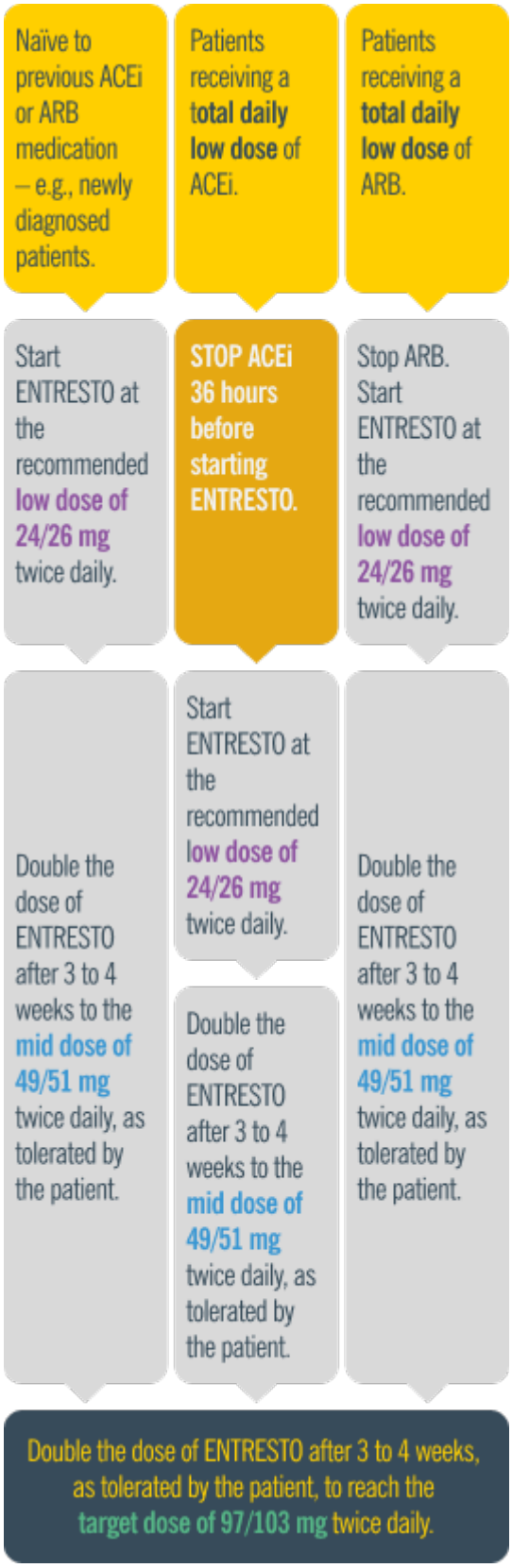
High dose: 97/103 mg

Switching from a low dose or not currently on ACEi or ARB to ENTRESTO (sacubitril/valsartan)

The starting dose of ENTRESTO and its titration schedule to target dose should be based on current treatment.[1-3]

Image


Naïve to previous ACEi or ARB medication – e.g., newly diagnosed patients.
Patients receiving a total daily low dose of ACEi.
Patients receiving a total daily low dose of ARB.
Start ENTRESTO at the recommended low dose of 24/26 mg twice daily.
STOP ACEi 36 hours before starting ENTRESTO.
Stop ARB. Start ENTRESTO at the recommended low dose of 24/26 mg twice daily.
Double the dose of ENTRESTO after 3 to 4 weeks to the mid dose of 49/51 mg twice daily, as tolerated by the patient.
Start ENTRESTO at the recommended low dose of 24/26 mg twice daily.
Double the dose of ENTRESTO after 3 to 4 weeks to the mid dose of 49/51 mg twice daily, as tolerated by the patient.
Double the dose of ENTRESTO after 3 to 4 weeks to the mid dose of 49/51 mg twice daily, as tolerated by the patient.
Double the dose of ENTRESTO after 3 to 4 weeks, as tolerated by the patient, to reach the target dose of 97/103 mg twice daily.
Image



A starting dose of 24/26 mg twice daily is recommended in patients on low-dose ACEi or ARB, or not previously on ACEi or ARB. Then, slow ENTRESTO dose titration doubling every 3 to 4 weeks as tolerated, to the target dosage of 97/103 mg twice daily.[1-3]

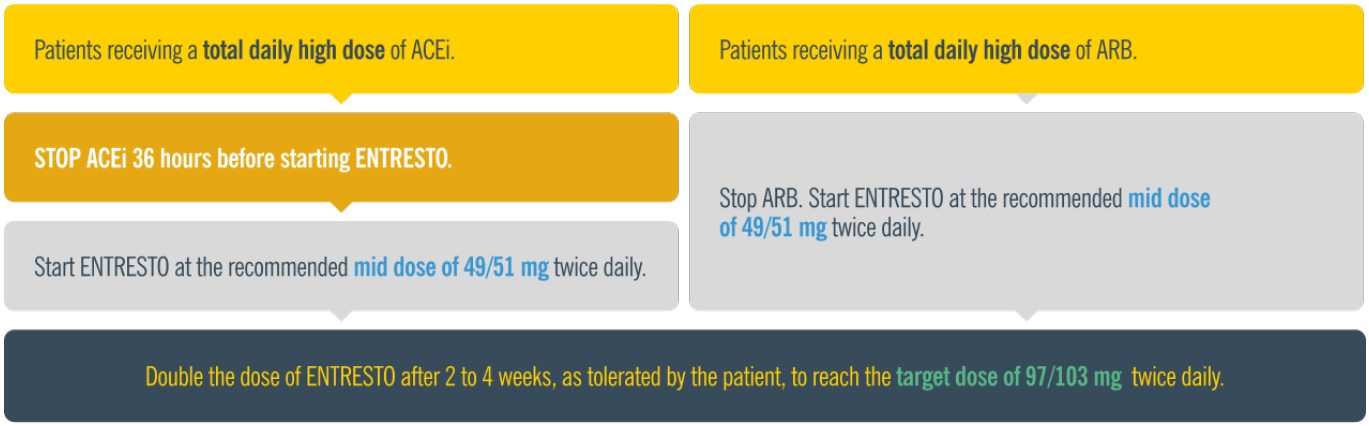
- **Low-dose ACEi:** total daily dose of ≤10 mg of enalapril or therapeutically equivalent dose of another ACEi (e.g., ramipril ≤5 mg)[1-3]

- **Low-dose ARB:** total daily dose of ≤160 mg valsartan or therapeutically equivalent dose of another ARB (e.g., candesartan ≤16 mg)[1-3]

Switching from a high dose of ACEi or ARB to ENTRESTO (sacubitril/valsartan)

The starting dose of ENTRESTO and its titration schedule to target dose should be based on current treatment.[1-3]

Image



- **High-dose ACEi:** total daily dose of >10 mg of enalapril or therapeutically equivalent dose of another ACEi (e.g., ramipril >5 mg)[3]

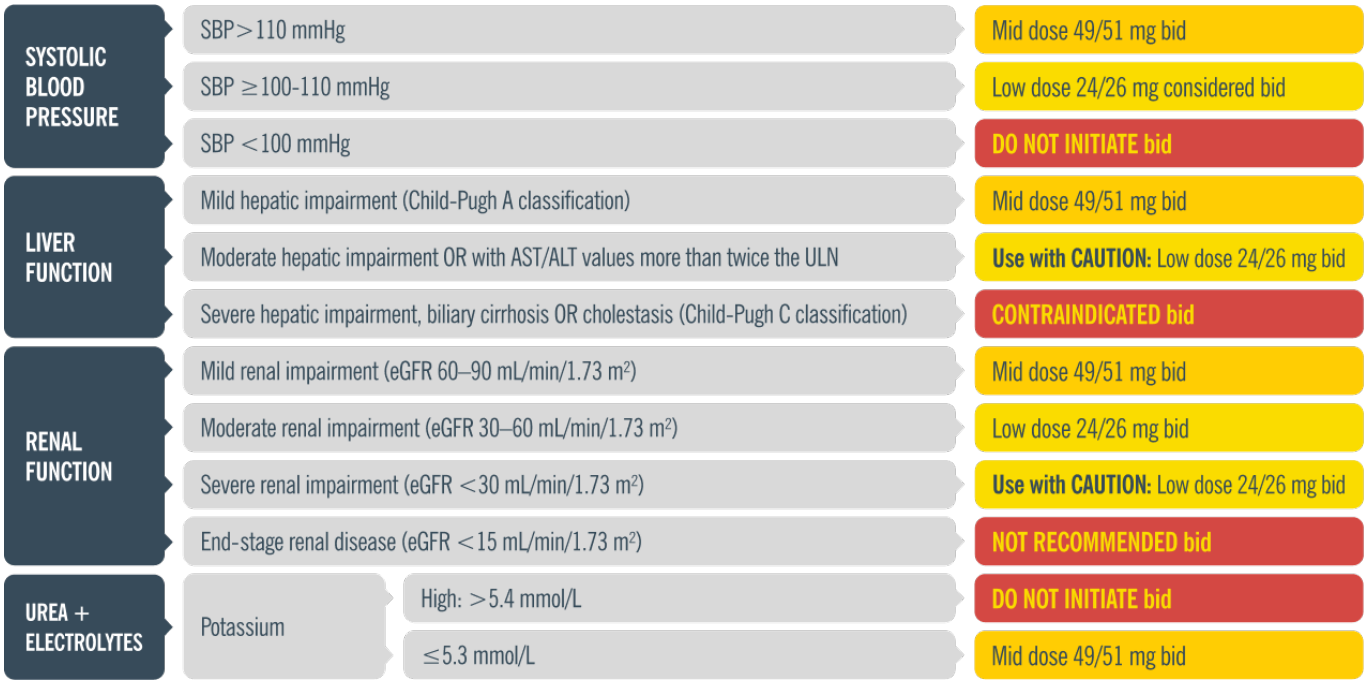
- **High-dose ARB:** total daily dose of >160 mg valsartan or therapeutically equivalent dose of another ARB (e.g., candesartan >16 mg)[3]

The combination of sacubitril/valsartan with an ACEi is contraindicated due to the increased risk of angioedema. Starting ENTRESTO after an ACEi requires the patient to undergo a 36-hour washout period to lower the angioedema risk.[1-3]

ENTRESTO should not be co-administered with another ARB containing medicinal product, since ENTRESTO contains the ARB valsartan. A 36-hour washout is NOT required for patients switching from an ARB to ENTRESTO.

ENTRESTO (sacubitril/valsartan) dosing considerations

Image



ENTRESTO (sacubitril/valsartan) and pregnancy

The use of ENTRESTO is not recommended during the first trimester of pregnancy and is contraindicated during the second and third trimesters of pregnancy.[1,2]

- Blood pressure dosing adjustments
- Renal function and dosing in patients with renal impairment
- Urea and electrolytes

Blood pressure dosing adjustments

If hypotension occurs, consider:

- Dose adjustment of concomitant medicinal products such as diuretics, concomitant antihypertensives and treatment of other causes of hypotension (e.g., hypovolaemia)

Please note: symptomatic hypotension is more likely to occur if the patient has been volume-depleted, e.g., by diuretic therapy, dietary salt restriction, diarrhoea or vomiting.[1,2]

Renal function and dosing in patients with renal impairment

When initiating therapy or during dose titration with ENTRESTO, renal function should be monitored routinely.[1,2]

Caution is required in patients with renal artery stenosis and monitoring of renal function is recommended because ENTRESTO may increase blood urea and serum creatinine levels in patients with bilateral or unilateral renal artery stenosis.[1,2]

Monitoring of renal function is recommended when initiating or modifying treatment in patients on ENTRESTO who are concomitantly taking NSAIDs.[1,2]

Patients with severe renal or moderate hepatic impairment should initiate Entresto at a low dose, doubling the dose after 3 to 4 weeks, as tolerated by the patient, to reach the target dose of 97/103 mg twice daily.

Patients with renal impairment with an eGFR <30 mL/min/1.73 m2 should be started with ENTRESTO 24/26 mg tablets twice daily; however, they may remain at heightened risk of developing hypotension.[1–3]

There is very limited clinical experience in patients with severe renal impairment (eGFR <30 mL/min/1.73 m2) and these patients may be at greatest risk of hypotension. There is no experience in patients with end-stage renal disease and use of ENTRESTO is not recommended.[1,2]

Urea and electrolytes

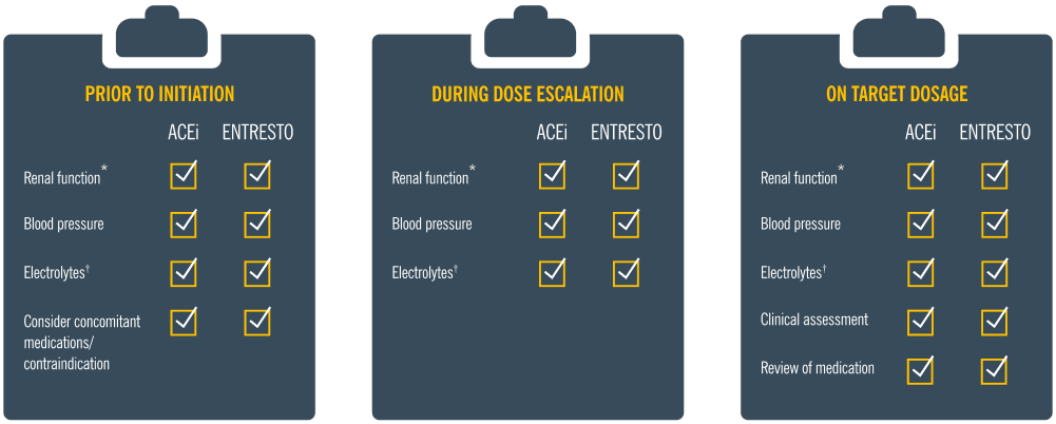
Monitoring of serum potassium is recommended, especially in patients with the following risk factors: renal impairment, diabetes mellitus or hypoaldosteronism or high-potassium diet or on mineralocorticoid antagonists.[1,2]

If patients experience clinically significant hyperkalaemia adjustment of concomitant medicinal products OR temporary down-titration OR discontinuation of ENTRESTO is recommended. If serum potassium level is >5.4 mmol/l, ENTRESTO discontinuation should be considered.[1,2]

Sodium and/or volume depletion should be corrected before starting treatment with ENTRESTO, however, such corrective action must be carefully weighed against the risk of volume overload.[1,2]

Monitoring for patients treated with ENTRESTO is similar to that for treatment with an ACEi (e.g., enalapril).

Image



*eGFR, urea, creatinine. †e.g., potassium, sodium.

Please refer to the Summary of Product Characteristics (SmPC) for all dosing considerations and contraindications prior to initiating ENTRESTO.
If there are any changes in renal function, blood pressure, electrolytes, or liver function while taking ENTRESTO please refer to the SmPC.

If patients experience tolerability issues (systolic blood pressure [SBP] ≤95 mmHg, symptomatic hypotension, hyperkalaemia, renal dysfunction), adjustment of concomitant medicinal products, temporary down–titration or discontinuation of Entresto is recommended.

Select Entresto special warnings and precautions.

Please visit the SmPC for all special warnings.

If a dose of ENTRESTO is missed, the patient should take the next dose at the scheduled

time.[1,2]

There is a potential for serious adverse drug reactions in breastfed infants from ENTRESTO. Hence, breastfeeding is not recommended during ENTRESTO treatment.[1,2]

Angioedema

ENTRESTO may cause angioedema. Angioedema associated with laryngeal oedema may be fatal.[1,2]

ENTRESTO has been associated with a higher rate of angioedema in Black patients and in patients with a prior history of angioedema. ENTRESTO should not be used in patients with hereditary angioedema.[1,2]

If angioedema occurs, discontinue ENTRESTO immediately, provide appropriate therapy and monitoring until complete and sustained resolution of signs and symptoms has occurred. ENTRESTO must not be re-administered.[1,2]

As patients with prior history may be at higher risk for angioedema, caution is recommended if Entresto is used.

Entresto is contraindicated in patients with a known history of angioedema related to previous ACE inhibitor or ARB therapy or with hereditary or idiopathic angioedema.

ENTRESTO (sacubitril/valsartan) drug interactions

Caution should be exercised when co-administering Entresto with statins or sildenafil or another PDE5 inhibitor.

Monitoring of renal function is recommended when initiating or modifying treatment in patients on Entresto who are taking NSAIDs concomitantly.

Entresto should not be co-administered with lithium or direct renin inhibitors such as aliskiren.

Please see ENTRESTO SmPC for further information.

Please click here for safety information

ACEi, angiotensin-converting enzyme inhibitor; ALT, alanine aminotransferase; ARB, angiotensin receptor blocker; AST, aspartate aminotransferase; bid, twice daily; ULN, upper limit of normal.

References:

1. ENTRESTO (sacubitril/valsartan) Summary of Product Characteristics.

2. Enalapril Summary of Product Characteristics. Electronic medicines compendium website, UK. Available at: https://www.medicines.org.uk/emc/product/561/smpc.

UK | October 2024 | FA-11283250

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Novartis online through the pharmacovigilance intake (PVI) tool at www.novartis.com/report, or alternatively email medinfo.uk@novartis.com or call 01276 698370.

Source URL:
https://www.pro.novartis.com/uk-en/medicines/cardio-metabolic/entresto/dosing