

SUMMARY

sacubitril/valsartan

**ENTRESTO 6 mg/6 mg,
15 mg/16 mg, 24 mg/26 mg,
49 mg/51 mg and
97 mg/103 mg,**

granules in capsules for opening and film-coated tablets

**Inclusion of new dosages and indication
extension**

**Original French opinion adopted by the Transparency Committee on 6
December 2023**

The legally binding text is the original French opinion version

Transparency Committee's Conclusions

Clinical Benefit

- ➔ Heart failure in children and adolescents is a condition capable of progressing to more advanced and severe stages with potentially life-threatening complications.
- ➔ This is a curative medicinal product.
- ➔ The efficacy/adverse effects ratio is high, with however an additional impact on morbidity-mortality or on quality of life for which there is no evidence to date, and with a product efficacy based in paediatrics on the extrapolation of the efficacy results in respect of the sacubitril/valsartan combination from adults to children.

This is a first-line treatment for children and adolescents who have symptomatic chronic heart failure with left ventricular systolic dysfunction in view of the therapies available

➔ Public health benefit

In view of:

- the seriousness of the condition and its low prevalence in paediatrics;
- the insufficiently met medical need;

- the partial response to the identified need with:
 - an additional impact on morbidity-mortality or on quality of life for which there is no evidence to date, but with a validated extrapolation of efficacy data of the sacubitril/valsartan combination to children using existing data from adults providing evidence of a reduction in cardiovascular morbidity-mortality;
 - an additional impact on the delivery of care with the provision of a new pharmaceutical form which are granules in capsules for opening suitable for paediatric use for children from 1 year of age;

ENTRESTO (sacubitril/valsartan) is likely to have an additional impact on public health.

Considering all of these elements, the Committee deems that the clinical benefit of ENTRESTO (sacubitril/valsartan), granules in capsules for opening and film-coated tablets, is substantial for children and adolescents aged one year or over for treatment of symptomatic chronic heart failure with left ventricular systolic dysfunction.

The Committee approves the inclusion of ENTRESTO (sacubitril/valsartan), granules in capsules for opening at the dosages of 6 mg/6 mg and 15 mg/16 mg, and the indication extension of ENTRESTO (sacubitril/valsartan), granules in capsules for opening and film-coated tablets, in the list of covered drugs for outpatients and in the list of covered drugs for inpatients for children and adolescents aged one year or over for treatment of symptomatic chronic heart failure with left ventricular systolic dysfunction and at the marketing authorisation dosages.

→ **Recommended reimbursement rate for inclusion in the list of covered drugs for outpatients: 65%**

Clinical Added Value

In view of:

- the extrapolation deemed to be valid of the efficacy data of the sacubitril/valsartan combination to children based on the results of the PARADIGM-HF study in adults which provided evidence of a reduction in cardiovascular morbidity-mortality;
- an insufficiently met medical need with therapeutic alternatives having a low level of evidence in children and with pharmaceutical forms not suited to paediatrics;
- the provision of a pharmaceutical form of the sacubitril/valsartan combination suitable for children aged from 1 year;
- an acceptable safety profile in children, which is comparable to that already known in adults;

but in the light of:

- the lack of evidence of superiority of the sacubitril/valsartan combination in relation to enalapril on clinical morbidity-mortality outcome measures in the PANORAMA-HF paediatric study, with however results deemed clinically relevant in both treatment groups based on experts opinion;

- suboptimal representativeness of the studied population in the PANORAMA-HF study with a small sample of children aged under 1 year (population excluded from the marketing authorisation), the exclusion of the perioperative period (pre-heart surgery, pre-heart transplantation and immediate postoperative period) and the exclusion of congenital hypertrophic and restrictive cardiomyopathies which are rare but largely relevant to paediatric heart failure;

the Committee deems that ENTRESTO (sacubitril/valsartan), granules in capsules for opening at the dosages of 6 mg/6 mg and 15 mg/16 mg and film-coated tablets at the dosages of 24 mg/26 mg, 49 mg/51 mg and 97 mg/103 mg, provides minor clinical added value (CAV IV) in the current therapeutic strategy in respect of symptomatic chronic heart failure with left ventricular systolic dysfunction in children and adolescents aged one year or overolder.