HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
8 DECEMBER 2021

The legally binding text is the original French opinion version

alirocumab
PRALUENT 75 mg, 150 mg and 300 mg solution for injection

Re-evaluation

Key points

Favourable opinion for reimbursement in the event of contraindication or known intolerance to statins and/or ezetimibe:

- in adults with heterozygous familial hypercholesterolaemia, at very high cardiovascular risk, inadequately controlled and requiring LDL-apheresis treatment,

- in adults with inadequately controlled (LDL-c ≥ 0.7 g/L) atherosclerotic cardiovascular disease established by a history of ACS (secondary prevention),

in combination with an optimised lipid-lowering therapy or alone in the event of contraindication or known intolerance to both statins and ezetimibe.

What therapeutic improvement?

No clinical added value in the therapeutic strategy.

Role in the care pathway?

Role of the medicinal product in the care pathway

In the event of contraindication or known intolerance to statins and/or ezetimibe, PRALUENT (alirocumab) should be used:

- in adults with heterozygous familial hypercholesterolaemia, at very high cardiovascular risk, inadequately controlled and requiring LDL-apheresis treatment,

- in adults with inadequately controlled (LDL-c ≥ 0.7 g/L) atherosclerotic cardiovascular disease established by a history of ACS (secondary prevention),

in combination with an optimised lipid-lowering therapy or alone in the event of contraindication or known intolerance to both statins and ezetimibe.

As a reminder, optimised lipid-lowering treatment for patients with a contraindication or known intolerance to statins and/or ezetimibe is therefore defined as follows:
- the maximum tolerated dose of a statin, alone in the event of contraindication or intolerance to ezetimibe;
- ezetimibe in the event of contraindication or known intolerance to statins.

Special recommendations

The Committee warns that there is a risk of misuse in populations not eligible for treatment, including, in particular:
- patients who are not at very high cardiovascular risk,
- patients not receiving an optimised treatment where this is possible.

The Committee will pay particularly close attention to the real conditions of use of PRALUENT (alirocumab) at its next assessments.

COMMITTEE'S CONCLUSIONS

Considering all of this information and further to debate and voting, the Committee considers:

Clinical benefit

◗ The cerebro- and cardiovascular diseases promoted by hypercholesterolaemia and mixed dyslipidaemia can be life-threatening as a result of complications, and impact quality of life as a result of disabling sequelae.

◗ These proprietary medicinal products are part of a preventive treatment regimen.

◗ The efficacy/adverse effects ratio is high in the event of contraindication or known intolerance to statins and/or ezetimibe:
- in adults with heterozygous familial hypercholesterolaemia, at very high cardiovascular risk, inadequately controlled and requiring LDL-apheresis treatment;
- in adults with inadequately controlled (LDL-c ≥ 0.7 g/L) atherosclerotic cardiovascular disease established by a history of ACS (secondary prevention),

in combination with an optimised lipid-lowering therapy or alone in the event of contraindication or known intolerance to both statins and ezetimibe.

◗ There are therapeutic alternatives (see section 05 Clinically relevant comparators).

◗ As a reminder, PRALUENT (alirocumab) should be used <u>as third-line treatment</u> as an adjunct to lifestyle and dietary measures and in combination with an optimised lipid-lowering treatment (including at least one statin at the maximum tolerated dose + ezetimibe).
In the event of contraindication or known intolerance to statins and/or ezetimibe, PRALUENT (alirocumab) should be used:
- in adults with heterozygous familial hypercholesterolaemia, at very high cardiovascular risk, inadequately controlled and requiring LDL-apheresis treatment;
- in adults with inadequately controlled (LDL-c ≥ 0.7 g/L) atherosclerotic cardiovascular disease established by a history of ACS (secondary prevention),

in combination with an optimised lipid-lowering therapy or alone in the event of contraindication or known intolerance to both statins and ezetimibe.

Optimised lipid-lowering treatment for patients with a contraindication or known intolerance to statins and/or ezetimibe is therefore defined as follows:
- the maximum tolerated dose of a statin, alone in the event of contraindication or intolerance to ezetimibe;
- ezetimide in the event of contraindication or known intolerance to statins.

<u>Public health impact</u>

Considering:
- the seriousness of cardiovascular diseases promoted by inadequately controlled LDL-c levels in secondary prevention, or by heterozygous familial hypercholesterolaemia, and their long-term consequences on the high risk of cardiovascular diseases and/or death;
- the low prevalence of patients with a contraindication or known intolerance to statins and/or ezetimibe;
- the medical need:
    - identified and unmet in inadequately controlled patients with a contraindication or known intolerance to both statins and ezetimibe;
    - identified and partially met in inadequately controlled patients with a contraindication or known intolerance to statins or ezetimibe;
- the absence of an additional response to the identified medical need due to the demonstrated impact on biological endpoints alone (LDL-c levels) and in an exploratory manner in this

subpopulation on morbidity and mortality, but the absence of a demonstrated additional impact on morbidity and mortality, and on quality of life;
- the absence of demonstration of an impact on the organisation of care,

PRALUENT (alirocumab) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of PRALUENT (alirocumab) is <u>substantial</u> in the event of contraindication or known intolerance to statins and/or ezetimibe:
- **in adults with heterozygous familial hypercholesterolaemia, at very high cardiovascular risk, inadequately controlled and requiring LDL-apheresis treatment;**
- **in adults with inadequately controlled (LDL-c ≥ 0.7 g/L) atherosclerotic cardiovascular disease established by a history of ACS (secondary prevention),**

in combination with an optimised lipid-lowering therapy or alone in the event of contraindication or known intolerance to both statins and ezetimibe.

The Committee issues a favourable opinion for inclusion in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use, at MA dosages, in the event of contraindication or known intolerance to statins and/or ezetimibe:
- **in adults with heterozygous familial hypercholesterolaemia, at very high cardiovascular risk, inadequately controlled and requiring LDL-apheresis treatment;**
- **in adults with inadequately controlled (LDL-c ≥ 0.7 g/L) atherosclerotic cardiovascular disease established by a history of ACS (secondary prevention),**

in combination with an optimised lipid-lowering therapy or alone in the event of contraindication or known intolerance to both statins and ezetimibe.

- **Recommended reimbursement rate: 65%**

Clinical Added Value

Considering:

- Initial data having demonstrated an effect of alirocumab on cardiovascular morbidity and mortality versus placebo, via a composite endpoint, in patients in secondary prevention with a history of recent ACS (ODYSSEY OUTCOMES study),
- But in view of the absence of robust data demonstrating a benefit in terms of morbidity and mortality in patients with a contraindication or intolerance to statins and/or ezetimibe,

the Committee considers that PRALUENT (alirocumab) in combination with an optimised lipid-lowering therapy or in the event of known intolerance provides no clinical added value (CAV V) in the event of contraindication or known intolerance to statins and/or ezetimibe:

- **in adults with heterozygous familial hypercholesterolaemia, at very high cardiovascular risk, inadequately controlled and requiring LDL-apheresis treatment,**
- **in adults with inadequately controlled (LDL-c ≥ 0.7 g/L) atherosclerotic cardiovascular disease established by a history of ACS (secondary prevention),**

in combination with an optimised lipid-lowering therapy Erreur ! Signet non défini. **or alone in the event of contraindication or known intolerance to both statins and ezetimibe.**