SUMMARY

évolocumab

REPATHA 140 mg,

solution for injection in pre-filled pen

Reassessment

Original French opinion adopted by the Transparency Committee on 27 March 2024

The legally binding text is the original French opinion version

Summary of opinion

Approval of retention of reimbursement for the following indications:

➔ **Homozygous familial hypercholesterolaemia**

In adults and children aged 10 years and over with homozygous familial hypercholesterolaemia (HoFH) in combination with other lipid-lowering therapies

➔ **Heterozygous familial hypercholesterolaemia**

In patients with heterozygous familial hypercholesterolaemia (HeFH):

- Adults, at a very high cardiovascular risk, insufficiently controlled with optimised lipid-lowering treatment and requiring LDL apheresis treatment:
  - In combination with optimised lipid-lowering treatment;
  - Or as monotherapy in cases of contraindication or established intolerance both to statins and ezetimibe.
- Children and adolescents aged 10 years and over insufficiently controlled (LDL-C > 130 g/L) with the maximum tolerated dose of a lipid-lowering treatment, as an adjunct to diet:
  - In combination with optimised lipid-lowering treatment;
  - Or as monotherapy in cases of contraindication or established intolerance both to statins and ezetimibe.

➔ **Established atherosclerotic cardiovascular disease**

In adults with established atherosclerotic cardiovascular disease with a history of symptomatic myocardial infarction (MI), non-haemorrhagic stroke (NHS) and/or peripheral arterial disease (PAD) (secondary prevention), whose disease is uncontrolled (LDL-C ≥ 0.7 g/L) despite optimised lipid-lowering treatment:

- In combination with optimised lipid-lowering treatment;
- Or as monotherapy in cases of contraindication or established intolerance both to statins and ezetimibe.

Transparency Committee's Conclusions

Clinical Benefit

- Cardiovascular disease and stroke promoted by hypercholesterolaemia and mixed dyslipidaemia are potentially life-threatening due to complications, and impact quality of life due to disabling sequelae.
- This is a preventive medicinal product.
- The efficacy/adverse effects ratio remains high.
- There are therapeutic alternatives.
- This is a third-line treatment in view of the therapies available, for:
  - Adults and paediatric patients aged 10 years and over with homozygous familial hypercholesterolaemia (HoFH) in combination with other lipid-lowering therapies;
  - Patients with heterozygous familial hypercholesterolaemia (HeFH):
    - Adults, at a very high cardiovascular risk, insufficiently controlled with optimised lipid-lowering treatment and requiring LDL apheresis treatment:
      - in combination with optimised lipid-lowering treatment;
      - or as monotherapy in cases of contraindication or established intolerance both to statins and ezetimibe.
    - Children and adolescents aged 10 years and over, insufficiently controlled (LDL-C > 1.30 g/L) with the maximum tolerated dose of a lipid-lowering treatment, as an adjunct to diet:
      - in combination with optimised lipid-lowering treatment;
      - or as monotherapy in cases of contraindication or established intolerance both to statins and ezetimibe.
  - Adults with established atherosclerotic cardiovascular disease with a history of symptomatic myocardial infarction (MI), non-haemorrhagic stroke (NHS) and/or peripheral arterial disease (PAD) (secondary prevention), whose disease is uncontrolled (LDL-C ≥ 0.7 g/L) despite optimised lipid-lowering treatment:
    - in combination with optimised lipid-lowering treatment;
    - or as monotherapy in cases of contraindication or established intolerance both to statins and ezetimibe.

Public health benefit

In view of the retention of the previous conclusions, namely:

- the seriousness of cardiovascular disease promoted by uncontrolled LDL-C levels in secondary prevention, or by heterozygous and homozygous familial hypercholesterolaemia, and its long-term consequences on the high risk of cardiovascular disease and/or death;
- the high prevalence of cardiovascular disease promoted by dyslipidaemia;
- the partially met medical need;
- the lack of additional response to the identified medical need on account of the evidence of an impact on cardiovascular morbidity but in the absence of evidence of an additional impact on mortality and on quality of life in the whole marketing authorisation population;
- the lack of evidence of an impact on delivery of care;

REPATHA (evolocumab) is unlikely to have an additional impact on public health.

Considering all of these elements, the Committee deems that the clinical benefit of REPATHA (evolocumab) 140 mg, solution for injection in pre-filled pen, remains substantial in the following indications:

➔ **Homozygous familial hypercholesterolaemia**

In adults and children aged 10 years and over with homozygous familial hypercholesterolaemia (HoFH) in combination with other lipid-lowering therapies

➔ **Heterozygous familial hypercholesterolaemia**

In patients with heterozygous familial hypercholesterolaemia (HeFH):

- Adults, at a very high cardiovascular risk, insufficiently controlled with optimised lipid-lowering treatment and requiring LDL apheresis treatment:
  - In combination with optimised lipid-lowering treatment;
  - Or as monotherapy in cases of contraindication or established intolerance both to statins and ezetimibe.
- Children and adolescents aged 10 years and over insufficiently controlled (LDL-C > 130 g/L) with the maximum tolerated dose of a lipid-lowering treatment, as an adjunct to diet:
  - In combination with optimised lipid-lowering treatment;
  - Or as monotherapy in cases of contraindication or established intolerance both to statins and ezetimibe.

➔ **Established atherosclerotic cardiovascular disease**

In adults with established atherosclerotic cardiovascular disease with a history of symptomatic myocardial infarction (MI), non-haemorrhagic stroke (NHS) and/or peripheral arterial disease (PAD) (secondary prevention), whose disease is uncontrolled (LDL-C ≥ 0.7 g/L) despite optimised lipid-lowering treatment:

- In combination with optimised lipid-lowering treatment;
- Or as monotherapy in cases of contraindication or established intolerance both to statins and ezetimibe.

The Committee approves continued inclusion of REPATHA (evolocumab) 140 mg, solution for injection in pre-filled pen, in the list of covered drugs for outpatients and in the list of covered drugs for inpatients in the indication mentioned above and at the dosages of the marketing authorisation.

Clinical Added Value

The new data presented based on exploratory and interim analyses of the FOURIER-OLE extension study with a median treatment follow-up of 5 years are not of a nature to modify the Committee's previous conclusions, namely:

➔ **Homozygous familial hypercholesterolaemia**

REPATHA (evolocumab) provides minor clinical added value (**CAV IV**) in the therapeutic strategy for adults and children aged 10 years and over with homozygous familial hypercholesterolaemia (HoFH) in combination with other lipid-lowering therapies (opinion of 16/12/2015 and 06/04/2022).

➔ **Heterozygous familial hypercholesterolaemia**

REPATHA (evolocumab) provides no clinical added value (**CAV V**) in the therapeutic strategy of patients with heterozygous familial hypercholesterolaemia (HeFH):

- Adults, at a very high cardiovascular risk, insufficiently controlled with optimised lipid-lowering treatment and requiring LDL apheresis treatment:
  - In combination with optimised lipid-lowering treatment;
  - Or as monotherapy in cases of contraindication or established intolerance both to statins and ezetimibe.
- Children and adolescents aged 10 years and over insufficiently controlled (LDL-C > 130 g/L) with the maximum tolerated dose of a lipid-lowering treatment, as an adjunct to diet:
  - In combination with optimised lipid-lowering treatment;
  - Or as monotherapy in cases of contraindication or established intolerance both to statins and ezetimibe.

➔ **Established atherosclerotic cardiovascular disease (secondary prevention)**

REPATHA (evolocumab) provides no clinical added value (**CAV V**) in the therapeutic strategy of adults with established atherosclerotic cardiovascular disease with a history of symptomatic myocardial infarction (MI), non-haemorrhagic stroke (NHS) and/or peripheral arterial disease (PAD) (secondary prevention), whose disease is uncontrolled (LDL-C ≥ 0.7 g/L) despite optimised lipid-lowering treatment:

- In combination with optimised lipid-lowering treatment;
- Or as monotherapy in cases of contraindication or established intolerance both to statins and ezetimibe.