SUMMARY

artesunate

ARTESUNATE AMIVAS 110 mg

powder and solvent for solution for injection

First listing

Original French opinion adopted by the Transparency Committee on 3 July 2024

The legally binding text is the original French opinion version

Summary of opinion

Favourable opinion for reimbursement in "the initial treatment of severe malaria in adults and children".

Transparency Committee's conclusions

Clinical Benefit

- Malaria is a serious disease, with *P. falciparum* forms being potentially fatal. Strains that are resistant to conventional treatments are increasingly common. This parasitic disease is the subject of a WHO control programme.
- This is a curative medicinal product.
- The efficacy/adverse effects ratio is high.
- It is a first-line treatment. The WHO now recommends IV artesunate as the first-line treatment for severe malaria, due to its superior efficacy and safety compared to IV quinine.
- There is a medicinal alternative: MALACEF (artesunate) available in France since the end of May 2011, via the named-patient temporary authorisation for use mechanism (ATUn), then as part of the compassionate access mechanism (AAC). The use of quinine during a severe malaria episode remains possible in some situations, such as when immediate treatment with artesunate is not possible (unavailability of the drug), in the event of known allergy to artemisinin or when the patient has returned from an artesunate-resistant region (South-East Asia).

➔ Public health benefit

Considering:

- the seriousness of the disease due to its potentially fatal nature;
- the partially met medical need in the initial treatment of severe malaria in adults and children;
- the response to the identified need given:
  - a demonstrated additional impact on mortality of artesunate compared to quinine (former reference treatment) but for which the impact in terms of reduction in the incidence of neurological sequelae remains to be demonstrated;
  - an expected impact on the organisation of care due to an administration method that is generally simpler, shorter and more effective (with a rapid reduction in parasite levels) and a better safety than quinine, which needs to be administered under strict monitoring due to its side effects in order to prevent complications;

ARTESUNATE AMIVAS (artesunate) is likely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of ARTESUNATE AMIVAS (artesunate) is substantial in the MA indication.

The Committee issues a favourable opinion for inclusion of ARTESUNATE AMIVAS (artesunate) in the list of covered drugs for inpatients approved for use in the MA indication and at the MA dosages.

Clinical Added Value

Considering:

- the partially met medical need in the initial treatment of severe malaria in adults and children;
- the effect size of artesunate in terms of reduction in hospital mortality compared to quinine, in patients with a severe form of *P. falciparum* malaria, which was statistically significant in:
  - the ITT population of the SEAQUAMAT trial (1,259 adults and 202 children < 15 years from Asia): 14.7% (107/730) versus 22.4% (164/731), i.e. an HR = 0.60, $CI_{95\%}$ = [0.45; 0.79], p = 0.0002;
  - the ITT population of the AQUAMAT trial (5,425 children < 15 years from Africa): 8.5% (230/2,712) versus 10.9% (297/2,713), i.e. an OR = 0.75; $CI_{95\%}$ = [0.63; 0.90], p = 0.0022;
- a safety profile that is satisfactory but marked by cases of anaemia, haemoglobinuria and blackwater fever in clinical trials. The important potential risk (risk management plan) is reproductive toxicity (particularly during the first trimester of pregnancy);

but:

- the transposability of the results limited to the *P. falciparum* species isolated in clinical trials only; but which remains the species of particular concern since it causes potentially serious or even fatal forms;
- the lack of evidence of an impact on reduction in the incidence of neurological sequelae (SEAQUAMAT and AQUAMAT trials);

the Committee deems that ARTESUNATE AMIVAS (artesunate) provides a moderate clinical added value (CAV III) compared to IV quinine in the initial treatment of severe malaria in adults and children.