Vaccine
Sector: Hospital

HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
3 NOVEMBER 2021

The legally binding text is the original French opinion version

Dengue quadrivalent vaccine (live, attenuated)
DENGVAXIA powder and solvent for solution for injection

First assessment

Key points

Favourable opinion for reimbursement in the prevention of dengue disease caused by dengue virus serotypes 1, 2, 3 and 4 in individuals 9 to 45 years of age **with previous dengue infection, living in endemic regions and only in the populations recommended by the current vaccine strategy.**

The Committee considers that access to an effective and validated diagnostic test to confirm previous dengue infection is essential.

What therapeutic improvement?

No clinical added value in the prevention of symptomatic virologically-confirmed dengue infections.

Role in the care pathway?

In its vaccine recommendations published in 2019, the HAS does not recommend the use of DENGVAXIA (Dengue quadrivalent vaccine [live, attenuated]):

- For individuals living in or travelling to Reunion island;
- For individuals living in French territories in America (except for those providing documented evidence of confirmed infection);
- For individuals travelling to French territories in America;
- For individuals living in or travelling to Mayotte.

The HAS considers that vaccination with the DENGVAXIA vaccine may be offered to individuals living in French territories in America and providing documented evidence of previous virologically-confirmed dengue virus infection.

This HAS position may be revised in the future, firstly in the event of a resumption of active circulation of dengue disease in French territories in America or depending on the evolution of the epidemiology of dengue disease on Reunion Island and in Mayotte, and secondly, if a test, whose performance for the assessment of past dengue infection is validated by an independent evaluation, becomes available .

The HAS recommends the conduct of a study assessing the seroprevalence in children aged 9 to 18 years in the French Caribbean region.

Role of the medicinal product in the care pathway

The Transparency Committee considers that DENGVAXIA dengue quadrivalent vaccine (live, attenuated) must be used in accordance with its MA and following current vaccine recommendations. It should be used in the prevention of dengue disease caused by dengue virus serotypes 1, 2, 3 and 4 in individuals 9 to 45 years of age with previous dengue infection, living in endemic regions. The Committee considers that, for this use, access to an effective and validated diagnostic test to confirm previous dengue infection is essential.

It highlights that the conditions of use of this vaccine are not optimal due to the current absence of a robust and validated test to diagnose previous dengue virus infection and the additional risk of virologically-confirmed dengue disease leading to hospitalisation or severe virologically-confirmed dengue disease if a seronegative individual is vaccinated (false positive).

Special recommendations

The Transparency Committee supports the request formulated in the HAS vaccine recommendations of January and March 2019 to conduct a study assessing the seroprevalence in children aged 9 to 18 years in the French Caribbean region.

In addition, it highlights that it will re-evaluate this opinion if the vaccine recommendations relative to the dengue disease control strategy, particularly in French overseas regions, are revised, and within a maximum period of 2 years.

COMMITTEE'S CONCLUSIONS

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

Clinical benefit

◗ Dengue disease is a viral disease transmitted by mosquitoes in tropical and subtropical regions, which, in rare cases (1% of symptomatic cases) can progress to potentially fatal (estimated fatality rate of around 0.5%) severe or haemorrhagic forms. Severe dengue disease occurs more frequently in children under the age of 15 years.

◗ The medicinal product DENGVAXIA dengue quadrivalent vaccine (live, attenuated) is a preventive treatment.

◗ The efficacy (immunogenicity)/adverse effects ratio is high in individuals aged 9 to 45 years with previous dengue infection (seropositive), living in endemic regions, pending the availability of a robust and validated dengue diagnostic test.

◗ There are no vaccine or medicinal alternatives.

◗ DENGVAXIA dengue quadrivalent vaccine (live, attenuated) can be used in accordance with its MA in the context of current vaccine recommendations.

Public health impact

Considering:

- the potential seriousness of dengue in endemic regions and its seroprevalence of more than 90% in the French Caribbean and around 70% in French Guiana,
- the unmet medical need apart from vector transmission control methods,
- an expected impact of the medicinal product DENGVAXIA on reduction of the incidence of symptomatic VCD and on the associated morbidity and mortality (hospitalisation and severe form) in view of the available immunogenicity, safety and efficacy data,
- the expected impact on the organisation of care in endemic regions,
- but due to the current absence of a robust and validated test to diagnose previous dengue virus infection and the additional risk of virologically-confirmed dengue disease leading to hospitalisation or severe virologically-confirmed dengue disease in the event of vaccination of a seronegative individual (false positive),

DENGVAXIA dengue quadrivalent vaccine (live, attenuated) is unlikely to have an impact on public health, to prevent dengue disease.

Considering all these elements, the Committee deems that the clinical benefit of DENGVAXIA is low in the prevention of dengue disease caused by dengue virus serotypes 1, 2, 3 and 4 in individuals 9 to 45 years of age with previous dengue infection, living in endemic regions only in the populations recommended by the HAS in 2019, unless a validated diagnostic test to confirm previous dengue infection is funded.

The Committee issues a favourable opinion for inclusion in the hospital formulary list of reimbursed proprietary medicinal products approved for use in the prevention of dengue disease caused by dengue virus serotypes 1, 2, 3 and 4 in individuals 9 to 45 years of age with previous dengue infection, living in endemic regions and only in the populations recommended by the HAS in 2019 and at the MA dosages.

The Committee highlights that it considers that access to an effective and validated diagnostic test to confirm previous dengue infection is essential.

Clinical Added Value

Considering:

- **clinical data having demonstrated a vaccine efficacy (relative reduction in symptomatic forms of virologically-confirmed dengue disease of around 60%) irrespective of the severity and serotype of dengue virus infection,**

But taking into account:

- **the additional risk of virologically-confirmed dengue disease leading to hospitalisation or severe virologically-confirmed dengue disease in seronegative individuals (at the time of vaccination),**
- **the difficulties in identifying subjects with previous dengue virus infection (seropositive) in the absence of a robust and validated diagnostic test,**

the Transparency Committee considers that, on the basis of currently available data, DENGVAXIA dengue quadrivalent vaccine (live, attenuated) provides no clinical added value (CAV V) in the prevention of dengue disease in individuals 9 to 45 years of age with previous dengue infection, living in endemic regions.