SUMMARY

Four-component live attenuated nasal influenza vaccine

FLUENZ TETRA,

suspension for nasal spray

New indication and reassessment

Original French opinion adopted by the Transparency Committee on 20 December 2023

The legally binding text is the original French opinion version

Transparency Committee's Conclusions

Clinical Benefit

Children with comorbidities

- Influenza is a highly contagious acute viral illness. Potentially serious complications occur more readily in people weakened by underlying conditions and/or over 65 years of age.
- The proprietary medicinal product FLUENZ TETRA (four-component live attenuated nasal influenza vaccine) is a preventive medicinal product.
- The efficacy (immunogenicity)/adverse effects ratio is high.
- There are alternative vaccines, namely FLUARIXTETRA, FLUCELVAX TETRA, INFLUVAC TETRA and VAXIGRIPTETRA.
- FLUENZ TETRA (four-component live attenuated nasal influenza vaccine) may be used according to its marketing authorisation within the scope of the vaccination guidelines in force.

Public health benefit

In view of:

- the frequency (2.5 million people affected each year) and the severity profile of influenza which can cause serious complications in particular in people with specific risk factors (almost 3,000 severe cases admitted to intensive care departments for the 2017-2018 season),
- the public health objective of lowering morbidity and mortality from this infection,
- the fact that vaccination is the most effective prevention tool against influenza and its complications,

- the objective of improving vaccination coverage to reach at least 75% in vaccination target populations,
- the medical need to expand the range available in order to be able to ensure the seasonal vaccination of all recommended populations in future influenza seasons,
- the comparable immunogenicity and safety between the four-component influenza vaccines available,
- the expected impact of vaccination on the delivery of care,
- the expected additional impact on the care and/or life pathway on account of its intranasal route of administration allowing better acceptability of this vaccine among children given that needles are not used.

FLUENZ TETRA is likely to have an additional impact on public health in the same way as the other four-component vaccines available (FLUARIXTETRA, FLUCELVAX TETRA, INFLUVAC TETRA and VAXIGRIPTETRA) for infants and children over 2 years of age to prevent influenza. This impact remains dependent, on one hand, on achieving sufficient vaccination coverage in the target populations and, on the other, on the protection provided by the seasonal vaccine against circulating viral strains.

Considering all of these elements, the Committee deems that the clinical benefit of FLUENZ TETRA (four-component live attenuated nasal influenza vaccine), remains substantial for seasonal influenza prevention in children with comorbidities from 2 to 17 years of age, according to the HCSP guidelines in force of 10 July 2014.

The Committee approves inclusions in the list of drugs covered for outpatients and continued inclusion in the list of covered drugs for inpatients of FLUENZ TETRA (four-component live attenuated nasal influenza vaccine) for seasonal influenza prevention in children with comorbidities from 2 to 17 years of age, according to the HCSP guidelines in force of 10 July 2014 and at the MA dosages.

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

Children without comorbidities

- ➔ Influenza is a highly contagious acute viral illness. Potentially serious complications occur more readily in people weakened by underlying conditions and/or over 65 years of age.
- ➔ The proprietary medicinal product FLUENZ TETRA (four-component live attenuated nasal influenza vaccine) is a preventive medicinal product.
- ➔ The efficacy (immunogenicity)/adverse effect ratio is significant.
- ➔ There are alternative vaccines, namely FLUARIXTETRA, FLUCELVAX TETRA, INFLUVAC TETRA and VAXIGRIPTETRA.
- ➔ FLUENZ TETRA (four-component live attenuated nasal influenza vaccine) may be used according to its marketing authorisation within the scope of the vaccination guidelines in force.

➔ Public health benefit

Considering:

- the frequency (2.5 million people affected each year) and the severity profile of influenza which can cause serious complications in particular in people with specific risk factors (almost 3,000 severe cases admitted to intensive care departments for the 2017-2018 season),
- the public health objective of lowering morbidity and mortality from this infection,
- the fact that vaccination is the most effective prevention tool against influenza and its complications,
- the objective of improving vaccination coverage to reach at least 75% in vaccination target populations,
- the medical need to expand the range available in order to be able to ensure the seasonal vaccination of all recommended populations in future influenza seasons,
- the comparable immunogenicity and safety between the four-component influenza vaccines available,
- the expected impact of vaccination on the delivery of care,
- the expected additional impact on the care and/or life pathway on account of its intranasal route of administration allowing better acceptability of this vaccine among children given that needles are not used.

FLUENZ TETRA is likely to have an additional impact on public health in the same way as the other four-component vaccines available (FLUARIXTETRA, FLUCELVAX TETRA, INFLUVAC TETRA and VAXIGRIPTETRA) for infants and children over 2 years of age to prevent influenza. This impact remains dependent, on one hand, on achieving sufficient vaccination coverage in the target populations and, on the other, on the protection provided by the seasonal vaccine against circulating viral strains.

Considering all of these elements, the Committee deems that the clinical benefit of FLUENZ TETRA (four-component live attenuated nasal influenza vaccine), is substantial for seasonal influenza prevention in children without comorbidities from 2 to 17 years of age, according to the HAS guidelines in force of 2 February 2023.

The Committee approves inclusions in the list of drugs covered for outpatients and continued inclusion in the list of covered drugs for inpatients of FLUENZ TETRA (four-component live attenuated nasal influenza vaccine) for seasonal influenza prevention in children without comorbidities from 2 to 17 years of age, according to the HAS guidelines in force of 2 February 2023 and at the MA dosages.

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

Clinical Added Value

Children with comorbidities

In the light of the data available, the Committee deems that FLUENZ TETRA (four-component live attenuated nasal influenza vaccine) provides no clinical added value (CAV V) for seasonal influenza prevention in children with comorbidities from 2 to 17 years of age, according to the HCSP guidelines in force of 10 July 2014.

Children without comorbidities

In view of:

- the non-inferior immunogenicity induced by FLUENZ TETRA (four-component live attenuated nasal influenza vaccine) to that of three-component live attenuated influenza vaccine (FLUENZ) against the three common strains in both vaccines, with a superior immune response against the additional B strain and a satisfactory safety profile (MI-CP208 study);
- the lack of specific clinical data with FLUENZ TETRA vaccine, the clinical efficacy of which is extrapolated from the three-component vaccine FLUENZ;
- the evidence of vaccination efficacy (VE) with live attenuated vaccines in lowering the incidence of laboratory-confirmed influenza cases (VE of 78%, $CI_{95\%}$ = [59; 89]) and influenza syndromes (VE of 31%, $CI_{95\%}$ = [20; 40]) based on the Cochrane review of 2018;
- the evidence of superiority of the three-component live attenuated nasal vaccine in relation to the three-component inactivated vaccine in terms of lowering the incidence of laboratory-confirmed influenza cases: RR of influenza (inactivate versus live attenuated) = 0.52, $CI_{95\%}$ = [0.22; 0.82] (meta-analysis by Minozzi et al. 2022);
- the possible benefit of a four-component live attenuated nasal influenza vaccine in terms of the better acceptability of this vaccine among children given that needles are not used, which may have a potential positive impact on vaccination coverage;
- the lack of evidence of an impact in terms of lowering the incidence of acute otitis media, pneumonia, hospital admissions and mortality and without sufficient evidence making it possible to differentiate the four-component influenza vaccines available (inactivated vaccines or attenuated vaccines) on these clinical outcome measures of interest (Cochrane reviews 2018 and 2017, Minozzi 2022, Stuurman 2021 and Sinnathamby study 2022);

the Committee deems that FLUENZ TETRA (four-component live attenuated nasal influenza vaccine) provides no clinical added value (CAV V) for seasonal influenza prevention in children without comorbidities from 2 to 17 years of age, according to the HAS guidelines in force of 2 February 2023.