HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
7 JULY 2021

The legally binding text is the original French opinion version

ceftazidime/avibactam
ZAVICEFTA 2 g/0.5 g powder for concentrate for solution for infusion

New indication

Key points

Favourable opinion for reimbursement in the MA indications only as a last resort for the treatment of **paediatric patients aged 3 months to less than 18 years** with infections due to Enterobacteriaceae susceptible to the ceftazidime/avibactam combination and for whom recourse to other beta-lactams and carbapenems (meropenem or imipenem-cilastatin) cannot be envisaged in the event of resistance, in particular via the production of KPC or OXA-48 type carbapenemase.

Unfavourable opinion for reimbursement in other situations.

What therapeutic improvement?

Moderate therapeutic improvement in the treatment of infections due to Enterobacteriaceae susceptible to ceftazidime/avibactam and for whom recourse to other beta-lactams and carbapenems (meropenem or imipenem-cilastatin) cannot be envisaged in the event of resistance.

Role in the care pathway?

In June 2019, the HAS drew up guidelines to specify the role of carbapenems and their alternatives in the treatment of infections due to Enterobacteriaceae and *P. aeruginosa* in adults.

In the MA indications, the use of antibiotics in children is largely extrapolated from the results observed in adults. Treatment is based on antibiotics appropriate to the identified or probable bacteria.

Role of the medicinal product in the care pathway

As in adults, it is recommended that the ceftazidime/avibactam combination should not be used as an alternative to carbapenems for the treatment of TGC-resistant Enterobacteriaceae.

ZAVICEFTA (ceftazidime/avibactam) is a last resort treatment reserved for paediatric patients aged 3 months to less than 18 years with infections due to Enterobacteriaceae susceptible to the ceftazidime/avibactam combination and for whom recourse to carbapenems cannot be envisaged in the event of resistance, in particular with a KPC or OXA-48 type resistance mechanism.

Special recommendations

Given the product characteristics and the need to restrict its use to a last resort treatment only in order to preserve it, the therapeutic decision should be taken with the help of an antibiotic expert, with systematic reassessment 48 hours after the start of treatment.

COMMITTEE'S CONCLUSIONS

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

Clinical benefit

◗ The infections concerned by this proprietary medicinal product are life-threatening to the paediatric patient, either immediately or as a result of complications.

◗ ZAVICEFTA (ceftazidime/avibactam) is a curative medicinal product.

◗ The efficacy/adverse effects ratio is high.

◗ There are therapeutic alternatives.

◗ It is a last-resort treatment in carbapenem-resistant infections.

Public health impact

Considering:

- the frequency and seriousness of the infections concerned,
- the medical need to have access to new antibiotics in order to respond to the spread of resistance to the antibiotics currently recommended in the treatment of these infections,
- the response to the identified need, due to its activity on carbapenem-resistant Enterobacteriaceae, in particular via the production of KPC or OXA-48 type carbapenemase,
- the expected impact on morbidity and mortality in patients with infections due to Enterobacteriaceae susceptible to ceftazidime/avibactam and for whom recourse to other beta-lactams and carbapenems is not possible,
- the expected impact on the care and life pathway of patients,

ZAVICEFTA (ceftazidime/avibactam) is likely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of ZAVICEFTA (ceftazidime/avibactam) is:

- **substantial in the MA indications only as a last resort for the treatment of paediatric patients aged 3 months to less than 18 years with infections due to Enterobacteriaceae susceptible to the ceftazidime/avibactam combination and for whom recourse to other beta-lactams and carbapenems (meropenem or imipenem-cilastatin) cannot be envisaged in the event of resistance, in particular via the production of KPC or OXA-48 type carbapenemase;**
- **insufficient to justify public funding cover in all other clinical situations.**

The Committee issues a favourable opinion for inclusion in the hospital formulary list of reimbursed proprietary medicinal products approved for use in the MA indications and dosages, only as a last resort for the treatment of paediatric patients aged 3 months to less than 18 years with infections due to Enterobacteriaceae susceptible to the ceftazidime/avibactam combination and for whom recourse to other beta-lactams and carbapenems (meropenem or imipenem-cilastatin) cannot be envisaged in the event of resistance, in particular via the production of KPC or OXA-48 type carbapenemase.
The Committee issues an unfavourable opinion for maintenance of inclusion in the hospital formulary list of reimbursed proprietary medicinal products approved for use in the other situations.

Clinical Added Value

Considering:

- **the significant medical need to have access to new antibiotics for the treatment of infections due to Enterobacteriaceae resistant to third-generation cephalosporin (TGC), and carbapenemase-producing bacteria as one of WHO's priorities (critical priority),**
- **its *in vitro* activity on *Pseudomonas aeruginosa* and Extended-Spectrum Beta-lactamase-Producing Enterobacteriaceae (ESBL-PE), particularly KPC and OXA-48,**
- **experience acquired with ceftazidime, a TGC widely used in the treatment of severe nosocomial infections due to Gram-negative bacteria with high suspicion of *P. aeruginosa,***
- **limited data in children and adolescents suggesting an efficacy comparable to that described in adults,**
- **the fact that the ceftazidime/avibactam combination is one of the few current antibiotics active on certain carbapenemase-producing Enterobacteriaceae,**

the Committee considers that, as in adults, ZAVICEFTA (ceftazidime/avibactam) provides a moderate clinical added value (CAV III) in the treatment of paediatric patients aged 3 months to less than 18 years with infections due to Enterobacteriaceae susceptible to the ceftazidime/avibactam combination and for whom recourse to other beta-lactams and carbapenems (meropenem or imipenem-cilastatin) cannot be envisaged in the event of resistance.