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

Reevaluation

Key points

Favourable opinion for reimbursement in the MA indications only as a last resort for the treatment of patients with enterobacteria infections 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 the other clinical situations.

What therapeutic improvement?

Moderate therapeutic improvement in the treatment of enterobacteria infections 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 published guidelines relating to the antibiotic treatment of Enterobacteriaceae and *Pseudomonas aeruginosa* infections in adults, specifying the role of carbapenems and their alternatives.

**Role of the medicinal product in the care pathway**

The ceftazidime/avibactam combination should not be used as an alternative to carbapenems for the treatment of TGC-resistant enterobacteria and for the treatment of *P. aeruginosa* infections.

ZAVICEFTA (ceftazidime/avibactam) is a last resort treatment reserved for patients with enterobacteria infections susceptible to ceftazidime/avibactam 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.
CONCLUSION

Clinical Benefit

- The infections concerned by this proprietary medicinal product are life-threatening to the patient, either immediately or as a result of complications.
- It is a curative treatment.
- The efficacy/adverse effects ratio is high.
- There are therapeutic alternatives.
- It is a last-resort treatment in carbapenem-resistant infections.

- Public health impact
Consideration:
  - 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 enterobacteria, in particular via the production of KPC or OXA-48 type carbapenemase,
  - the expected impact on morbidity and mortality in patients with enterobacteria infections 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 impact on public health.

Considering these elements, the Committee deems that the clinical benefit of ZAVICEFTA (ceftazidime/avibactam):
- remains substantial in the marketing authorisation indications only as a last resort for the treatment of patients with enterobacteria infections 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, in particular via the production of KPC or OXA-48 type carbapenemase;
- becomes insufficient to justify its funding by the French national health insurance system in all other clinical situations.

The Committee issues a favourable opinion for maintenance of 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 patients with enterobacteria infections 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 clinical situations.
Clinical Added Value

Considering:
- 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 third-generation cephalosporin (TGC) widely used in the treatment of severe nosocomial infections due to Gram-negative bacteria with high suspicion of *P. aeruginosa*,
- its demonstrated efficacy in moderate to mild complicated urinary tract infections (including pyelonephritis) and complicated intra-abdominal infections, particularly on ceftazidime-resistant strains; and in hospital-acquired pneumonia, including ventilator associated pneumonia,
- limited clinical data in severe forms and/or forms due to multi-drug resistant bacteria,
- the fact that the ceftazidime/avibactam combination is one of the few current antibiotics active on certain carbapenemase-producing enterobacteria,

the Committee considers that ZAVICEFTA (ceftazidime/avibactam) provides a moderate clinical added value (CAV III) in the treatment of enterobacteria infections 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.