TRANSPARENCY COMMITTEE
OPINION
22 JANUARY 2020

ceftolozane/tazobactam
ZERBAXA 1 g/0.5 g powder for concentrate for solution for infusion
Reevaluation and new indication

Key points

Favourable opinion for reimbursement in the MA indications only as a last resort for the treatment of patients with P. aeruginosa infections susceptible to the ceftolozane/tazobactam combination and for whom recourse to other beta-lactams and/or carbapenems (meropenem or imipenem-cilastatin) cannot be envisaged in the event of resistance.

Unfavourable opinion for reimbursement in the other clinical situations.

What therapeutic improvement?

Moderate therapeutic improvement in the treatment of P. aeruginosa infections susceptible to ceftolozane/tazobactam and for whom recourse to other beta-lactams and/or 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.

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<th>Role of the medicinal product in the care pathway</th>
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<tr>
<td>The ceftolozane/tazobactam combination should not be used as an alternative to carbapenems for the treatment of 3GC-resistant enterobacteria.</td>
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<tr>
<td>ZERBAXA (ceftolozane/tazobactam) is a last resort treatment reserved for patients with <em>P. aeruginosa</em> infections susceptible to ceftolozane/tazobactam and for whom recourse to other beta-lactams and/or carbapenems (meropenem or imipenem-cilastatin) cannot be envisaged in the event of resistance.</td>
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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

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.

- 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 possible use in certain situations, in particular in infections caused by *P. aeruginosa* in the event of beta-lactamase resistance,
  - the expected impact on morbidity and mortality in patients with *P. aeruginosa* infections susceptible to ceftolozane/tazobactam and for whom recourse to other beta-lactams is not possible,
  - the expected impact on the care and life pathway of patients.

*ZERBAXA* (ceftolozane/tazobactam) is likely to have an impact on public health.

Considering these elements, the Committee deems that the clinical benefit of ZERBAXA (ceftolozane/tazobactam):
- remains substantial in the marketing authorisation indications only as a last resort for the treatment of patients with *P. aeruginosa* infections susceptible to the ceftolozane/tazobactam combination and for whom recourse to other beta-lactams and/or carbapenems (meropenem or imipenem-cilastatin) cannot be envisaged in the event of resistance;
- 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 *P. aeruginosa* infections susceptible to the ceftolozane/tazobactam combination and for whom recourse to other beta-lactams and/or carbapenems (meropenem or imipenem-cilastatin) cannot be envisaged in the event of resistance.

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 extended-spectrum beta-lactamase-producing Enterobacteriaceae (ESBL-PE), particularly *Pseudomonas aeruginosa*,
- its demonstrated efficacy in moderate to mild complicated urinary tract infections (including pyelonephritis) and complicated intra-abdominal infections; and in hospital-acquired pneumonia, including ventilator associated pneumonia,
- limited clinical data in severe forms and/or forms due to multi-drug resistant *Pseudomonas aeruginosa*,
that fact that the ceftolozane/tazobactam combination is one of the few drugs currently active against *P. aeruginosa* resistant to other beta-lactams, the Committee considers that ZERBAXA (ceftolozane/tazobactam) provides a moderate clinical added value (CAV III) in the treatment of *P. aeruginosa* infections susceptible to the ceftolozane/tazobactam combination and for whom recourse to other beta-lactams and/or carbapenems (meropenem or imipenem-cilastatin) cannot be envisaged in the event of resistance.