ceftolozane/tazobactam

ZERBAXA 1 g/0.5 g,

powder for solution for dilution for infusion

New indication(s)

Adopted by the Transparency Committee on 14 December 2022

SUMMARY

The legally binding text is the original French opinion version

Key points

Approval of reimbursement as for adults, in the marketing authorisation indications only as a last resort for the treatment of children (from birth to under 18 years) infected with ceftolozane/tazobactam-susceptible *P. aeruginosa* and for whom it is not possible to envisage the use of other beta-lactams and/or carbapenems (meropenem or imipenem-cilastatin) in cases of resistance.

Disapproval of reimbursement for other clinical contexts.

Therapeutic improvement?

As for adults, therapeutic improvement in the treatment of ceftolozane/tazobactam-susceptible *P. aeruginosa* infections, for which it is not possible to envisage the use of other beta-lactams and/or carbapenems (meropenem or imipenem-cilastatin) in cases of resistance.

Role of medicinal product in therapeutic strategy?

In June 2019, HAS drafted guidelines to specify the role of carbapenems and their alternatives in the treatment of enterobacteria and *P. aeruginosa* infections in adults. In the marketing authorisation indications, the use of antibiotics in children is largely extrapolated from the outcomes observed in adults. The treatment is based on antibiotics suitable for the identified or probable bacteria.
Role of the medicinal product

As for adults, it is recommended not to use the ceftolozane/tazobactam association as an alternative carbapenems for the treatment of C3G-resistant enterobacteria.

ZERBAXA (ceftolozane/tazobactam) is a last-resort treatment reserved for children from birth and aged under 18 years infected with ceftolozane/tazobactam association-susceptible *P. aeruginosa* and for whom it is not possible to envisage the use of other beta-lactams and/or carbapenems (meropenem or imipenem-cilastatin) in cases of resistance.

Committee’s conclusions

Clinical Benefit

- The conditions concerned by this proprietary medicinal product are life-threatening for the patient in the immediate term or following complications.
- The proprietary medicinal product ZERBAXA (ceftolozane/tazobactam) is a curative treatment.
- The efficacy/adverse effect ratio of ZERBAXA (ceftolozane/tazobactam) is significant only as a last resort for the treatment of patients infected with ceftolozane/tazobactam-susceptible *P. aeruginosa* and for whom it is not possible to envisage the use of other beta-lactams and/or carbapenems (meropenem or imipenem-cilastatin) in cases of resistance.
- Therapeutic alternatives are available.
- The product is a last-resort treatment for infections resistant to other beta-lactams and/or carbapenems (meropenem or imipenem-cilastatin).

Public health benefit

Considering:
- the frequency and severity of the infections in question,
- the medical need for new antibiotics to control the spread of resistance to the antibiotics currently recommended for the treatment of these infections,
- the response to the identified need, on account of its possible use in certain contexts, in particular for infections caused by *P. aeruginosa* in cases of beta-lactam resistance,
- an expected impact on morbidity-mortality among patients with an infection caused by ceftolozane/tazobactam-susceptible *P. aeruginosa* and for whom it is not possible to use other beta-lactams,
- an expected impact on patients’ care and/or life pathway.

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

Considering all of these elements, the Committee deems that the clinical benefit of ZERBAXA (ceftolozane/tazobactam) is:
- significant in the marketing authorisation indications only as a last resort for the treatment of children aged from birth to under 18 years infected with ceftolozane/tazobactam-susceptible *P. aeruginosa* and for whom it is not possible to envisage the use of
other beta-lactams and/or carbapenems (meropenem or imipenem-cilastatin) in cases of resistance;
- insufficient to justify public funding in the other contexts.

The Committee approves inclusion in the list of proprietary medicinal products approved for community use in the indications and at the dosages of the marketing authorisation, only as a last resort for the treatment of children aged from birth to under 18 years infected with ceftolozane/tazobactam-susceptible *P. aeruginosa* and for whom it is not possible to envisage the use of other beta-lactams and/or carbapenems (meropenem or imipenem-cilastatin) in cases of resistance;

The Committee disapproves inclusion in the list of proprietary medicinal products approved for community use for the other clinical contexts.

### Clinical Added Value

Considering:
- the medical need for new antibiotics for the treatment of enterobacteria resistant to third-generation cephalosporins (C3G), and carbapenemase-producing bacteria at the top of WHO priorities (critical priority),
- its *in vitro* activity on *Pseudomonas aeruginosa* and on extended-spectrum beta-lactamase-secreting enterobacteria (ESBLSE),
- the experience acquired with ceftazidime, a C3G widely used in the treatment severe nosocomial infections induced by Gram-negative bacteria with a strong suspicion of *P. aeruginosa*,
- limited data in children and adolescents suggesting comparable efficacy to that described in adults,
- that the ceftolozane/tazobactam association is one of the rare current antibiotics active on *P. aeruginosa* strains resistant to other beta-lactams,

the Committee deems that, as for adults, ZERBAXA (ceftolozane/tazobactam) provides moderate clinical added value (CAV III) in children aged from birth to under 18 years infected with ceftolozane/tazobactam-susceptible *P. aeruginosa* and for whom it is not possible to envisage the use of other beta-lactams and/or carbapenems (meropenem or imipenem-cilastatin) in cases of resistance.

In this way, the paediatric target population of ZERBAXA (ceftolozane/tazobactam) can therefore be estimated at approximately 200 patients per year.

However, based on the current epidemiological context, these figures represent the upper limit of the target population ZERBAXA (ceftolozane/tazobactam) as this antibiotic must only be used in cases of infection caused by multiresistant Gram-negative aerobic bacteria susceptible to the ceftolozane/tazobactam association. The size of the target population may however be subject to change according to the prevalence of infections caused by Gram-negative aerobic bacteria resistance to other beta-lactams and/or carbapenems (meropenem or imipenem-cilastatin).