HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE

SUMMARY

23 SEPTEMBER 2020

The legally binding text is the original French opinion version

imipenem/cilastatin/relebactam

RECARBRIO 500 mg/500 mg/250 mg powder for solution for infusion

First assessment

Key points

Positive opinion for reimbursement in the market authorisation (MA) indications, only as a last resort for patients' treatment with enterobacteria infections, sensitive to the imipenem/cilastatin/relebactam combination, and for whom recourse to other beta-lactams and carbapenems (meropenem or imipenem-cilastatin) cannot be considered in case of resistance, in particular through KPC-type carbapenemase production.

Negative opinion for reimbursement in other situations.

What therapeutic improvement?

Therapeutic improvement in patient care management.

Role in the care pathway?

In June 2019, the HAS published guidelines relating to antibiotics management therapy 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

RECARBRIO (imipenem/cilastatin/relebactam) is a last resort treatment, in the same way as VABOREM (meropenem/vaborbactam), restricted for patients with enterobacteria infections sensitive to the imipenem/cilastatin/relebactam combination and for whom recourse to carbapenems cannot be considered in case of resistance, in particular with a KPC type resistance mechanism.

RECARBRIO (imipenem/cilastatin/relebactam) should not be used as an alternative to carbapenems for the treatment of TGC-resistant enterobacteria and for the treatment of *P. aeruginosa* infections.

It should not be used as probabilistic treatment but solely on the basis of microbiological documentation.

Special recommendations

Given the product characteristics and the need to restrict its use to a last resort treatment only to preserve it, the therapeutic decision should be taken alongside antibiotic experts, with systematic reassessment 48 hours after treatment initiation.

Clinical benefit

◗ The infections concerned by this proprietary medicinal product are life-threatening for patient's prognosis, either directly or as a result of complications.
◗ It is a curative treatment.
◗ The efficacy/adverse effects ratio is high.
◗ There are few 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 antibiotics' resistance, of those currently used.
- the response to the identified need, due to its possible use in particular therapeutic pathway, as infections caused by carbapenem-resistant and extended-spectrum beta-lactamase-producing Enterobacteriaceae (ESBL-PE),
- the expected impact on morbidity and mortality in patients with enterobacteria infections sensitive to imipenem/cilastatin/relebactam and for whom recourse to carbapenems cannot be considered in case of resistance, in particular through KPC-type carbapenemase production,
- the expected impact on the care and life pathway of patients.

RECARBRIO (imipenem/cilastatin/relebactam) is likely to have, in the same way as VABOREM (meropenem/vaborbactam), an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of RECARBRIO (imipenem/cilastatin/relebactam) is:

- **substantial only as a last resort for patients' treatment with enterobacteria infections sensitive to the imipenem/cilastatin/relebactam combination and for whom recourse to other beta-lactams and carbapenems (meropenem or imipenem/cilastatin) cannot be considered in case of resistance, in particular through KPC-type carbapenemase production;**
- **insufficient to justify public funding cover in all other clinical situations.**

The Committee issues a positive opinion for RECARBRIO's inclusion (imipenem/cilastatin/relebactam) 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 patients' treatment with enterobacteria infections sensitive to the imipenem/cilastatin/relebactam combination and for whom recourse to other beta-lactams and carbapenems (meropenem or imipenem/cilastatin) cannot be considered in case of resistance, in particular through KPC-type carbapenemase production.
The Committee issues a negative opinion for RECARBRIO's inclusion (imipenem/cilastatin/relebactam) in the hospital formulary list of reimbursed proprietary medicinal products approved for use in other situations.

Clinical Added Value

Considering:

- **its *in vitro* activity on class A Extended-Spectrum Beta-Lactamase-Producing Enterobacteriaceae (ESBL-PE), particularly KPC type;**
- **experience acquired with imipenem/cilastatin, a carbapenem widely used in the treatment of severe nosocomial infections due to Gram-negative bacteria;**
- **the demonstrated efficacy of the imipenem/cilastatin/relebactam combination in mild to moderate hospital-acquired pneumonia, with a satisfactory safety profile;**
- **limited clinical data (RESTORE-IMI-1 study) suggesting high efficacy in patients with carbapenem-resistant enterobacteria infections (CRE), primarily through KPC-type carbapenemase production;**
- **the fact that the imipenem/cilastatin/relebactam combination is one of the few current antibiotics active on certain carbapenemase-producing enterobacteria;**

the Committee considers that RECARBRIO (imipenem/cilastatin/relebactam), in the same way as VABOREM (meropenem/vaborbactam), provides a moderate clinical added value (CAV III) in the treatment of enterobacteria infections sensitive to the imipenem/cilastatin/relebactam combination and for whom recourse to other beta-lactams and carbapenems (meropenem or imipenem-cilastatin) cannot be considered in case of resistance.