TRANSPARENCY COMMITTEE
SUMMARY
20 JANUARY 2021
The legally binding text is the original French opinion version

**cefiderocol**
FETCROJA 1 g powder for concentrate for solution for infusion

First assessment

### Key points

Favourable opinion for reimbursement in the MA indication **only as a last resort** for the treatment of patients with infections due to multiresistant Gram-negative bacteria (particularly in the event of Enterobacterales and *Pseudomonas aeruginosa*, with a KPC, oxacillinase or metallo-β-lactamase resistance mechanism [NDM, VIM, IMP]) and when the use of the other available options is not possible.

Unfavourable opinion for reimbursement in other situations.

### What therapeutic improvement?

Therapeutic improvement in management.

### Role in the care pathway?

In June 2019, the HAS published guidelines relating to the antibiotic treatment of Enterobacterales and *Pseudomonas aeruginosa* infections in adults, specifying the role of carbapenems and their alternatives.

**Role of the medicinal product in the care pathway**
FETCROJA (cefiderocol) is a last-resort antibiotic reserved for patients with infections due to multiresistant Gram-negative bacteria (particularly in the event of Enterobacterales and *Pseudomonas aeruginosa*, with a KPC, oxacillinase or metallo-β-lactamase resistance mechanism [NDM, VIM, IMP]), with the exception of *Acinetobacter baumannii* and *Stenotrophomonas maltophilia*.

FETCROJA (cefiderocol) should not be used as an alternative to carbapenems for the treatment of third-generation cephalosporin-resistant Enterobacterales and for the treatment of carbapenem-susceptible *P. aeruginosa* infections.

The use of this antibiotic should only be considered as a last resort, i.e. when the other available options are not possible.

The Committee specifies that, despite the favourable response observed in studies, the uncertainties related to the higher mortality observed with cefiderocol in the CREDIBLE-CR study, which currently remains unexplained, particularly in the event of pneumonia, bacteraemia and/or sepsis due to *Acinetobacter baumannii*, mean that it is not possible to reach a conclusion with respect to the benefit of this antibiotic in the event of infection caused by this microorganism. In addition, the clinical efficacy has not been established in *Stenotrophomonas maltophilia* infections (only 5 patients in the CREDIBLE-CR study). The Committee would like to have additional data.

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 in order to preserve it, the decision to initiate treatment with FETCROJA (cefiderocol) should be taken following a documented proposal based on a treatment review meeting with an antibiotic expert, with systematic reassessment 48 hours after the start of treatment.

The Committee is awaiting additional data from the pharmaceutical company in order to better assess the clinical value of cefiderocol in the event of infections due to non-fermenter bacteria, such as *Acinetobacter baumannii* and *Stenotrophomonas maltophilia*. Depending on the content of this data, the Committee may revise its opinion.
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 in infections due to cefiderocol-susceptible and carbapenem-resistant aerobic Gram-negative bacteria (Enterobacterales and Pseudomonas aeruginosa, with a KPC, oxacillinase or metallo-β-lactamase resistance mechanism [NDM, VIM, IMP]),
  - not established in infections caused by non-fermenter bacteria such as Acinetobacter baumannii and Stenotrophomonas maltophilia due to the higher mortality observed in the CREDIBLE-CR study, which currently remains unexplained, particularly in the event of pneumonia, bacteraemia and/or sepsis due to A. baumannii and limited data in the event of S. maltophilia infection,
- There are few or no therapeutic alternatives in the last-resort situations concerned by this medicinal product.
- 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 the possibility of its use in certain situations, particularly in infections due to cefiderocol-susceptible and carbapenem-resistant aerobic Gram-negative bacteria (Enterobacterales and Pseudomonas aeruginosa, with a KPC, oxacillinase or metallo-β-lactamase resistance mechanism [NDM, VIM, IMP]),
- the expected impact on morbidity and mortality and on the care and life pathway, with the exclusion of A. baumannii and Stenotrophomonas maltophilia infections for which the clinical benefit is still to be demonstrated,

FETCROJA (cefiderocol) is likely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of FETCROJA (cefiderocol) is:
- substantial only as a last resort for the treatment of patients with infections due to multiresistant Gram-negative bacteria (particularly in the event of Enterobacterales and Pseudomonas aeruginosa, with a KPC, oxacillinase or metallo-β-lactamase resistance mechanism [NDM, VIM, IMP]) and when the use of the other available options is not possible.
- insufficient to justify public funding cover in other clinical situations, including infections with Acinetobacter baumannii or Stenotrophomonas maltophilia, pending additional data.

The Committee issues a favourable opinion for inclusion of FETCROJA (cefiderocol) 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 infections due to multiresistant Gram-negative bacteria (particularly in the event of Enterobacterales and Pseudomonas aeruginosa, with a KPC, oxacillinase or metallo-β-lactamase resistance mechanism [NDM, VIM, IMP]) and when the use of the other available options is not possible.

HAS - Medical and Economic Evaluation and Public Health Division
The Committee issues an unfavourable opinion for inclusion of FETCROJA (cefiderocol) 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 a broad variety of Gram-negative bacteria, such as Enterobacterales and *Pseudomonas aeruginosa*, with a KPC, oxacillinase or metallo-β-lactamase resistance mechanism [NDM, VIM, IMP] or non-fermenter bacteria such as *Acinetobacter baumannii* or *Stenotrophomonas maltophilia*,
- the fact that cefiderocol is one of the few current antibiotics active against these microorganisms,
- the results of 2 clinical studies demonstrating its efficacy in terms of non-inferiority compared to the imipenem/cilastatin combination in the treatment of urinary tract infections on microbiological eradication (APEKS-cUTI study) and compared to high-dose meropenem in the treatment of nosocomial pneumonia on all-cause mortality (APEKS-NP study), due to carbapenem-sensitive Gram-negative bacteria,
- the limited clinical data in situations where the other therapeutic options have been exhausted (CREDIBLE-CR study) suggesting a favourable response in terms of clinical recovery and microbiological eradication in patients with carbapenem-resistant infections, particularly those with a metallo-β-lactamase resistance mechanism for whom few or no alternatives are available,
- the need to have access to new antibiotics with improved efficacy, safety and resistance profiles,

But:
- a higher mortality observed in the CREDIBLE-CR study, which is still unexplained, particularly in the event of pneumonia, bacteraemia and/or sepsis due to *Acinetobacter baumannii* and limited data in *Stenotrophomonas maltophilia* infections,
- pending additional data enabling better assessment of the therapeutic contribution of cefiderocol in the event of infection with non-fermenter bacteria such as *Acinetobacter baumannii* or *Stenotrophomonas maltophilia*,

the Committee considers that FETCROJA (cefiderocol) provides a minor clinical added value (CAV IV) in the treatment of patients with infections due to multiresistant Gram-negative bacteria (particularly in the event of Enterobacterales and *Pseudomonas aeruginosa*, with a KPC, oxacillinase or metallo-β-lactamase resistance mechanism [NDM, VIM, IMP]) and when the use of the other available options is not possible.