HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
21 APRIL 2021

The legally binding text is the original French opinion version

amikacin
ARIKAYCE LIPOSOMAL 590 mg nebuliser dispersion

First assessment

Key points

Favourable opinion for reimbursement in the treatment of non-tuberculous mycobacterial (NTM) lung infections caused by *Mycobacterium avium* Complex (MAC) in adults with limited treatment options who do not have cystic fibrosis.

What therapeutic improvement?

Therapeutic improvement in management of the condition.

Role in the care pathway?

The treatment of lung infections caused by *Mycobacterium avium* Complex (MAC) is well standardised in the international guidelines and is based on a combination of antibiotics: multiple drug regimen (MDR). This is composed of rifampicin or rifabutin, a macrolide (clarithromycin or azithromycin) and ethambutol continued for 12 months following conversion to negative sputum cultures. The addition of parenteral amikacin is envisaged in cavitary or severe forms and for macrolide-resistant infections.

In the event of non-response (patients without sputum culture conversion after 6 consecutive months of MDR), the use of inhaled liposomal amikacin in conjunction with MDR is recommended.

Role of the medicinal product in the care pathway

Considering demonstration of its microbiological efficacy (durable sputum culture conversion in heavily pretreated patients), the Transparency Committee considers that ARIKAYCE LIPOSOMAL (amikacin) is a salvage therapy, in conjunction with MDR, in the event of failure of oral MDR therapy alone (at least 6 months of treatment), in patients with lung infections caused by MAC sensitive to amikacin, with limited treatment options and who do not have cystic fibrosis. Patients with cystic fibrosis were not included in the pivotal study.

Special recommendations

The Committee highlights the fact that treatment should be initiated and monitored by physicians experienced in the management of these incapacitating and difficult-to-treat infections. In addition, patients should be informed about both the benefits of the treatment and the safety issues, i.e., the poor respiratory tolerance (related to aerosolization), the long-term risks, in particular tinnitus, which can impair quality of life, and ototoxicity, which may be more problematic and irreversible. To limit this risk, approximate cumulative doses with an increased probability of ototoxicity must be determined, particularly when there is a risk of renal impairment.

COMMITTEE'S CONCLUSIONS

Considering all of this information and further to debate and voting, the Committee considers:

Clinical benefit

◗ *Mycobacterium avium* Complex (MAC) infections are rare and serious infections that can be life-threatening following complications.

◗ The proprietary medicinal product ARIKAYCE LIPOSOMAL (amikacin) is a curative medicinal product.

◗ Its efficacy/adverse effects ratio is high.

◗ There are no therapeutic alternatives in the treatment of non-tuberculous mycobacterial (NTM) lung infections caused by *Mycobacterium avium* Complex (MAC) in adults with limited treatment options who do not have cystic fibrosis.

◗ This is a salvage therapy in patients with limited treatment options who do not have cystic fibrosis.

Public health impact

Considering:

- the seriousness of non-tuberculous mycobacterial (NTM) lung infections, for which treatment is complex (on average, 15 to 18 months of treatment, 3 antibiotics combined, narrow therapeutic index),
- the small number of patients concerned in France,
- the significant medical need to have access to enough second-line antibiotics to be used in combination in order to be able to adjust treatment in the event of contraindication or intolerance, non-response or resistance to first-line options,
- the fact that ARIKAYCE LIPOSOMAL (amikacin) may provide a partial response to the identified medical need in patients in whom the treatment options have been exhausted (multi-drug resistant bacteria) due to durable bacteriological culture conversion, but for which the impact on morbidity and mortality and/or quality of life cannot be assessed on the basis of the limited data available,
- an expected impact on the care and life pathway related to durable bacteriological culture conversion (microbiological cure), while preserving the veins (inhaled route),

ARIKAYCE LIPOSOMAL (amikacin) is likely to have an impact on public health.

Given all these elements, the Committee deems that the clinical benefit of ARIKAYCE LIPOSOMAL (amikacin) is substantial in the MA indication.

The Committee issues a favourable opinion for inclusion in the hospital formulary list of reimbursed proprietary medicinal products approved for use in the MA indication and dosages.

Clinical Added Value

Considering:

- **the identified substantial medical need to have access to additional therapeutic options in situations in which the treatment options are limited in order to avoid all the options being exhausted,**
- **demonstration of the superiority of liposomal amikacin in combination with a multiple drug regimen (MDR), composed of an average of three antibiotics, compared to MDR alone in terms of sputum culture conversion after 6 months: 29.0% *versus* 8.9% (OR = 4.220; [2.078; 8.570]; p < 0.0001) and durable sputum culture conversion up to 12 months of treatment and 3 months after discontinuation of treatment (16.1% (36/224) *versus* 0%) in patients with previous non-response to MDR,**

but taking into account:

- **an impact on morbidity and mortality and on quality of life that is difficult to assess on the basis of the limited data available and the short follow-up confirming a clinical benefit,**
- **a safety protocol marked by otocochlear and pulmonary toxicity that could potentially be related to chronic exposure to nebulised amikacin, along with a non-negligible proportion of respiratory adverse events leading to temporary (approximately 30%) or permanent (approximately 11%) discontinuation of liposomal amikacin,**

the Committee considers that ARIKAYCE LIPOSOMAL (amikacin), in combination with a multiple drug regimen, provides a minor clinical added value (CAV IV) in the care pathway for the treatment of lung infections caused by MAC in patients with limited treatment options who do not have cystic fibrosis.