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Contact
Ms P. Pasman
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2020051391

Date 15 December 2020
Subject Amikacin liposome inhalation suspension (Arikayce® liposomal)

Our reference
2020051391

Dear Ms van Ark,

In your letter of 7 September 2020 (CIBG-20-0910), you asked the National Health Care Institute to assess (using the CBG-ZIN parallel procedure) the reimbursement application of the medicinal product amikacin liposome inhalation suspension (Arikayce® liposomal) for inclusion in the medication reimbursement system (GVS). In the Parallel Procedure CBG-ZIN pilot, the reimbursement process was started while the registration process had not yet been completed. Medicinal products that go through this parallel procedure, rather than the current sequential procedures, will become available to patients more quickly. The EMA registration of amikacin liposome inhalation suspension (ALIS) was published on the EMA website on 18 November 2020. This is normally the time when a reimbursement dossier can be submitted. Due to the parallel procedure, the National Health Care Institute can now rule on the reimbursement immediately after registration. The National Health Care Institute has since completed its assessment. The considerations are included in the GVS report attached to this letter, with the pharmaco-therapeutic report and the budget impact analysis.

The market authorisation holder is asking for inclusion on List 1B of the Health Insurance Regulation.

Amikacin liposome inhalation suspension (Arikayce® liposomal) is an orphan drug. It is registered for *the treatment of non-tuberculous mycobacterial (NTM) lung infections caused by Mycobacterium avium complex (MAC) in adult patients with limited treatment options, who do not have cystic fibrosis.*
Consideration should be given to official guidance on the appropriate use of antibacterial agents.

ARIKAYCE liposome inhalation suspension (ALIS) should be used in conjunction with other antibacterial agents active against *Mycobacterium avium* Complex lung infections.
The recommended dose is one vial (590 mg) administered once a day, by oral inhalation. Treatment should be continued for 12 months after sputum culture conversion. The maximum duration of treatment with inhaled liposomal amikacin should not exceed 18 months. Treatment with ALIS should not continue beyond a maximum of 6 months if sputum culture conversion has not been confirmed by

then.

Review of interchangeability
None of the medicinal products included in the GVS is for the indication for which amikacin liposome inhalation suspension is registered. ALIS is not interchangeable with any of the other medicinal products that are included in the GVS.

Based on the above, ALIS cannot be placed on List 1A. The question of whether amikacin liposome inhalation suspension is eligible for inclusion on List 1B needs to be reviewed.

Therapeutic value conclusion
One randomised controlled open-label phase III study directly investigated the desirable and undesirable effects of ALIS in the treatment of patients with the above indication, when added to an antibacterial treatment regimen. Treatment with ALIS results in a higher proportion of patients (13%) with sustained culture conversion (up to 3 months after treatment was discontinued) compared to patients treated with an antibacterial treatment regimen (0%). However, treatment with ALIS is associated with more adverse effects (98% vs 91% respectively) and a clinically relevant increase in the number of dropouts resulting from adverse effects. On the other hand, account should be taken of the fact that patients for whom ALIS is registered have an evident unmet medical need. The five-year mortality of patients with this NTM lung disease is estimated to be approximately 27%. In addition, these patients experience a reduced quality of life.

The main measure of outcome is the difference in the number of patients with a sustained culture conversion. Patients with a sustained sputum culture conversion may discontinue the antibiotic treatment regimen for the MAC lung infection. The National Health Care Institute, like the medical experts, considers the difference in the number of patients with sustained culture conversion to be clinically relevant. It should be noted, however, that sustained culture conversion will only occur in 13% (about 1 in 8) of patients. Furthermore, the translation of sustained culture conversion into a clinical benefit for patients has only been demonstrated indirectly.

The National Health Care Institute, advised by the Scientific Advisory Board (WAR), has concluded that, when added to an antibacterial treatment regimen, amikacin liposome inhalation suspension has added value in the treatment of non-tuberculous mycobacterial lung infections caused by the *Mycobacterium avium* Complex in adults with limited treatment options, who do not have cystic fibrosis.

Budget impact analysis
Taking into account the different assumptions with regard to patient numbers, treatment duration, market penetration and patient compliance, the inclusion of ALIS on List 1B of the GVS for the treatment of persistent *Mycobacterium avium* Complex lung infection will be associated with additional costs charged to the pharmaceutical budget of €5.7 to €6.9 million, depending on the treatment duration involved. This concerns 70 patients in the third year after inclusion in the Dutch basic healthcare insurance package. Based on an average treatment duration of 7.7 months, the cost per patient amounts to €86,523. Assuming a treatment duration of 9.6 months, the cost per patient amounts to €107,873.

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Appropriateness
The Summary of Product Characteristics states that treatment with ALIS should be initiated and managed by physicians experienced in the treatment of non-tuberculous lung diseases due to the *Mycobacterium avium* complex. The marketing authorisation holder (MAH) proposes that treatment with ALIS should be linked to a discussion of the patient within the context of the Multidisciplinary Consultation Meeting offered by the NTM Centre of Expertise every 2 weeks. This proposal is primarily motivated by a wish to establish, with greater certainty, whether the patient is a candidate for treatment with ALIS, and to secure the correct advice and 'supervision', especially in terms of managing the adverse effects. In addition, the occupational group and the patients' association have indicated that it is important to centralise treatment in centres of expertise.

Advice on inclusion in the GVS
Amikacin liposome inhalation suspension (ALIS; Arikayce® liposomal) is not interchangeable with any product in the GVS. Based on the considerations mentioned above, we recommend that you include ALIS in List 1B and List 2 of the Healthcare Insurance Regulations. Inclusion in List 1B will lead to additional costs.

Condition regarding amikacin liposome suspension
Only for an insured person with a non-tuberculous mycobacterial lung infection caused by *Mycobacterium avium* Complex, who does not have cystic fibrosis, and who has not achieved culture conversion after at least 6 months of treatment involving a guideline-based antibacterial regimen in accordance with the guidelines accepted by the relevant professional practitioners in the Netherlands.

Yours sincerely,

Sjaak Wijma
Chair of the Executive Board