Aclidinium bromide in COPD: Proof of considerable added benefit for certain patients

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The drug aclidinium bromide (aclidinium for short; trade name: Eklira, Bretaris) has been approved since July 2012 and is used to relieve the symptoms of chronic obstructive pulmonary disease (COPD) in adults. The German Institute for Quality and Efficiency in Health Care (IQWiG) has now reexamined the added benefit of the drug pursuant to the Act on the Reform of the Market for Medicinal Products (AMNOG).

In contrast to the first dossier assessment from 2012, IQWiG now sees proof of considerable added benefit on the basis of newly submitted data. This only applies to one patient group, however, namely adults with COPD grade III and fewer than two exacerbations (flare-ups) per year. These patients have fewer flare-ups under aclidinium bromide.

Manufacturer applied for a new dossier assessment

IQWiG had assessed the drug twice already: as monotherapy (2012) and in the fixed-dose combination with the drug formoterol (2015). The Institute had determined an added benefit for the fixed-dose combination, but not for the monotherapy.

Referring to new scientific findings, the drug manufacturer had applied for reassessment of the single agent at the Federal Joint Committee (G-BA) and submitted a new dossier.

Formoterol as appropriate comparator therapy

The G-BA specified different appropriate comparator therapies depending on the severity grade of the disease: From COPD grade II (research question 1), the drug was to be compared with a long-acting beta-2 sympathomimetic (such as formoterol) and/or tiotropium. From grade III and at least two exacerbations per year (research question 2), the patients in the comparator arm were to receive an additional inhaled corticosteroid (ICS).

The manufacturer followed these specifications and chose formoterol as appropriate comparator therapy for research question 1. According to the company, there was no sufficient new evidence for research question 2, and therefore no reassessment was required.

Two suitable studies with direct comparisons

Data from two double-blind, randomized controlled trials in patients with moderate to severe COPD, in which the drug combination was directly compared with formoterol, were relevant for the reassessment. These studies had not been completed in 2012 and had therefore not been included in the first assessment of the single agent. The manufacturer had used them in its dossier on the fixed-dose combination from 2015, however.

In contrast to the G-BA's specifications, all patients included in these studies could continue ongoing treatment with an ICS, irrespective of their severity grade and the frequency of exacerbations. However, only the data of those patients who were treated in accordance with the G-BA's specifications were included in the analyses presented.

Advantage in exacerbations depends on COPD grade

Overall, there were mixed results on the outcome "exacerbations" (non-severe/non-serious events). Further data analysis showed that they largely depended on the severity grade of the disease. According to the findings, adults with severity grade III with fewer than two exacerbations per year have fewer flare-ups under aclidinium than under formoterol. Such an advantage of aclidinium was not notable in patients with severity grade II.

Heterogeneous results or no relevant differences

For further outcomes (e.g. COPD symptoms, quality of life or side effects), the analyses either showed no relevant differences between the treatment groups or the results were heterogeneous and showed no clear direction.

No data were available for COPD grade IV with fewer than two exacerbations per year.

Hence proof of considerable added benefit only remains for one patient group, namely adults with severity grade III with fewer than two exacerbations per year. In contrast, there is still no hint of an added benefit for further patients.

More information: www.iqwig.de/download/A15-45_A … ertung-35a-SGB-V.pdf

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