Tiotropium/olodaterol in COPD: Disadvantages in some patients, advantages in others

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The fixed-dose combination of tiotropium and olodaterol (trade name: Spiolto Respimat) has been approved since July 2015 for maintenance treatment in adults with chronic obstructive pulmonary disease (COPD). The German Institute for Quality and Efficiency in Health Care (IQWiG) examined in a dossier assessment whether this drug combination offers an added benefit over the appropriate comparator therapy.

According to the findings, there were no statistically significant differences between the treatment groups for the totality of adults with moderate COPD symptoms (severity grade II) and higher severity grades (III-IV) and fewer than two flare-ups (exacerbations) per year. Indications of a minor added benefit could only be derived for women in these COPD groups who inhaled the fixed-dose combination.

In adults with higher severity grades (

Comparator therapy depends on severity and frequency of exacerbations

The Federal Joint Committee (G-BA) specified different appropriate comparator therapies depending on the severity of the disease: From a moderate COPD severity grade (stage II), the new drug combination was to be compared with a long-acting beta-2 sympathomimetic (LABA, e.g.

formoterol, salmeterol) and/or tiotropium (research question 1). From severity grade III and at least two flare-ups (exacerbations) per year, the patients in the comparator arm were to receive an additional inhaled corticosteroid (ICS) (research question 2).

Assessment based on subpopulations

The manufacturer presented data from two approval studies (TONADO 1 and 2) with patients diagnosed with moderate to severe COPD. In contrast to the G-BA's specifications, all patients included in these studies could continue ongoing treatment with an ICS. Hence for both research questions, the assessment was based on subpopulations treated in compliance with the G-BA specifications.

The average age of the patients in the subpopulations was 60 years, and the majority were men: depending on the subpopulation, there were twice to four times as many men as women.

Analyses on longest possible treatment duration

For maintenance treatment in a chronic disease, such as tiotropium/olodaterol, analyses over a longer period of time are more suitable for drawing conclusions on long-term effects. Analyses after 52 weeks were therefore used for all outcomes in the present assessment. The manufacturer, in contrast, had also considered analyses after week 24 in some outcomes.

Advantages only for women with rare flare-ups

For most adults in the subpopulation with severity grade II or severity grade III and IV with fewer than two exacerbations per year, no relevant differences between the treatment groups were shown, or data were lacking, for most outcomes (e.g. COPD symptoms, exacerbations,

quality of life, severe side effects).

Positive effects regarding health-related quality of life and COPD symptoms (shortage of breath) under the fixed-dose combination were only shown for women in this subpopulation. In each case, an indication of minor added benefit of tiotropium/olodaterol in comparison with tiotropium can be derived from this. The data provided neither positive nor negative effects for men.

Disadvantages in severe/very severe COPD with several exacerbations

No relevant differences between the treatment groups occurred or data were lacking also for the second research question (adults with severity grade higher than III and at least two exacerbations per year) in most outcomes.

However, severe exacerbations were more frequent in patients who had inhaled the fixed-dose combination. This resulted in proof of lesser benefit of tiotropium/olodaterol plus ICS in comparison with tiotropium plus ICS.

G-BA decides on the extent of added benefit

This dossier assessment is part of the early benefit assessment according to the Act on the Reform of the Market for Medicinal Products (AMNOG) supervised by the G-BA. After publication of the dossier assessment, the G-BA conducts a commenting procedure and makes a final decision on the extent of the added benefit.

More information: www.iqwig.de/download/A15-31_T … ertung-35a-SGB-V.pdf