Rilpivirine combination product in pretreated HIV-1 patients: Added benefit not proven

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The German Institute for Quality and Efficiency in Health Care (IQWiG) reassessed the antiviral drug combination rilpivirine/emtricitabine/tenofovir. In early 2012, the combination was approved for the treatment of adults infected with human immunodeficiency virus type 1 (HIV-1) who have not received previous antiretroviral treatment. For men, the Institute then found proof, and for women, indications of a considerable added benefit of the fixed combination in comparison with the appropriate comparator therapy.

In the end of 2013, the approval was expanded to people with previous antiretroviral treatment, and the drug manufacturer submitted a dossier for this new therapeutic indication, in which it claimed an added benefit again. IQWiG came to a different conclusion: The only study cited in the dossier was too short for the assessment of an added benefit, and the appropriate comparator therapy was not implemented. Hence an added benefit of rilpivirine/emtricitabine/tenofovir in the treatment of adults infected with HIV-1 with previous antiretroviral treatment is not proven.

New therapeutic indication, new comparator therapy

According to the expansion of approval from November 2013, the fixed drug combination can now also be used in HIV-1 infected adults with a viral load of no more than 100,000 RNA copies per millilitre who have already received antiretroviral treatment – provided that their virus has

no mutations associated with known resistance to the drugs.

Since these patients had already received antiretroviral treatment, which possibly did not have a satisfactory effect or had to be discontinued, the Federal Joint Committee (G-BA) specified a different appropriate comparator therapy than in 2012 for non-pretreated patients: Antiretroviral treatment was now to be specified individually, depending on the previous treatment and the reason for treatment switching, e.g. treatment failure or side effects.

Comparator therapy not implemented

In its dossier, the manufacturer presented one single study, in which the drug combination was compared with an individual antiretroviral treatment. However, no switch of treatment was possible in the control group. Instead, the patients continued their previous treatment – although approximately 10% of them complained of side effects in the beginning, and about 20% claimed to be worried about longterm side effects of their previous treatment.

Randomized controlled phase far too short

Moreover, the rilpivirine/emtricitabine/tenofovir combination was only compared with the appropriate comparator therapy for 24 weeks in the study. But the research question of the benefit assessment cannot be answered on the basis of such a short study; this would require at least one to two years.

For these reasons, an added benefit of rilpivirine/emtricitabine/tenofovir is not proven for HIV-1 infected adults with previous antiretroviral treatment whose viruses do not have mutations associated with resistance.

G-BA decides on the extent of added benefit

The dossier assessment is part of the overall procedure for early benefit assessments supervised by the G-BA. After publication of the manufacturer's dossier and IQWiG's assessment, the G-BA conducts a commenting procedure, which may provide further information and result in a change to the benefit assessment. The G BA then decides on the extent of the added benefit, thus completing the early benefit assessment.

More information: An overview of the results of IQWiG's benefit assessment is given by a German-language executive summary. In addition, the website " www.gesundheitsinformation.de, published by IQWiG, provides easily understandable and brief German-language information on rilpivirine/emtricitabine/tenofovir.

The G-BA website contains both general English-language information on benefit assessment pursuant to §35a Social Code Book (SGB) V and specific German-language information on the assessment of rilpivirine/emtricitabine/tenofovir. More English-language information will be available soon (Sections 2.1 to 2.6 of the dossier assessment as well as subsequently published health information on " www.informedhealthonline.org).

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