Ombitasvir/paritaprevir/r in hepatitis C: Indication of added benefit in certain patients

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The fixed-dose drug combination ombitasvir/paritaprevir/ritonavir (trade name Viekirax) has been available since January 2015 for the treatment of adults with chronic hepatitis C infection. 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 are indications of an added benefit in patients who have not yet developed cirrhosis of the liver and who are infected with the hepatitis C virus (HCV) genotype 1a. In case of genotype 1b, this only applies to treatment-naive, but not to treatment-experienced patients. The extent of added benefit is non-quantifiable, however. No added benefit can be derived from the dossier for 13 other patient groups.

Differentiated approvals result in a large number of patient groups

The new fixed-dose combination is only approved in combination with other drugs (dasabuvir and/or ribavirin). The Summaries of Product Characteristics specify partly different treatment regimens both for these drugs or drug combinations and for the respective comparator therapies. This results in as many as 16 patient groups for this benefit assessment, which mainly differ in type of virus, pretreatment and stage of disease.

Two direct comparative studies

All 16 groups were reflected in the dossier compiled by the drug manufacturer, but the data were informative for only 3 of these groups. The benefit assessment was based on two randomized controlled approval studies (MALACHITE I and II), in which ombitasvir/paritaprevir/ritonavir in combination with dasabuvir and/or ribavirin was directly compared with triple therapy consisting of telaprevir, pegylated interferon and ribavirin.

In compliance with the approval, the new fixed-dose combination was administered in the intervention arm for a period of 12 weeks, whereas treatment in the comparator arm could last up to 48 weeks, depending on response to the treatment.

Patients in the intervention arm were free of the virus more frequently

These two studies provided conclusive results for patients who have not yet developed cirrhosis of the liver and who are infected with a virus of genotype 1a or 1b. In genotype 1a, this applies both to treatment-naive patients and to patients who had relapsed after initially successful treatment. In genotype 1b, appropriate data were available only for treatment-naive patients.

In these three patient groups, the data showed a statistically significant difference in sustained virologic response (SVR) in favour of the new fixed-dose combination. IQWiG derived an indication of an added benefit from this. Its extent is non-quantifiable, however. It remained unclear in how many patients in whom the virus is no longer detectable, late complications, and liver cancer in particular, can actually be prevented.

Quality of life: advantage in treatment-naive patients

For the first time in the assessment of a hepatitis C drug, the manufacturer dossier contained evaluable data on health-related quality of life, which is of particular importance regarding interferon, which is considered to be very burdensome. These data on quality of life showed an advantage of ombitasvir/paritaprevir/ritonavir at least for the duration of treatment. This applies to certain treatment-naive genotype 1a or 1b patients, but not to treatment-experienced patients (genotype 1a). It depends on the severity of the disease whether they have an advantage and how big this advantage is.

IQWiG derived a hint of an added benefit with differing extent from these data.

Data on side effects partly not conclusively interpretable

The important differences in treatment duration between intervention and control arm, which could be up to 36 weeks, partly made it impossible to interpret differences in side effects. Since the observation periods also differed, the results were probably biased. In certain patient groups or aspects of side effects (serious adverse events and treatment discontinuation), however, the data were robust and therefore conclusions could be drawn. In each case, the results were in favour of the new fixed-dose combination.

IQWiG therefore sees a hint or an indication of lesser harm in treatment-naive genotype 1b patients and an indication of lesser harm in treatment-experienced genotype 1a patients for individual aspects of side effects. Overall, greater or lesser harm is not proven.

Robust data were lacking for further patient groups

The dossier contained no suitable data for the remaining 13 patient groups (genotype 1 or 4). Since direct comparative studies were lacking, the manufacturer referred to studies on ombitasvir/paritaprevir/ritonavir, in which the fixed-dose combination was not tested against the appropriate comparator therapy, however. No systematic comparison with data on the appropriate comparator therapy was conducted. Since there was also no systematic search for studies on the comparator therapies, it can be assumed that the data were incomplete.

Overall, an indication of a non-quantifiable added benefit can be derived from the dossier for three patient groups: patients without cirrhosis of the liver infected with genotype 1a (treatment-naive and treatment-experienced) and with genotype 1b who have not been pretreated.

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/A15-04_K … ertung-35a-SGB-V.pdf

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