Dasabuvir and ombitasvir/paritaprevir/ritonavir: Hint of added benefit in further patients

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Dasabuvir (trade name Exviera) and the fixed-dose drug combination ombitasvir/paritaprevir/ritonavir (trade name Viekirax) have 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) had examined their added benefit in a dossier assessment completed in April 2015.

In an addendum, the Institute now assessed study data subsequently submitted by the drug manufacturer in the commenting procedure. According to the findings, the results of an indirect comparison show a hint of an added benefit of both drugs also in pretreated patients with genotype 1b infection without cirrhosis. The extent of this added benefit is non-quantifiable.

Differentiated approvals result in a large number of patient groups

Both dasabuvir and ombitasvir/paritaprevir/ritonavir are only approved in combination with further drugs, including dasabuvir plus ombitasvir/paritaprevir/ritonavir. Since the Summaries of Product Characteristics recommend partly different treatment regimens both for these two drugs and for the respective comparator therapies, there are different patient groups for the benefit assessment, which mainly differ in type of virus, pretreatment and stage of disease.

The Federal Joint Committee (G-BA) specified either dual therapy (peginterferon plus ribavirin) or triple therapy, i. e. a combination of a protease inhibitor with peginterferon and ribavirin, as appropriate comparator therapies.

Studies suitable for indirect comparison

In the commenting procedure, the manufacturer now subsequently submitted results of an indirect comparison. This comparison was based on two randomized controlled trials (RCTs): The first study (PEARL II) compared dasabuvir plus ombitasvir/paritaprevir/ritonavir with dasabuvir plus ombitasvir/paritaprevir/ritonavir plus ribavirin. The second study (MALACHITE II) compared the latter combination with triple therapy. Hence dasabuvir plus ombitasvir/paritaprevir/ritonavir plus ribavirin was suitable as a so-called common comparator. Since the studies and their participants were sufficiently similar, the comparison is principally possible and suitable. The results are less informative than in a direct comparison, however.

Advantage in virologic response

This indirect comparison showed a statistically significant difference in favour of dasabuvir plus ombitasvir/paritaprevir/ritonavir in "sustained virologic response" (SVR). A hint of an added benefit can be derived from this for one further group of patients, for which initially this was not possible on the basis of the dossier.

This patient group consists of pretreated patients infected with genotype 1b virus who have not (yet) developed cirrhosis. The extent of this added benefit cannot be quantified, however. It remains unclear in how many patients in whom the virus is no longer detectable, late complications, and liver cancer in particular, can actually be prevented.

Now added benefit for approximately 90% of the patients

In the dossier assessment from May 2015, IQWiG had determined an indication of a non-quantifiable added benefit of dasabuvir and ombitasvir/paritaprevir/ritonavir in a total of three patient groups, which was primarily justified by an advantage in SVR and derived from studies of direct comparisons. These were pretreated and treatment-naive patients with genotype 1a infection and treatment-naive patients with genotype 1b. Pretreated patients with genotype 1b now form the fourth group. The limitation that the patients have not yet developed cirrhosis applies to all four groups.

The data still do not show an advantage for the remaining groups of patients. But these populations are comparably small. Overall, IQWiG now sees an added benefit in approximately 90% of the patients for whom the two drugs are approved.

G-BA decides on the extent of added benefit

The 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 manufacturer's dossier and the IQWiG dossier assessment, the manufacturer submitted additional information in the commenting procedure. The G-BA subsequently commissioned IQWiG to assess the data subsequently submitted. IQWiG now presents this assessment in the form of an addendum. The G-BA makes a final decision on the extent of added benefit.

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