Boceprevir: Indication of added benefit for specific patients

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The active ingredient boceprevir has been available since the middle of 2011 as a treatment for chronic hepatitis C of genotype 1. In an early benefit assessment pursuant to the "Act on the Reform of the Market for Medicinal Products" (AMNOG), the German Institute for Quality and Efficiency in Health Care (IQWiG) has now examined to establish whether boceprevir offers added benefit in comparison with the previous standard therapy.

According to this assessment, the dossier submitted by the pharmaceutical company provides indications of added benefit for patients who have not yet developed liver cirrhosis. However, the extent of this added benefit cannot be classified.

The pharmaceutical company provided no data - or inadequate data - for two other indications - patients with liver cirrhosis and patients for whom prior treatment was totally ineffective (zero response to prior interferon-based therapy) - and therefore added benefit for these patients is not proven.

An addition to previous standard drug therapy

Hepatitis C viruses attack the liver and can trigger inflammation there. If this becomes chronic, cirrhosis can develop and liver function progressively deteriorates. Moreover, the risk of liver cancer (hepatocellular carcinoma, HCC) increases. Boceprevir (trade name

Victrelis®, manufacturer MSD Sharp & Dohme) inhibits the reproduction of hepatitis C viruses. Experts assume that if no viruses are detectable in the blood over a sustained period after treatment (sustained virological response, SVR), the risk of secondary disease is reduced.

Boceprevir is administered in addition to the active ingredients peginterferon alfa and ribavirin, which are already on the market. In accordance with the approval status, different patient groups are treated for different periods, as was allowed for in the assessment. The dual combination of peginterferon alfa and ribavirin has been the standard therapy and this was compared with boceprevir given in a triple combination with the former two drugs.

Reduction in secondary diseases: extent cannot be classified.

For the two indications of pretreated (treatment-experienced) and non-pretreated (treatment-naive) patients without cirrhosis, data from one approval study each (SPRINT-2 and RESPOND-2) were available. With the available studies, it is not possible to assess directly whether the new active ingredient influences secondary diseases, such as the development of liver cancer. This is partly because the studies have not lasted long enough for these patient-relevant outcomes to be recorded.

With respect to SVR, there was a clear advantage for boceprevir, both for pretreated patients and for non-pretreated patients without liver cirrhosis. However, SVR is not itself a patient-relevant outcome and cannot be equated with "cure", and there are no studies in which SVR is validated as a surrogate outcome in accordance with the usual criteria employed by IQWiG. Nevertheless, the Institute accepts SVR in the context of the assessment as a surrogate for the reduced incidence of liver cancer. This is because it is currently accepted that patients with no

detectable hepatitis C virus in the blood are at lower risk of liver cancer. However, it is unclear how many cases of liver cancer can in fact be prevented by boceprevir.

For the outcome "secondary diseases", IQWiG recognizes an "indication" of a benefit for boceprevir. The requirements for a "proof" are not fulfilled, one reason being that the data are only derived from a single study each, with a comparatively small number of patients. Moreover, the scientific data do not permit a conclusive assessment of the number of patients in whom liver cancer is actually prevented. It is therefore unclear whether the added benefit is "minor", "considerable" or "major". For such a case, the corresponding legal ordinance specifies the assessment category of "unquantifiable".

Indication of greater harm for patients without prior treatment

The indication of greater benefit is in contrast to the indication of greater harm, but only in previously untreated patients. In these patients, boceprevir more often led to anaemia, although this was rarely serious. IQWiG classified the extent of this greater harm as "considerable". In contrast, in patients with prior treatment, anaemia was no more frequent than with standard treatment.

Effect on mortality unclear

IQWiG established that the approval studies contained inadequate data on quality of life for patients with or without prior treatment. There were no statistically significant differences in mortality between the treatment groups. It thus remains unclear if and how boceprevir influences mortality.