Daclatasvir for hepatitis C: Hint of added benefit in genotype 4

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Daclatasvir (trade name Daklinza) has been approved since August 2014 for the treatment of adults with chronic hepatitis C (CHC) infection. According to the dossier assessment conducted by the German Institute for Quality and Efficiency in Health Care (IQWiG) in December 2014, no added benefit could be derived for daclatasvir.

In an addendum, the Institute now examined information subsequently submitted by the drug manufacturer in the commenting procedure: According to the findings, there is a hint of an added benefit for treatment-naive patients with genotype 4. The extent is non-quantifiable, however. The study for patients infected with hepatitis C virus (HCV) of genotype 3, which was presented for the first time, is unsuitable to derive an added benefit.

Genotype 4: Additional analyses reinforce advantage of daclatasvir

In the dossier, the manufacturer had analysed one study (AI444042) for treatment-naive HCV genotype 4 patients. Since many patients had discontinued treatment, however, numerous values were missing in the analysis. These missing values had not been considered adequately in the analysis of the study data. The manufacturer dossier last year therefore provided no robust results for the valid surrogate outcome "sustained virologic response (SVR)".

The manufacturer presented further information on the SVR in its comment on IQWiG's dossier assessment. According to the assessment of these data and supplementary analyses by IQWiG, the results on the outcome "SVR" in favour of daclatasvir were shown to be robust: On completion of the treatment, virus particles (HCV RNA) were detectable in more patients in the control arm than in the daclatasvir arm. Overall however, the study results were so uncertain that no more than a hint of an added benefit can be derived from them.

The extent of this added benefit is non-quantifiable, also because it cannot be derived from the results on SVR how many cases of liver cancer can actually be prevented.

HCV genotype 3: uncontrolled study provided no comparator data

In the commenting procedure on the dossier assessment, the manufacturer presented data from a study (ALLY 3) on HCV genotype 3 patients for the first time. This study is unsuitable for conclusions on the added benefit, however: The presentation of study characteristics and results was incomplete, and the analyses were not comprehensible. In addition, the study participants were treated differently than recommended by the Summary of Product Characteristics. Due to the uncontrolled design, the study additionally provided no results on the comparison with the appropriate comparator therapy so that no added benefit can be derived.

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 conclusively decides on the extent of added benefit.

Provided by Institute for Quality and Efficiency in Health Care