Vandetanib: IQWiG assessed data subsequently submitted by the manufacturer

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Vandetanib (trade name: Caprelsa) has been approved in Germany since February 2012 for the treatment of adult patients who have a particular form of aggressive thyroid cancer. On the inclusion of additional study data subsequently provided by the drug manufacturer in the commenting procedure, the German Institute for Quality and Efficiency in Health Care (IQWiG) came to a different conclusion in an addendum: According to the findings, there is a hint of a minor added benefit in people aged under 65 years, but a hint of greater harm (lesser benefit) in older patients in comparison with standard therapy ("best supportive care").

Additional analyses on pain and side effects

In IQWiG's dossier assessment from June 2013, important data for the harm side were missing. The Institute was therefore unable to balance positive and negative effects, and could therefore not accord an added benefit.

In the commenting procedure conducted by the Federal Joint Committee (G-BA), the pharmaceutical company now submitted additional analyses both on side effects (adverse events) and on the degree of pain. The G-BA subsequently commissioned the Institute to investigate whether, using these additional data, an added benefit of vandetanib is proven with regards to morbidity (symptoms, here: pain) and the uncertainties regarding harm are resolved.

Pain rated as severe or serious

The dossier assessment concluded that pain occurs later or gets worse later in patients aged under 65 years if they are treated with vandetanib. In people aged over 65 years, however, there was no difference in comparison with "best supportive care".

The data provided in the manufacturer's dossier did not allow to rate the severity of the pain. The additional analysis now showed that this pain in patients with this kind of pain progression is to be rated as "severe" or "serious" symptoms. IQWiG therefore considers there to be a hint of an added benefit, the extent of which is to be rated as "considerable" – and not only "minor" as in the dossier assessment from June 2013.

More side effects under vandetanib

The additional analysis on side effects (adverse events) now allowed to assess the data although the patients in the two study arms were treated and observed for different lengths of time. It showed that vandetanib causes side effects more frequently than "best supportive care" – independent from the patients' age. This applies to severe adverse events and skin rash. There was no difference between the study arms regarding serious adverse events and discontinuations of treatment due to side effects. IQWiG rated the extent of harm as "major" (severe adverse events) and "considerable" (skin rash).

People aged under 65 years: negative effects do not outweigh positive effects

IQWiG considers there to be both positive and negative effects in people aged under 65 years: The delay in pain progression is not outweighed by more frequent side effects. But IQWiG downgraded the extent of added

benefit from "considerable" to "minor".

The assessment only found negative effects in the group of people aged over 65 years: There is only "major" and "considerable" harm in the form of side effects.

Overall, IQWiG concludes that there is a hint of minor added benefit in patients aged under 65 years, but a hint of lesser benefit in patients aged over 65 years of vandetanib compared with "best supportive care".

G-BA decides on the extent of added benefit

The dossier assessment is part of the overall procedure for early benefit assessment conducted by the G-BA. After publication of the manufacturers' dossiers and the IQWiG dossier assessments, the G-BA conducted commenting procedures, in which the manufacturer submitted additional information. The G-BA subsequently commissioned IQWiG to undertake a new assessment, with the additional data included.

If, in the course of the discussions on a commission of the G-BA, a need for further revision arises, IQWiG presents its report in the form of an addendum. The Institute sent the addendum on vandetanib to the contracting agency on 8 August 2013. The G-BA then decides on the extent of the added benefit in each case, thus completing the early benefit assessment.

Provided by Institute for Quality and Efficiency in Health Care