Enzalutamide: IQWiG assessed data subsequently submitted by the manufacturer

February 21 2014

Enzalutamide (trade name: Xtandi) has been approved since June 2013 for men with metastatic prostate cancer in whom the commonly used hormone blockade is no longer effective and who have already been treated with the cytostatic drug docetaxel. In an early benefit assessment pursuant to the Act on the Reform of the Market for Medicinal Products (AMNOG) in November 2013, the German Institute for Quality and Efficiency in Health Care (IQWiG) determined an added benefit of this new drug over the appropriate comparator therapy specified by the Federal Joint Committee (G-BA).

However, due to insufficient data, not more than a "hint" was found. Moreover, this hint only had the extent "considerable" in patients with visceral metastases, i.e. secondaries in internal organs. Based on data subsequently provided by the manufacturer in the commenting procedure, the Institute now came to a different conclusion in an addendum: There is an indication of a major added benefit in the patient group without visceral metastases. In patients with visceral metastases, there is a hint of a major added benefit.

Pain therapy adequately implemented

Metastatic prostate cancer is incurable, but treatment may relieve symptoms, for example. Such palliative treatment, adapted to the individual needs of the patients, is called "best supportive care" (BSC). The benefit assessment was based on data from the approval study

AFFIRM, in which enzalutamide with BSC was tested against BSC alone. It was unclear at first whether patients received adequate pain therapy throughout the entire study and whether therefore the criteria of BSC were fulfilled.

No more than "hints" could be derived from the manufacturer's dossier because of this uncertainty. The study data subsequently submitted in December 2013 remedied this shortcoming: The manufacturer was able to show that the pain therapy was consistently optimized to the individual patient, and that therefore the appropriate comparator therapy was implemented correctly. Hence for the group of patients without visceral metastases, instead of a hint, there is an indication of a major added benefit of the new drug versus BSC.

Added benefit in side effects can now be quantified

For patients with visceral metastases, no significant increase in survival time could be derived from the original study data, but an advantage in morbidity. However, on the basis of these data, the extent of added benefit was not "major", but only "considerable" for this patient group.

The data on side effects in the original dossier were not evaluable. The documents subsequently submitted now facilitated a description of the differences in the side effects of the treatment alternatives. This results in a major advantage of enzalutamide versus BSC in serious and severe adverse events in patients with and without visceral metastases. Strong painkillers, which are often associated with severe side effects, had to be used less frequently than under BSC alone, for example.

This also increased the extent of added benefit for patients without visceral metastases to "major".

Higher rating for added benefit

Overall, there is an indication of a major added benefit of the new drug for patients without metastases in internal organs due to the improved reliability of the conclusions in the implementation of the comparator therapy. The Institute now also determined a hint of a higher, i.e. also major, added benefit for patients with visceral metastases due to quantifiable data on side effects.

G-BA decides on the extent of added benefit

The dossier assessment is part of the overall procedure for early benefit assessments supervised by the G-BA. After publication of the manufacturer's dossier and the IQWiG dossier assessment, the G-BA conducted commenting procedures, in which the manufacturer submitted additional information. The G-BA subsequently commissioned IQWiG to assess the data subsequently submitted.

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 enzalutamide to the commissioning agency on 30 January 2014.

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