Cobimetinib in advanced melanoma with BRAF V600 mutation: Added benefit now considerable

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Cobimetinib (trade name: Cotellic) has been approved since November 2015 in combination with vemurafenib for the treatment of adults with advanced, i.e. metastatic or unresectable, melanoma with a BRAF V600 mutation. In a dossier assessment from March 2016, the German Institute for Quality and Efficiency in Health Care (IQWiG) found both advantages and disadvantages of cobimetinib in combination with vemurafenib in comparison with the appropriate comparator therapy vemurafenib alone. This resulted in an indication of a minor added benefit.

In the subsequent commenting procedure, the drug manufacturer presented further data analyses, which were now included in the assessment in a so-called addendum. This increased the extent of the added benefit: There is now an indication of a considerable added benefit of cobimetinib plus vemurafenib in comparison with vemurafenib monotherapy.

Third data cut-off of the approval study decisive

The manufacturer dossier was based on the study coBRIM, which was decisive for the approval. In this study, cobimetinib in combination with vemurafenib was directly compared with vemurafenib. Besides advantages, particularly in overall survival, several disadvantages also resulted from the data.

In the commenting procedure conducted by the Federal Joint Committee (G-BA) after IQWiG's dossier assessment, the manufacturer now in particular presented more informative analyses on symptoms and health-related quality of life from the third data cut-off, as well as further results for the fourth and fifth data cut-off. The third data cut-off was decisive for the benefit assessment because the recording of symptoms and health-related quality of life was discontinued shortly afterwards. It was investigated whether the data from the later cut-off dates raised doubts about the overall conclusion on the added benefit - which was not the case.

Additional positive effects in symptoms and quality of life

In contrast to the unchanged considerable negative effects of the combination therapy, there were now additional positive effects, which had a major extent for benign, malignant and unspecified neoplasms. There were further advantages in symptoms (insomnia) and health-related quality of life; these were only found for patients under 65 years of age, however. Moreover, the advantages of the drug combination in the outcome "pain" now applied to the total population and not only to under 65-year-olds as before.

Overall, there is now an indication of considerable added benefit of cobimetinib in combination with vemurafenib in comparison with the appropriate comparator therapy.

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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