Perampanel for epilepsy: No proof of added benefit

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The drug perampanel (trade name Fycompa) has been approved since July 2012 as adjunctive ("add-on") therapy for adults and children aged 12 years and older with epileptic fits (seizures). In an early benefit assessment according to the German Act on the Reform of the Market for Medicinal Products (AMNOG), the German Institute for Quality and Efficiency in Health Care (IQWiG) examined whether perampanel offers an added benefit over the previous standard therapy. However, no such added benefit can be derived from the dossier, because the manufacturer failed to present any relevant data in it for the comparison with the drugs lamotrigine or topiramate.

Lamotrigine and topiramate as appropriate comparator therapy

Fits that affect only a small part of the brain are called "focal" or "partial seizures". In this type of fit, the muscle twitches and spasms remain limited to isolated parts of the body. They may, however, spread over the entire body and this process is then called a "secondary generalization". Perampanel is approved as add-on therapy for the treatment of partial seizures with or without secondary generalization in people aged 12 years and older.

When the Federal Joint Committee (G-BA) specified the appropriate comparator therapy, it distinguished between two treatment situations: if the first-line (basic) anti-epileptic treatment does not contain lamotrigine

, perampanel as add-on therapy should be compared with lamotrigine as add-on therapy. If, on the other hand, lamotrigine is already part of the basic treatment, then perampanel as add-on therapy should be compared with topiramate as add-on therapy.

Topiramate not considered in the dossier

However, in its dossier, the pharmaceutical company deviated from this specification of the G-BA and considered only lamotrigine. In those cases where lamotrigine was already contained in the basic treatment, the manufacturer stated that a comparison with topiramate was "not productive". But IQWiG does not accept this explanation from the manufacturer.

Comparisons with lamotrigine not adequate

In order to demonstrate the added benefit over lamotrigine, the manufacturer provided data on a direct and an indirect comparison. However, ultimately the former comparison was with a dummy drug (a placebo). Although in this case a placebo comparison can prove a benefit, it cannot prove an added benefit.

For various reasons, the indirect comparison is also inadequate. Amongst other things, perampanel was not tested here against lamotrigine (in each case as add-on therapy), but instead a combination of perampanel and lamotrigine against lamotrigine, in each case in addition to basic treatment, was tested.

Since neither the indirect nor the direct comparisons are suitable for answering the research question, no relevant study results are available for the benefit assessment. Hence there is also no proof of an added benefit.

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 IQWiG's assessment, the G-BA conducts a commenting procedure, which may provide further information and result in a change to the benefit assessment. The G-BA then decides on the extent of the added benefit, thus completing the early benefit assessment.

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