Nalmefene for alcohol dependence: Added benefit not proven

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Nalmefene (trade name Selincro) has been approved since February 2013 for people with alcohol dependence who currently drink a lot of alcohol, but who do not have physical withdrawal symptoms and who do not require immediate detoxification. The German Institute for Quality and Efficiency in Health Care (IQWiG) examined in a dossier assessment whether the drug offers an added benefit over the appropriate comparator therapy in this patient group.

According to the findings, such an added benefit is not proven: In its dossier, the drug manufacturer only presented data for an indirect comparison with the appropriate comparator therapy naltrexone. These data are unsuitable, however. In six out of seven studies on naltrexone, patients and treatment goals differ fundamentally from the ones in the nalmefene studies. In the seventh study, naltrexone was temporarily not used in compliance with the approval, and there were no analyses for relevant periods of time in the study.

Treatment goal: reduce alcohol consumption

Nalmefene is approved for people with alcohol dependence who do not have physical withdrawal symptoms and who do not require immediate detoxification. The drug is an option for people who want to reduce their current high level of alcohol consumption (approximately three bottles of beer for men, and approximately two bottles of beer for women), but are unable to do so of their own accord within two weeks. Nalmefene

influences the release of transmitters in the brain to help reduce the urge to drink alcohol, thus decreasing the amount of alcohol intake for alcohol-dependent men and women. According to the approval, the drug is used together with psychosocial support, e.g. in combination with counselling, behavioural therapy or psychotherapy.

For the therapeutic indication of nalmefene, the Federal Joint Committee (G-BA) specified naltrexone as the appropriate comparator therapy. The Pharmaceutical Directive was to be taken into account, which specifies the use of nalmefene in alcohol-dependent men and women who are to undergo abstinence treatment, but are still waiting for a therapy place.

Indirect comparison using placebo

The manufacturer conducted an adjusted indirect comparison in its dossier because there were no direct comparative studies on nalmefene versus naltrexone. It included a total of eleven studies, in which the drug was compared with placebo. Hence the placebo was used as the so-called common comparator.

Four studies investigated the effect of nalmefene in comparison with placebo in alcohol-dependent people with the goal to reduce alcohol consumption. The manufacturer presented analyses of those study participants who still drank alcohol with at least a high risk level at the start of the study. These patients correspond to the research question and the data would, in principle, be evaluable for an indirect comparison.

Different patients and different treatment goals in comparator studies

Seven studies investigated the effect of naltrexone in comparison with

placebo. In six of them however, the treatment goals were abstinence and prevention of relapse. Only patients who had abstained from drinking alcohol for several days before the start of the study were included in these six studies. However, these patients do not concur with the research question for the benefit assessment, which particularly considered patients who currently drink alcohol at a high risk level. A comparison with nalmefene patients with a current high level of alcohol consumption with naltrexone patients who are already abstinent cannot be interpreted in a meaningful way also with regard to outcomes like change in drinking behaviour. Hence these studies provide no suitable data for the indirect comparison of nalmefene and naltrexone.

The seventh naltrexone study is not relevant because the drug was not administered in compliance with the approval over the entire course of the study, and no suitable results were available. Hence no suitable data for the indirect comparison resulted from the seven naltrexone studies, and IQWiG therefore concluded: An added benefit of nalmefene is not proven.

G-BA decides on the extent of added benefit

The dossier assessment is part of the overall procedure for early benefit assessments 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 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.

More information: www.iqwig.de/download/A14-30_N … ertung-35a-SGB-V.pdf