RECOMMENDATION ON ZOLBETUXIMAB IN THE FIRST-LINE TREATMENT OF GASTRIC OR GASTRO-OESOPHAGEAL JUNCTION ADENOCARCINOMA

At its meeting of 28 August 2025, the Council for Choices in Health Care in Finland (COHERE Finland) adopted a recommendation on zolbetuximab in the first-line treatment of gastric or gastro-oesophageal junction (GEJ) adenocarcinoma.

Zolbetuximab, in combination with fluoropyrimidine- and platinum-containing chemotherapy, is not included in the national range of services for the first-line treatment of adult patients with locally advanced unresectable or metastatic HER2-negative gastric or gastro-oesophageal junction (GEJ) adenocarcinoma whose tumours are Claudin (CLDN) 18.2 positive.
The evidence from two phase III studies shows that the median PFS rates were 2.1 months and 1.4 months and the median OS rates 2.6 months and 2.1 months for patients treated with zolbetuximab compared to patients who received placebo. Thus, zolbetuximab was found to have little clinically significant effect. Applying this evidence to the Finnish patient population involves uncertainty. According to the research evidence, patients treated with zolbetuximab experienced more adverse reactions than those in the control group.

The evidence for the efficacy and safety of zolbetuximab is based on two phase III studies in patients with good performance status. In these studies, zolbetuximab was used as first-line treatment in combination with platinum-based chemotherapy. The differences between the median PFS rates for the primary outcome variable were 2.1 months and 1.4 months when comparing zolbetuximab with the placebo arm. The differences between the median OS rates for the secondary outcome variable were 2.6 months and 2.1 months when comparing zolbetuximab treatment with the placebo arm. In both arms, over 70% of patients had died by the time of the analysis. In one of these studies, the overall response rate was 48% in both the zolbetuximab and placebo arms. The median duration of response was 9.0 months for zolbetuximab and 8.1 months for placebo treatment. In the other study, the overall response rate was 43% in the zolbetuximab arm and 39% in the

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placebo arm. The median duration of response was 6.1 months in both the zolbetuximab and placebo arms. No statistically significant differences were observed between the overall response rate and the duration of response. When assessing the health-related quality of life, baseline measurement results were similar between the treatment arms in both studies, and no statistically significant differences were observed during the studies. A combined analysis of the indicators showed that the quality of life was similar in both treatment arms. In COHERE's opinion, the clinical efficacy of zolbetuximab in combination with chemotherapy in patients with gastric adenocarcinoma whose performance status is good remains minimal. The clinical significance of outcomes for Finnish patients remains uncertain. Almost all patients experienced at least one adverse event and approximately half experienced a severe adverse event. The most common adverse events included nausea, vomiting, decreased appetite, anaemia and diarrhoea. The most common severe or life-threatening adverse events were vomiting, nausea, neutropenia, neutrophil count decreased and anaemia. An adverse event leading to the permanent discontinuation was associated with treatment in 10.5% of the patients who received zolbetuximab and in 3.2% of the patients who received placebo. The most common adverse events leading to permanent discontinuation were nausea and vomiting.

The marketing authorisation holder compared zolbetuximab with two PD-(L)1 inhibitors, nivolumab and pembrolizumab, through indirect comparison. Their use in combination with chemotherapy is the comparator therapy most in line with the standard of care practice. Based on these results, no statistically significant differences were observed between zolbetuximab and PD-(L)1 inhibitors. According to the Finnish Medicines Agency (Fimea), the cost of zolbetuximab at list prices would be approximately EUR 21,000 more than the cost of nivolumab and around EUR 28,000 less than the cost of pembrolizumab.

This is a summary of a recommendation adopted by the Council for Choices in Health Care in Finland (COHERE Finland). The actual recommendation and the related background material are available in Finnish on the website of COHERE Finland under Valmiit suositukset.

The summary of the recommendation is also available in Finnish and Swedish on the website.

The Council for Choices in Health Care in Finland (COHERE Finland) is attached to the Ministry of Social Affairs and Health. Its mission is to issue recommendations on services that should be included in the range of public health services. Further information about service choices in healthcare is available on the COHERE Finland website.

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