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[C2H2201] Summary of cost-effectiveness evaluation of gefapixant (Lyfnua®)

1. Indications

Refractory or unexplained chronic cough

2. Price of the drug

Gefapixant (Lyfnua®) has been reimbursed since April 2022 at JPY 203.20 (as of May 2023). The price is calculated using a cost calculation method without a premium. This product is designated as an H1 cost-effectiveness evaluation item.

3. Scope of cost–effectiveness evaluation

This product is indicated for the treatment of refractory or unexplained chronic cough. The scope of evaluation agreed upon at the first session of the Expert Committee of Cost-Effectiveness Evaluation (ECCEE) is described below.

Population	Refractory or unexplained chronic cough
Comparator	Non-treatment or watchful waiting (including treatment* for the underlying cause)

*Treatment including inhaled corticosteroid/long-acting β2-agonist (ICS/LABA), histamine H1 receptor antagonists, proton pump inhibitors, and central antitussives drugs

4. Evaluation of additional benefits

In this systematic review, the randomized COUGH-1 and COUGH-2 trials were detected. The participants were randomly allocated (1:1:1) to one of three treatment groups: placebo, gefapixant 15 mg twice daily, or gefapixant 45 mg twice daily. The primary outcome was the mean change in 24-h cough frequency at 12 weeks in COUGH-1 and 24 weeks in COUGH-2.

Gefapixant 45 mg twice daily showed significant reductions in 24-h cough frequency compared with placebo at week 12 in COUGH-1 (18.45% [(95%CI 0.86 to 32.92, p=0.041) and at week 24 in COUGH-2 (95%CI 1.43 to 26.07, p=0.031). The number of participants experiencing taste-related adverse events was 141/243 (58.0%) in the gefapixant 45 mg group and 8/243 (3.3%) in the placebo group in COUGH-1, and 303/440 (68.6%) in the gefapixant 45 mg group and 36/432 (8.3%) in the placebo group in COUGH-2.

Consequently, the academic group concluded that Lyfnua has additional benefits for the comparator.

5. Results of the cost-effectiveness analysis

The manufacturer performed a cost–utility analysis for each population using Markov models consisting of three health states (on-treatment, off-treatment, and death).

The overall analysis by the manufacturer was considered appropriate. The academic group identified the following limitations of the manufacturer's analysis.

- Health states of the Markov model were not based on cough frequency or severity.
- The difference between the mean quality of life (QOL) scores of the gefapixant 45 mg group and placebo groups was not statistically significant in the COUGH-1 and COUGH-2 trials.

The ECCEE accepted the following criteria:

Population	Comparator	ICER (JPY/QALY)
Refractory or unexplained chronic cough	Non-treatment or watchful waiting	17,569,051