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[C2H2208] Summary of cost-effectiveness evaluation of molnupiravir (Lagevrio®)

1. Indications

Coronavirus disease 2019 (COVID-19)

2. Price of the drug

Molnupiravir has been reimbursed from August 2022 at JPY 2,357.80 (as of March 2024). The price was calculated using a cost calculation method with a usefulness premium (II) of 10%. This product was designated as an H1 cost-effectiveness evaluation item.

3. Scope of cost–effectiveness evaluation

This product is indicated for the treatment of COVID-19. The scope of evaluation agreed upon at the first session of the Expert Committee of Cost-Effectiveness Evaluation (ECCEE) is described below.

Population	Adults with COVID-19 who have an increased risk of progression to severe COVID-19 (aged 18 years and older) (except adults with severe COVID-19*) *The definition follows Clinical Management of Patients with COVID-19 by the MHLW version 8.1
Comparator	Standard of care (SoC)* * Except other medications indicated for treatment of COVID-19

4. Evaluation of additional benefits

The manufacturer performed a systematic review of randomized controlled trials (RCTs). Of these, they used the MOVe-OUT trial to evaluate additional benefits.

The manufacturer insisted on the additional benefits of molnupiravir over SoC because the MOVe-OUT trial showed that molnupiravir had statistically significant effect on the incidence of hospitalization or death at day 29 compared to placebo (molnupiravir: 7.3%, placebo: 14.1%, difference: -6.8%(95% CI：-11.3 to -2.4)).

The academic group noted that the MOVe-OUT trial was conducted in unvaccinated adults infected with the delta, gamma, and mu variants of SARS-CoV-2. Because the main variant of SARS-CoV-2 is Omicron and COVID-19 vaccination has become widespread in Japan, the generalizability of the study results to Japanese clinical practice is limited. Therefore, the academic group considered that the evaluation should be conducted according to the PANORAMIC trial (U.K., University of Oxford) for vaccinated adults infected with omicron variants. However, due to differences in the definition of risk factors for progression to severe COVID-19 and the SoC in Japan and the U.K., the PANORAMIC trial included some participants who were not necessarily defined as having risk factors in Japan and those who were treated with other medications indicated for COVID-19 when using molnupiravir. Therefore, the academic group evaluated the treatment effect of molnupiravir after extracting adults who met the Japanese definition of risk factors for progression to severe COVID-19 and the SoC in Japan from the PANORAMIC study. The post-hoc analysis of the PANORAMIC trial demonstrated that the odds ratio for hospitalization or death was 1.053 (95% CI: 0.775 to 1.396), and the difference in event rate was not significant between the molnupiravir plus usual care group and the usual care group. Thus, the academic group could not determine that molnupiravir had additional benefits for hospitalization or death. Clinical experts have suggested that molnupiravir may have additional benefits for older adults from subgroup analysis by age; however, the available evidence is limited, and further data are required to establish their benefits.

5. Results of the cost-effectiveness analysis

The manufacturer performed a cost-effectiveness analysis using a decision-tree model expressing the acute phase of COVID-19 and a Markov model expressing the post-acute phase of COVID-19. The academic group performed a cost-minimization analysis because molnupiravir did not show any additional benefits over the SoC. The ECCEE accepted the following results:

Population	Comparator	Additional benefit	ICER (JPY/QALY)
Adults with COVID-19 who have an increased risk of progression to severe COVID-19	SoC	No additional benefit	Cost increase