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November 30, 2021

# [C2H2001] Summary of cost-effectiveness evaluation of posaconazole (Noxafil)

1. Indications

Prevention of invasive fungal infection (IFI)

2. Price of the drug

Posaconazole is being reimbursed since April 2020 at JPY 3,109.1 (as of November 2021). The price is calculated using a cost calculation method. This product is designated as an H1 cost-effectiveness evaluation item.

3. Scope of cost-effectiveness evaluation

This product has been observed to help in the prevention of IFI among (a) the patients who have undergone allogeneic hematopoietic stem-cell transplantation and (b) those who have or are anticipated to have neutropenia. Hereafter, the scope of evaluation agreed upon at the first session of the Expert Committee of Cost-Effectiveness Evaluation (ECCEE) is described. The target population comprises population (a) and (b) described above. The cheapest fluconazole (capsule) in population (a) and itraconazole (oral solution) in population (b) are considered as the comparators.

| | |
|---|---|
| Population | (a) Patients who have undergone allogeneic hematopoietic stem-cell transplantation<br>(b) Patients who have or are anticipated to have neutropenia |
| Comparators | (a) fluconazole (capsule)<br>(b) itraconazole (oral solution) |

4. Evaluation of additional benefits

As a result of the systematic review, two randomized control trials (RCTs) corresponding to the research questions were detected: C/I98-316 trial for population (a) and P01899 trial for population (b). These are non-inferiority trials through which the superiority of posaconazole is tested if non-inferiority is proven. In the randomized C/I98-316 trial, patients were allocated to the posaconazole (N=301) and fluconazole (N=299) groups. Similarly, in the randomized P01899 trial, patients were allocated to the posaconazole (N=304) and fluconazole/itraconazole (N=298) groups. The primary endpoint is to ensure the prevention of IFI. In population (A), the incidence of IFI was 5.3% in the posaconazole group and 9.0% in the fluconazole group. The odds ratio was 0.56 [95%CI 0.30-1.07, P=0.07]. In population (B), the incidence of IFI was 2.3% in the posaconazole group and 8.4% in the fluconazole group. The difference between both the incidences was -6.09% [95%CI -9.68—2.50%, P=0.0009].

Manufacturers insisted that in population (A), in the secondary endpoint in which the observation period is changed, posaconazole significantly reduced the incidence of IFI, although the superiority of posaconazole was not shown, considering the results of the primary endpoint.

The academic group concluded as follows.

· (a) Population A: According to the results of the C/I98-316 trial, the superiority of posaconazole for all fungal infections was not supported. However, the trial shows a significant improvement in the prevention of aspergillosis infection. Considering these results, the group concluded that posaconazole has an additional benefit that helps in the prevention of the aspergillosis infection.

· (b) Population B: Posaconazole has an additional benefit because the P01899 trial shows that it is superior to the comparators….

5. Results of the cost-effectiveness analysis

The manufacturer performed a cost-effectiveness analysis. The academic group used the model adopted by the manufacturer, but some parameters such as the probability of IFI and demographic information, were changed. The ECCEE accepted the following.

| Population | ICER (JPY/QALY) |
|---|---|
| Patients who have undergone allogeneic hematopoietic stem-cell transplantation | 9,813,704 |
| Patients who have or are anticipated to have neutropenia | 1,271,646 |