

Table 1. Results of patch testing with probenazole in patients

| Materials                                       | Conc./vehicle | Case 1 |    |    | Case 2 |    |    | Case 3 |    |
|-------------------------------------------------|---------------|--------|----|----|--------|----|----|--------|----|
|                                                 |               | D2     | D3 | D7 | D2     | D3 | D6 | D2     | D3 |
| Oryzemat <sup>®</sup>                           | 1.0/pet       | +      | +  | +  | NT     | NT | NT | ++     | ++ |
|                                                 | 0.1/pet       | +      | +  | +  | NT     | NT | NT | NT     | NT |
|                                                 | 0.01/pet      | +      | +  | +  | NT     | NT | NT | NT     | NT |
|                                                 | 0.001/pet     | –      | –  | –  | NT     | NT | NT | NT     | NT |
| Probenazole                                     | 1.0/pet       | +      | +  | +  | NT     | NT | NT | NT     | NT |
|                                                 | 0.1/pet       | +      | +  | +  | NT     | NT | NT | ++     | ++ |
|                                                 | 0.05%/pet     | NT     | NT | NT | +      | +  | +  | +      | ++ |
|                                                 | 0.01/pet      | +      | +  | –  | +      | +  | +  | +      | +  |
| Other five ingredients of Oryzemat <sup>®</sup> | 0.001/pet     | +      | +  | –  | –      | +  | –  | NT     | NT |
|                                                 | 1.0/pet       | –      | –  | –  | –      | –  | –  | NT     | NT |
|                                                 | 0.1/pet       | –      | –  | –  | NT     | NT | NT | NT     | NT |
|                                                 | 0.01/pet      | –      | –  | –  | NT     | NT | NT | NT     | NT |
| Control (pet)                                   | 0.001/pet     | –      | –  | –  | NT     | NT | NT | NT     | NT |
|                                                 | As is         | –      | –  | –  | –      | –  | –  | –      | –  |

NT, not tested; pet, petrolatum.

Table 2. Results of patch testing controls for case 3

| Materials             | Conc./vehicle | D2 | Control 1 |     | Control 2 |    |
|-----------------------|---------------|----|-----------|-----|-----------|----|
|                       |               |    | D3        | D22 | D2        | D3 |
| Oryzemat <sup>®</sup> | 1%/pet        | –  | –         | ++  | –         | –  |
| Probenazole           | 0.1%/pet      | –  | –         | +   | –         | –  |
|                       | 0.05%/pet     | –  | –         | +   | –         | –  |
|                       | 0.01%/pet     | –  | –         | +   | –         | –  |
| Control (pet)         | As is         | –  | –         | –   | –         | –  |

Pet, petrolatum.

## Occupational contact dermatitis caused by probenazole in agricultural chemical factories

Contact Dermatitis 2009; 61: 350–351

Kazue Nishioka<sup>1,2</sup>, Hiroaki Takahata<sup>1</sup>, Hidetosi Yasuno<sup>3</sup> and Go-ichiro Muramoto<sup>4</sup>

<sup>1</sup>Department of Dermatology, Yamaguchi Red Cross Hospital, Yamaguchi, Japan,

<sup>2</sup>Joy Dermatological Clinic, Sanyo-onoda, Japan, <sup>3</sup>Yasuno Dermatological Clinic,

Yamaguchi, Japan, and <sup>4</sup>Muramoto Clinic, Yamaguchi, Japan

**Key words:** agricultural chemical; occupational contact dermatitis; Oryzemat<sup>®</sup>; probenazole.

Probenazole is an agricultural chemical with antifungal properties. It is known as a contact allergen through guinea pig maximization studies, but allergic contact dermatitis in humans has not been reported in the literature. We report three cases of occupational contact dermatitis caused by probenazole at two agricultural chemical factories in Japan.

### Patients/Methods and Results

**Case 1:** In April 2003, a 24-year-old male presented with a 1-week history of dermatitis on his face, neck,

forearms, and hands. He had been manufacturing the agricultural chemical Oryzemat<sup>®</sup> during the previous 2 weeks. A 2-day closed patch test with Oryzemat<sup>®</sup>, probenazole, and other ingredients of Oryzemat<sup>®</sup> in Finn Chambers<sup>™</sup> on Scanpor<sup>™</sup> tape was undertaken. Readings were according to the ICDRG recommendations. He showed positive reactions to Oryzemat<sup>®</sup> and probenazole (Table 1). On the 9th day after the testing, erythema appeared on his face, neck, and forearms. Eleven control cases were negative to probenazole 0.1% and 0.01% pet.

**Case 2:** In January 2007, a 35-year-old male presented with a 2-week history of dermatitis. For 2 months before presentation he had been working with Oryzemat<sup>®</sup> at the same factory as Case 1. He showed positive reactions to probenazole (Table 1).

**Case 3:** Seven employees of another agricultural chemical factory were affected by dermatitis in August 2004. They had been engaged in manufacturing Oryzemat<sup>®</sup>. In June 2006, one of the seven, a 52-year-old male, underwent patch testing. He showed

positive reactions to Oryzemat<sup>®</sup> and probenazole (Table 1). Two controls were negative for Oryzemat<sup>®</sup> and probenazole. One of the two, however, developed a late reaction after 20 days (Table 2). Later, seven further controls were tested using 0.01% probenazole and these were all negative.

### Discussion

Probenazole (3-allyloxy-1, 2-benzisothiazole 1, 1-dioxide; CAS No. 27605-76-1, Fig. 1) is a synthetic bactericide used for rice blast fungus (1). Oryzemat<sup>®</sup> contains approximately 8–48% probenazole. It first appeared on the Japanese market in 1974 and has been widely used in Asia. According to the toxicity information by the manufacturer, probenazole was negative in a skin irritation study but a potent allergen in guinea pig maximization studies. We report three cases of allergic contact dermatitis caused by probenazole. In case 1, erythema on the face, neck, chest, and both forearms recurred after patch testing. Although we conducted

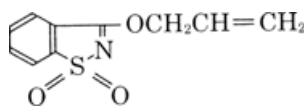


Fig. 1. Chemical structure of probenazole  
(3-allyloxy-1,2-benzisothiazole 1,1-dioxide)

patch testing only on one individual in case 3, six other individuals may have been sensitized to probenazole. One of the control subjects became actively sensitized during patch testing. A 1% dilution of probenazole seems to be too high for testing. All three cases reacted to 0.01% probenazole and two of them showed reactions to 0.001% concentration. Accordingly, a 0.01% concentration appears sufficient for diagnostic testing. A preferable number of controls is at least 20 to rule out false positive reactions (2). In our study, all 20 controls were negative reactions to 0.01% probenazole. We concluded that probenazole is a potent sensitizer for humans.

### References

1. Watanabe T, Igarashi H, Matsumoto K et al. The characteristics of probenazole (Oryzmate®) for the control of rice blast. *J Pesticide Sci* 1977; 2: 291–296.
2. Fregert S. Publication of allergens. *Contact Dermatitis* 1985; 12: 123–124.

Address:

Kazue Nishioka Joy  
Dermatological Clinic  
6-4-1 Nakagawa  
Sanyo-onoda  
Yamaguchi 756-0806  
Japan e-mail: info@joyhifuka.jp