September 2, 2002

Japan’s first domestically originated injectable new quinolone antibacterial agent
Sales release of pazufloxacin mesilate on September 2
Product names: PASIL; Pazucross INJECTION

Summary
On September 2, 2002, Toyama Chemical Co., Ltd. (president & CEO: Katsuhiko Nakano) and Mitsubishi Pharma Corporation (president & CEO: Teruo Kobori) released for sale a novel pazufloxacin mesilate (generic name).

Toyama Chemical manufactures the bulk drug, which is then formulated and sold separately by the two companies under two separate commercial names: PASIL by Toyama Chemical; and Pazucross INJECTION by Mitsubishi Pharma.

The drug discovery process for the new quinolone antibacterial pazufloxacin mesilate was the work of Toyama Chemical while development was carried out jointly with Mitsubishi Pharma. The manufacturing license was issued on April 11, 2002, and registration to the National Health Insurance (NHI) drug price list was performed on August 30.

Therapeutic significance of product (novel new quinolone injection solution increasing therapeutic options for infectious disease)
At present, cephem and carbapenem type beta-lactam drugs are generally seen as the drugs of first and second choice in the treatment of infectious diseases. It has been pointed out that this continued use of drugs with the same mechanism of action raises the risk of drug-resistant bacteria emerging in the future.

As a new quinolone drug, the product has potent antibacterial action and an alternative action mechanism to beta-lactam drugs while as an injection formulation it has superior safety to conventional quinolone drugs; its launch is expected to offer medical professionals a new option whose advantages include benefits from the viewpoint of combating the emergence of drug-resistant bacteria.

Sales release date
September 2, 2002
### Product standards and pharmaceutical tariff

<table>
<thead>
<tr>
<th>Manufacture and sale</th>
<th>Product name</th>
<th>Packaging</th>
<th>NHI price per bag</th>
</tr>
</thead>
<tbody>
<tr>
<td>Toyama Chemical Co., Ltd.</td>
<td>PASIL 300mg</td>
<td>100 mL/bag × 10</td>
<td>¥1,534</td>
</tr>
<tr>
<td>Toyama Chemical Co., Ltd</td>
<td>PASIL 500mg</td>
<td>100 mL/bag × 10</td>
<td>¥2,112</td>
</tr>
<tr>
<td>Mitsubishi Pharma Corporation</td>
<td>Pazucross INJECTION 300</td>
<td>100 mL/bag × 10</td>
<td>¥1,534</td>
</tr>
<tr>
<td>Mitsubishi Pharma Corporation</td>
<td>Pazucross INJECTION 500</td>
<td>100 mL/bag × 10</td>
<td>¥2,112</td>
</tr>
</tbody>
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### Product outline

1. Indications
   - Burn wound infection, surgical wound infection
   - Secondary infection in chronic respiratory disease (chronic bronchitis, diffuse panbronchiolitis, bronchiecstasis, pulmonary emphysema, pulmonary fibrosis, bronchial asthma, old pulmonary tuberculosis, etc.), pneumonia, pulmonary suppuration
   - Nephropyletitis, complex cystitis, prostatitis
   - Cholecystitis, choloangitis, hepatic abscess
   - Peritoneal abscess, peritonitis
   - Infection of internal genitalia (uterine adnexitis, parametritis) pelvic peritonitis

2. Administration and dosage
   The usual dosage in adults is 1000 mg/day of pazufloxacin divided into two doses and administered by intravenous infusion. Dosage may be reduced in line with age of patient and symptoms, for instance, to 600 mg/day divided into two doses and administered by intravenous infusion. Intravenous infusion should be performed over a period of 30 minutes to 1 hour.

### Characteristics of pazufloxacin mesilate injection solution

1. Developed as Japan's first domestically produced new quinolone antibacterial in highly safe injection form
   The product was developed with the aim of creating an antibacterial injection preparation which would achieve high blood concentration levels and excellent distribution to tissues at the same time as displaying equivalent clinical efficacy and safety to β-lactam drugs.

2. Indications in wide range of medical fields with excellent clinical efficacy in mild to severe infections
   The product has a wide range of indications for infectious diseases not only in the field of respiratory medicine, but also in areas such as surgery, urologic and cholangiic medicine,
gynecology and peritonitis, and displays excellent clinical efficacy in moderate to severe infection.

3. Efficacious in cases previous medication against bacterial infection has failed in all areas of medicine
   With its wide antibacterial spectrum and potent antibacterial action and an alternative mechanism of action to other antibacterial injection preparations including -lactam and aminoglycoside drugs, the product can be used with expectation of efficacy where these pharmaceuticals have failed.

4. No major adverse effects observed in clinical trials and rate of adverse effect incidence roughly equal to that of cephem pharmaceuticals
   The product has been confirmed to have a low rate of incidence for the central nervous system symptoms, hypersensitivity, and other major adverse effects which are a risk of conventional new quinolone drugs, with main clinical adverse effects being diarrhea and soft stool, flushing, eruption, nausea, and vomiting, and a rate of incidence roughly equal to that of cephem drugs.

A pazufloxacin mesilate with the characteristics outlined above should broaden therapeutic options across the range of infectious disease and contribute greatly to an improved quality of infectious disease treatment.

[Reference data]

**Market size (based on 2001 pharmaceutical tariff)**
Total market for injectable antibiotics: approx. 250 billion yen a year
Estimated size of market for cephem and penem type injection pharmaceuticals (most widely used injectable antibiotics): approx. 140 billion yen a year