CHUGAI PHARMACEUTICAL CO., LTD.
Corporate Communications Dept.
1-1, Nihonbashi-Muromachi 2-chome,
Chuo-ku Tokyo, 103-8324 Japan
TEL:+81-(0)3-3273-0881
FAX:+81-(0)3-3281-6607
E-mail:pr@chugai-pharm.co.jp
URL:http://www.chugai-pharm.co.jp

Translation

Synthetic Antibacterial Agent, Bactramin®
Approved for Additional Indication of
"Treatment and Prevention of *Pneumocystis* Pneumonia"

August 10, 2012-Chugai Pharmaceutical Co., Ltd. [Main Office: Chuo-ku, Tokyo. Chairman & CEO: Osamu Nagayama (hereafter, "Chugai")] announced today that on August 10, 2012, it received approval from the Japanese Ministry of Health, Labour and Welfare on the additional indication of "*Pneumocystis* pneumonia and prevention of its development*[1]" for Bactramin®. Bactramin® is a synthetic antibacterial trimethoprim - sulfamethoxazole (TMP-SMX) combination with brand names: "Bactramin® Combination Tablet" and "Bactramin® Combination Granule." In Japan, Bactramin® is currently approved for the indications of "pneumonia, secondary infection caused by chronic respiratory lesion, complicated cystitis, pyelonephritis, infectious enteritis, typhoid, or paratyphoid*[2]."

As a result of the evaluation by the "Review Committee on Unapproved Drugs and Indications with High Medical Needs*[3]" held on December 22, 2011, an application based on evidence in the public domain was found applicable when filing for this indication. Then, at the meeting of the Second Committee on New Drugs, Pharmaceutical Affairs and Food Sanitation Council, held on February 1, 2012, the Committee determined that filing the application based on evidence in the public domain would be reasonable. In response to this, Chugai submitted the application for this additional indication on February 13.

Pneumocystis pneumonia (PCP) is a so-called opportunistic infection occurring in immunocompromised patients due to HIV infection or the use of immunosuppressants. It is a serious disease with a mortality of almost 100% if left untreated. In patients with HIV infection, the incidence of PCP is highest (approximately 40%) among AIDS indicator diseases, and the mortality (per month) of PCP is estimated to be 15 to 20%. In non-HIV infected patients who are on immunosuppressants, symptoms often rapidly deteriorate, and the mortality (per month) is assumed to be approximately 40% for non-HIV infected patients, and as high as approximately 60% for patients requiring artificial respiratory management. Furthermore, the prognosis is often poor in patients with underlying lung disease, and PCP may progress to pulmonary impairment even after recovering.

Chugai strongly believes that, as a drug with the indication of *Pneumocystis* pneumonia and prevention of its development, where high unmet medical needs exist, Bactramin® can be a significant contribution to patient care.

*1 An applicable strain is *Pneumocystis jiroveci*.

*2 Applicable strains are sulfamethoxazole/trimethoprim-sensitive *Enterococcus*, *Escherichia coli*, *dysentery bacillus*, *typhoid bacillus, paratyphoid bacillus*, *Citrobacter*, *Klebsiella*, *Enterobacter*, *Proteus*, *Morganella morganii*, *Providencia rettgeri* and *Haemophilus influenza*.

*3 The "Review Committee on Unapproved Drugs and Indications with High Medical Needs" was established for the purpose of "enhancing development by the pharmaceutical companies of drugs and indications that have been approved for use in western countries but not yet approved in Japan, through activities such as evaluating medical needs and confirming the applicability of "application based on evidence in the public domain" and investigating the need for studies that should be additionally conducted."

[**Reference**]

Underlined information was added or changed.

Brand name:
Bactramin® Combination Tablet
Bactramin® Combination Granule

Generic name:
Trimethoprim
Sulfamethoxazole

Indications:
1. General infections
Applicable bacterial species:
- Sulfamethoxazole/trimethoprim-sensitive *Enterococcus, Escherichia coli, dysentery bacillus, typhoid bacillus, paratyphoid bacillus*, *Citrobacter*, *Klebsiella, Enterobacter*, *Proteus*, *Morganella morganii*, *Providencia rettgeri* and *Haemophilus influenza*

Indications:
- Pneumonia, secondary infection caused by chronic respiratory lesion, complicated cystitis, pyelonephritis, infectious enteritis, typhoid, and paratyphoid

2. Treatment and prevention of *Pneumocystis* pneumonia
Applicable bacterial species:
- *Pneumocystis jiroveci*

Indications:
- *Pneumocystis* pneumonia, prevention of *Pneumocystis* pneumonia

Dosage and administration:
1. General infections

The usual adult dosage for oral use is 4 tablets/day of Bactramin® (4 g/day for granules) divided into 2 doses.

The dosage should be adjusted as necessary according to age and symptoms.

2. Treatment and prevention of *Pneumocystis* pneumonia

(1) For treatment:

The usual adult dosage for oral use is 9 to 12 tablets/day of Bactramin® (9 to 12 g/day of granules) divided into 3 or 4 doses.

The usual dosage for children for oral use is 15 to 20 mg/kg/day of trimethoprim divided into 3 or 4 doses.

The dosage should be adjusted as necessary according to age and symptoms.

(2) For prevention:

The usual adult dosage for oral use is 1 to 2 tablets of Bactramin® (1 to 2 g/day of granules) once daily, every day or for 3 days/week.

The usual dosage for children for oral use is 4 to 8 mg/kg/day of trimethoprim divided into 2 doses, every day or for 3 days/week.

NHI Drug price:

Bactramin® Combination Tablet: JPY 60.80
Bactramin® Combination Granule: JPY 62.50