



23 June 2009

## Press Release

Nippon Boehringer Ingelheim Co., Ltd.  
Astellas Pharma Inc.

### **Sales of Micombi<sup>®</sup> Combination Tablets commenced -Telmisartan and HCTZ combination demonstrates potent hypertension reduction, broadening therapeutic options-**

Nippon Boehringer Ingelheim Co., Ltd. (Headquarters: Shinagawa-ku, Tokyo; Chairman & President: Dr. Thomas Heil) and Astellas Pharma Inc. (Headquarters: Chuo-ku, Tokyo; President & CEO: Masafumi Nogimori) announced today that on 23 June the sales of Micombi<sup>®</sup> Combination Tablets commenced. Micombi<sup>®</sup> is a combination drug of telmisartan, an angiotensin II receptor blocker (ARB), and hydrochlorothiazide (HCTZ), a diuretic of the thiazide class. Micombi<sup>®</sup> Combination Tablets are manufactured by Nippon Boehringer Ingelheim, distributed by Astellas Pharma, and co-promoted by both companies as are the telmisartan drug Micardis<sup>®</sup> Tablets.

Hypertension Treatment Guidelines 2009 (JSH2009) recommend that if blood pressure cannot be lowered adequately with the administration of a single drug, a combination of ARB and a small quantity of diuretic should be given.<sup>1</sup> The combined dosing of two drugs with differing modes of action is believed to bring synergistic antihypertensive effects and counteract the effect on serum potassium levels in the blood.<sup>2</sup>

Micombi<sup>®</sup> Combination Tablets are available in two formulations, “Micombi<sup>®</sup> Combination Tablets AP,” containing telmisartan 40 mg and hydrochlorothiazide 12.5 mg and “Micombi<sup>®</sup> Combination Tablets BP,” containing telmisartan 80mg and hydrochlorothiazide 12.5 mg.

In a Japanese clinical trial, Micombi<sup>®</sup> Combination Tablets AP demonstrated a very strong antihypertensive effect, lowering systolic blood pressure by -23.3 mmHg from baseline at the end of the trial.<sup>3</sup> Micombi<sup>®</sup> Combination Tablets offer a very strong antihypertensive effect by a convenient single dose administration which is expected to contribute to improving medication adherence.<sup>1</sup> In Japan, there are an estimated 40 million people suffering from hypertension.

However, survey results show that roughly 60% of patients, despite receiving hypertension treatment, have not achieved the blood pressure control target (casual blood pressure of <140 mmHg/90 mmHg).<sup>4</sup> In an awareness survey of drug dosing conducted on 277 hypertensive patients, 83.8% responded that they are reluctant to see their amount of medication increase<sup>5</sup>.

Professor Jitsuo Higaki, Department of Integrated Medicine and Informatics Ehime University Graduate School of Medicine, who initiated the Japanese clinical trial of the combination tablets of telmisartan and HCTZ (Micombi® Combination Tablets), explained the significance of the combination therapy for hypertension in an era of high sodium diet, saying, “Excessive sodium intake, which can be even called salt poisoning, has become a significant factor causing hypertension. Therefore, for the treatment for hypertension in this era, it is reasonable to enhance excretion of the salt. Especially, physicians have been realizing clinical benefits from a therapy of a renin-angiotensin system blocker, such as ARB, in combination with a small quantity of a pharmacologically compatible diuretic.” He subsequently mentioned the significance of combination drugs, saying, “From a viewpoint of patients, a combination drug is more reliable than those used for the combination therapy, because hypertension can be adequately controlled with one tablet, which won’t raise a psychological barrier to the increase in the number of drugs. Thus, adherence will be reasonably improved.” Finally, he summarised his comment, stating, “The combination drug of ARB and a diuretic is expected to be an effective solution for a situation in antihypertensive treatment where rigorous antihypertensive effects cannot be obtained with a single drug.”

**The following is a summary of the product:**

- Date of Approval: 22/4/2009
- Date of Drug Price Listing: 19/6/2009
- Date of Sales Commencement: 23/6/2009
- Product Name: Micombi® Combination Tablets AP, Micombi® Combination Tablets BP
- Generic Name: telmisartan/hydrochlorothiazide
- Ingredients/Content:
  - Micombi® Combination Tablets AP: telmisartan 40 mg and hydrochlorothiazide 12.5 mg.
  - Micombi® Combination Tablets BP: telmisartan 80 mg and hydrochlorothiazide 12.5 mg.
- Indication: Hypertension
- Use/Dose: Adults - 1 tablet once daily taken orally (as telmisartan/hydrochlorothiazide either 40 mg/12.5 mg or 80 mg/12.5 mg). This drug is not to be used as the first-line drug for antihypertensive treatment.
- Drug Price:
  - Micombi® Combination Tablets AP 157.30 Yen
  - Micombi® Combination Tablets BP 234.40 Yen

## About telmisartan

Telmisartan is a member of the angiotensin II receptor blocker (ARB)<sup>\*</sup> class and is undergoing many clinical studies for the verification of its efficacy. A single agent telmisartan is marketed as Micardis<sup>®</sup>, while Micombi<sup>®</sup> is to join the line-up as a combination drug. Landmark clinical trial programmes including ONTARGET<sup>®6</sup> and PRoFESS<sup>®7</sup> have been conducted, enrolling a total of 58,000 subjects or more for investigation of the efficacy of telmisartan in preventing cardiovascular events. These landmark trials proved the favourable profile of telmisartan in preventing cardiovascular events.

<sup>\*</sup>Angiotensin II receptor blocker (ARB): antihypertensive treatment drug that selectively blocks the angiotensin II AT<sub>1</sub> receptor. The blockade is thought to cause vasodilation and prevent cell proliferation.

Telmisartan was discovered and developed by Boehringer Ingelheim. The company markets either telmisartan mono-therapy or telmisartan and HCTZ combination therapy in approximately 90 countries, including USA, Japan and European countries. Telmisartan drugs (Micardis<sup>®</sup> Tablets/Micombi<sup>®</sup> Combination Tablets) are manufactured by Nippon Boehringer Ingelheim, distributed by Astellas Pharma, and co-promoted by both companies in Japan. Both Micardis<sup>®</sup> Tablets and Micombi<sup>®</sup> Combination Tablets are indicated for hypertension in Japan.

## References

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