

Kyorin Pharmaceutical Co., Ltd.
Eisai Co., Ltd.

**Partial Amendment of the Marketing Alliance Agreement
for the Migraine Treatment *MAXALT*[®]**

Kyorin Pharmaceutical Co., Ltd. (Headquarters: Tokyo, President: Ikuo Ogihara) and Eisai Co., Ltd. (Headquarters: Tokyo, President: Haruo Naito) have reached an agreement on partial amendment of the joint marketing agreement concluded in February 2003 for *MAXALT*[®] (generic name: rizatriptan benzoate/not yet launched in Japan), and the companies executed the amended contract today. *MAXALT*[®], a 5-HT_{1B/1D} receptor agonist, is a migraine treatment for which Kyorin has obtained import approval.

The principal change from the former agreement is that promotion of *MAXALT*[®] will be performed solely by Eisai instead of co-promotion by both companies. Other aspects of the previously announced arrangement whereby Kyorin will import the product from Merck & Co., Inc., and supply it to Eisai, and Eisai will distribute *MAXALT*[®] in Japan are unchanged.

Kyorin has been promoting a franchise customer strategy under which Kyorin concentrates marketing activities in the fields of respiratory disease, otorhinology, and urology. Eisai, which specializes in neurology as one of its franchises, will promote *MAXALT*[®] independently. Kyorin will concentrate its sales activities on the three other principal areas noted above.

The product will be launched following national health insurance price listing. Eisai aims to increase its presence in the field of neurology and establish *MAXALT*[®] as a top brand in the Japanese market for migraine treatment agents.

[The amended points in the contract, product outline, and explanations of terms are attached below for reference.]

Contacts:

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Eisai Co., Ltd.
Public Relations Department
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[Major contents of the marketing partnership agreement]

(Prior to the revision: as of February 26, 2003)

1. Kyorin Pharmaceutical Co., Ltd. will import the product (finished product) from Merck & Co., Inc., and supply it to Eisai Co., Ltd.
2. Eisai Co., Ltd. will sell the product in Japan and both Kyorin and Eisai will conduct sales promotion activities. (1 brand, 1 channel, 2 promotion scheme)
3. Both companies will share the profit* after deducting marketing expenses etc. from total sales.

(Revision: as of July 30, 2003)

1. Kyorin Pharmaceutical Co., Ltd. will import the product (finished product) from Merck & Co., Inc., and supply it to Eisai Co., Ltd.
2. Eisai Co., Ltd. will sell the product in Japan and Eisai will conduct sales promotion activity. (1 brand, 1 channel, 1 promotion scheme)

* Item 3 under the former scheme was deleted from the agreement, because only Eisai will promote the product.

[Product Outline of MAXALT® 10 mg Tablet, MAXALT RPD® *10 mg Tablet]

Product Name: MAXALT® 10 mg Tablet, MAXALT RPD® 10 mg Tablet

Generic Name: Rizatriptan benzoate

Indication: Migraine

Import Approval Date: July 17, 2003

Price: As yet not listed in the national health insurance list in Japan

Distributor: Eisai Co., Ltd.

Importer: Kyorin Pharmaceutical Co., Ltd.

*RPD: Rapid disintegration tablet

[Explanation of Terms]

1. Migraine

A throbbing headache that occurs repeatedly and episodically, often appearing unilaterally. The headache occurs one or several times in a month, and lasts from a few hours to several days. Onset may be preceded by sensory disorders such as scintillating scotoma, and is often accompanied by nausea, vomiting, or hypersensitivity to light or sound. The cause of migraine headaches has not yet been

definitively determined, but it is recognized that the trigeminal nerve or dilation of the cerebral blood vessels are involved with the onset of migraine headaches.

The prevalence rate of migraines in Japanese aged 15 years and older including suspected cases was reported as 8.4% (male: 3.6%, female: 13.0%). Approximately 8.4 million people are estimated to have experienced migraine in Japan. (Sakai F; Igarashi H. *Prevalence of migraine in Japan: a nationwide survey. Cephalalgia* 1997; 17: 15 - 22)

2. 5-HT_{1B/1D} receptor agonist-type migraine treatment agent

5-HT (serotonin) _{1B/1D} receptor agonist acts selectively on 5-HT_{1B/1D} receptors, constricting the blood vessels that expanded when symptoms of migraine develop, and controlling vascular inflammation. This treatment demonstrated superior control of migraines over current treatments.