



FOR IMMEDIATE RELEASE

October 27, 2010

Pfizer Japan Inc.
Eisai Co., Ltd

New Indication Approved for Lyrica® Capsules

Tokyo, Japan, October 27, 2010—Today, October 27, 2010, Pfizer Japan Inc. (Head Office: Tokyo; President: Ichiro Umeda; hereinafter “Pfizer”) received approval to replace the indication of “postherpetic neuralgia” that is currently approved for Lyrica® Capsules (generic name: pregabalin; hereinafter “Lyrica®”) in Japan with the new and broader indication of “peripheral neuropathic pain.”

Approval to produce and distribute Lyrica® with the indication postherpetic neuralgia was received on April 16 of this year, and it was launched on June 22. Pfizer and Eisai Co., Ltd. (Head Office: Tokyo; President: Haruo Naito) are jointly promoting the drug in Japan and providing information regarding the proper usage of the drug.

Lyrica® is a therapeutic agent for the treatment of pain developed by Pfizer Inc. (USA). It has been approved in 110 countries and regions worldwide (as of July 2010). The drug is recommended by the International Association for the Study of Pain and other key academic bodies as a first-line treatment for neuropathic pain. As its major mechanism of action, Lyrica® is thought to express its analgesic effect by inhibiting the release of various neurotransmitters in an overexcited nervous system.

The pathologies and pathogeneses of neuropathic pain are complex and varied, so it is considered to be a form of intractable pain for which NSAIDs (non-steroidal anti-inflammatory drugs) and other analgesics cannot be expected to have much effect.

Lyrica® has a mechanism of action that differs from those of conventional analgesic agents, so it is a new option for the treatment of pain. Its efficacy and safety have been confirmed in domestic Phase III trials and domestic long-term administration trials regarding pain accompanying diabetic neuropathy in addition to postherpetic neuralgia, a typical peripheral neuropathic disease for which it was already approved.

Pfizer Japan Inc. and Eisai Co., Ltd. will use the newly approved indication of peripheral neuropathic pain for Lyrica® to help improve the quality of life of patients suffering from pain accompanying various types of neuropathic disorders.

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Outline of Lyrica® Capsules

Product name:	Lyrica® Capsules (25mg, 75mg, 150 mg)
Generic name:	Pregabalin
Approval date:	April 16, 2010
NHI pricing date:	June 11, 2010
Launch date:	June 22, 2010
Manufactured/sold by:	Pfizer Japan Inc.
Co-promotion with:	Eisai Co., Ltd.
Effect/efficacy:	<u>Peripheral neuropathic pain</u> (NOTE: changed from postherpetic neuralgia)
Administration/dosage:	Normally, adults are orally administered an initial dosage of 150mg of pregabalin in two divided doses per day. The daily dosage is then titrated to 300mg over one week. The dosage may be adjusted according to age and symptoms. However, daily dosage should never exceed 600mg and should always be orally administered in two divided doses per day.

Properties:

1. Abundant evidence

Approved in 110 countries and regions around the world (as of July 2010). Recommended by the International Association for the Study of Pain and various other overseas academic societies as a first-line drug in the treatment of peripheral neuropathic pain.

2. New action mechanism

Has a new mechanism of action that differs from those of conventional analgesic treatments in that it expresses its analgesic effect by binding to calcium ion channel $\alpha_2\delta$ sub-units primarily distributed in the nervous system.

3. Superior analgesic effect

Expresses its effect quickly, starting the first week of administration. Maintains its effect even during long-term administration.

4. Safety profile

Postherpetic neuralgia

In a domestic dose-response trial, a domestic long-term administration trial, an overseas late stage Phase II trial, an overseas Phase III trial and an overseas long-term administration trial, side effects (including an abnormal clinical laboratory test results) were found to have occurred in 1,084 cases (64.5%) out of 1,680 cases. The most common side effects were floating dizziness (393 cases, 23.4%), somnolence (267 cases, 15.9%), and edema (179 cases, 10.7%) (based on the total of investigation data collected prior to approval).

Pain accompanying diabetic peripheral neuropathy

In a domestic double-blind comparative trial and domestic long-term administration trial, side effects (including abnormal clinical laboratory test results) were found in 199 cases (65.9%) out of 302 cases. The most common side effects were somnolence (74 cases, 24.5%), floating dizziness (68 cases, 22.5%), and edema (52 cases, 17.2%) (based on the total of investigation data collected prior to approval).

Regarding pain classifications

Pain is classified into three categories according to its mechanism and characteristics: neuropathic pain, nociceptive pain, and psychogenic pain. It is thought that these categories often overlap rather than existing independently.*

* Hosokawa, Toyoshi. Guidebook for the Treatment of Neuropathic Pain. Ed. Setsurō Ogawa. Tokyo: Nanzando, 2010. 3.

Neuropathic pain has been defined by the International Association for the Study of Pain (IASP) as “pain arising as a direct consequence of a lesion or disease affecting the somatosensory system.” In other words, it is pain that occurs as a result of nerve damage or a functional anomaly accompanying such damage, and it indicates a variety of pain types accompanied by disturbance of perception.

In addition, neuropathic pain can be categorized as peripheral or central according to the site of the nerve lesion. Typical peripheral neuropathic pain disorders include postherpetic neuralgia, painful diabetic neuropathy, and trigeminal neuralgia, whereas post-stroke pain is a central neuropathic pain disorder.

Nociceptive pain is pain that occurs when a pain-producing substance that is activated by a nociceptive stimulus or inflammation stimulates nociceptors. It has been defined by the IASP as “pain arising from activation of nociceptors.”

Nociceptive pain includes shoulder peri-arthritis pain and rheumatoid arthritis pain.

Some pain is a combination of neuropathic pain and nociceptive pain. Chronic back pain and cervico-omo-brachial syndrome are representative examples of this.

Nociceptive pain	Pain that is a combination of elements of neuropathic pain and nociceptive pain	Neuropathic pain
<ul style="list-style-type: none"> • Shoulder peri-arthritis pain • Tendonitis or tenosynovitis • Rheumatoid arthritis pain 	<ul style="list-style-type: none"> • Chronic back pain • Chronic neck pain (cervico-omo-brachial syndrome) • Carpal tunnel syndrome 	<p>Peripheral neuropathic pain</p> <ul style="list-style-type: none"> • Postherpetic neuralgia • Painful diabetic neuropathy • Trigeminal neuralgia • Chronic pain accompanied by nerve root compression (cervical vertebrae, thoracic vertebrae, lumbar vertebrae) <p>Central neuropathic pain</p> <ul style="list-style-type: none"> • Post-stroke pain • Post-spinal cord injury

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The World Health Organization classifies psychogenic pain as a somatoform disorder in the International Classification of Diseases, and it is incorporated into the entry “Pain Disorder” in the DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, 4th Edition) of the American Psychiatric Association.

Conceptually speaking, pain is considered to be psychogenic ① when there is no organic lesion and psychological factors account for all of the causes of the pain, or ② when an organic physical lesion exists as a source of the pain, but it does not sufficiently explain the pain complaint.**

** Hosokawa, Toyoshi. Psychogenic Pain. The Concept of Pain Has Changed. Ed. Setsurō Ogawa. Tokyo: Shinko Trading Company, 2008. 54.