ONO PHARMACEUTICAL CO.,LTD.

July 4, 2016

ONO Receives Manufacturing and Marketing Approval in Japan for KYPROLIS® (INN: Carfilzomib; development code: ONO-7057), a Proteasome Inhibitor, in Relapsed or Refractory Multiple Myeloma

ONO PHARMACEUTICAL CO., LTD. (Osaka, Japan; President, Representative Director and CEO: Gyo Sagara; hereinafter, "ONO") today announced that ONO has received a manufacturing and marketing approval for KYPROLIS® for Intravenous Injection 10 mg and 40 mg (hereinafter, "Kyprolis"), which is a proteasome inhibitor, for the treatment of patients with relapsed or refractory multiple myeloma.

Multiple myeloma results from an abnormality of plasma cells, usually in the bone marrow and there are nearly 18,000 patients* in Japan. Several regimens for multiple myeloma are currently available to patients; however, the disease relapses and progresses and eventually becomes no longer responding to therapies, also known as refractory disease. Additionally, adverse drug reactions and co-morbid conditions have been reported following long-term treatment, making continued treatment a challenge. The development of new therapeutic options for multiple myeloma is needed.

Kyprolis is in a class of drugs called proteasome inhibitors. ONO in-licensed Kyprolis for development and commercialization in Japan from U.S.-based Onyx Pharmaceuticals, Inc., now an Amgen subsidiary, in September 2010. Proteasome, an intra-cellular enzyme complex, functions to mediate degradation of polyubiquitinated proteins and control proliferation and differentiation of cells, as well as functional cell-death. Kyprolis inhibits certain proteasome activity, thereby inducing functional cell-death of myeloma.

In July 2012, the U.S. Food and Drug Administration (FDA) granted accelerated approval of Kyprolis as a single agent for the treatment of patients with multiple myeloma who have received at least two prior therapies including bortezomib and an immunomodulatory agent and have demonstrated disease progression on or within 60 days of completion of the last therapy. Also, in July 2015, the FDA approved supplemental New Drug Application (sNDA) of Kyprolis in combination with lenalidomide and dexamethasone for the treatment of patients with relapsed or refractory multiple myeloma who have received one to three prior therapies. The FDA subsequently granted a full approval in January 2016 for sNDA of Kyprolis as a single agent for the treatment of patients with relapsed or refractory multiple myeloma who have received one or more prior therapies. In Europe, the Marketing Authorization Application for Kyprolis in combination with lenalidomide and dexamethasone was approved in November 2015 for the treatment of patients with multiple myeloma who have received at least one prior therapy.

In Japan, the Ministry of Health, Labour and Welfare designated Kyprolis as an orphan drug with a proposed indication for the treatment of “relapsed or refractory multiple myeloma” on August 20, 2015.

ONO considers the accumulation of further clinical data important in ensuring that Kyprolis will be used properly and effectively. ONO is committed to taking actions necessary for the proper use of Kyprolis by implementing a post-marketing use-results survey (all-case surveillance) and collecting clinical data on the safety and efficacy of Kyprolis according to the conditions for its approval.

Overview of Kyprolis®

Product Name	KYPROLIS® for Intravenous Injection 10 mg KYPROLIS® for Intravenous Injection 40 mg
International nonproprietary name (INN)	Carfilzomib
Indication	Relapsed or refractory multiple myeloma
Dosage and administration	In combination with lenalidomide and dexamethasone, KYPROLIS is usually administered intravenously in adults once a day on Days 1, 2, 8, 9, 15 and 16 followed by a 12-day rest period. Each 28-day period is considered one treatment cycle, and the treatment is continued until Cycle 12. In Cycle 13 and onward, KYPROLIS is intravenously administered once a day on Days 1, 2, 15 and 16 followed by a 12-day rest period. KYPROLIS is administered intravenously over 10 minutes at a dose of 20 mg/m^2 (body surface area) as carfilzomib on Days 1 and 2 in Cycle 1 and then at 27 mg/m^2 (body surface area) afterwards. The dose should be reduced as needed according to each patient’s condition.
Manufacturer/ distributor	Ono Pharmaceutical Co., Ltd.
Conditions for approval	1. ONO should establish Risk Management Plan to be implemented appropriately. 2. Because of the very limited number of patients treated with KYPROLIS in Japanese clinical trials, ONO is required to perform a post-marketing use-results survey covering all cases until data on a certain minimum number of patients have been accumulated. Through these activities, ONO should identify the characteristics of patients to be treated with KYPROLIS and collect safety and efficacy data as soon as possible, thereby taking actions necessary to ensure the proper use of KYPROLIS.

*: Vital Statistics and Patients Survey, 2014 (Statistics and Information Department, Minister's Secretariat, Ministry of Health, Labour and Welfare).

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