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Eisai Co., Ltd.

EISAI CLEARS ALL-CASE SURVEILLANCE CONDITION FOR APPROVAL OF ANTICANCER DRUG GLIADEL® 7.7MG IMPLANT

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, “Eisai”) announced today that it has received notification from Japan's Ministry of Health, Labour and Welfare (MHLW) to the effect that the “all-case surveillance” survey condition required for approval of Gliadel® 7.7mg Implant (carmustine, “Gliadel”) has been lifted.

In September 2012, the MHLW approved Gliadel indicated for malignant glioma with the following condition for approval: “Because of the very limited number of subjects treated in the Japanese clinical trials, the applicant is required to conduct all-case drug use-results survey until data from a certain number of patients are accumulated after market launch, in order to identify the background information of patients treated with the product and collect safety and efficacy data on the product in the early post-marketing period, and thereby take necessary measures to ensure proper use of the product.”

The MHLW lifted this condition for approval after evaluating safety and efficacy data submitted by Eisai from patients with malignant glioma (558 cases for safety analysis, 536 cases for efficacy analysis). According to the results of the evaluation, the MHLW determined that the conditions for approval have been met.

Gliadel is the only sustained-release formulation approved for intracranial implantation in Japan. Each wafer contains the nitrosourea alkylating agent carmustine distributed in a biodegradable polymer matrix. Implanting the agent into the brain following surgical removal of malignant glioma allows for direct delivery of chemotherapy to the tumor site, allowing the agent to be used prior to initiating radiation, chemotherapy and other standard therapies. Gliadel is manufactured and distributed by Eisai, and the product is co-promoted by Eisai and Nobelpharma Co., Ltd.

Eisai will continue to promote and provide information on the proper use of Gliadel while making further contributions to improve the quality of life of patients.

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[Notes to editors]

1. About Gliadel

Gliadel 7.7 mg Implant is the only sustained-release formulation approved for intracranial implantation in Japan. Each wafer contains the nitrosourea alkylating agent carmustine distributed in a biodegradable polymer matrix. Implanting the agent into the brain following surgical removal of malignant glioma allows for direct delivery of chemotherapy to the tumor site, allowing the agent to be used prior to initiating radiation, chemotherapy and other standard therapies.

2. About Glioma

Glioma is the general term for primary brain tumors originating from the glial cells that exist in parenchymal brain tissue. They are mostly malignant with poor prognosis. Gliomas account for approximately 30% of all primary brain tumors and in many cases are difficult to completely remove as they characteristically spread and develop (infiltrate) in the brain or spinal cord without a distinct tumor boundary, with normal brain tissue and tumor cells both being present in surrounding areas. In these cases, the tumor has a poor survival prognosis of 25% or less within the first five years.

Surgical removal (craniotomy) of the tumor is usually performed as standard treatment for glioma and in the majority of cases radiation and/or chemotherapy is administered adjunctively post-surgery. However, the active ingredients in chemotherapeutic agents administered during systemic chemotherapy regimens are often unable to be sufficiently delivered to the brain tumor site at the required dose because of the blood-brain barrier and the actual dose required also cannot be sufficiently administered without systemic adverse events. These difficulties are another reason for poor prognosis in patients with malignant glioma.

3. Results of the All-Case Surveillance Survey

Among the 558 patients included for safety analysis, a total of 365 adverse drug reactions were observed in 199 patients, giving an adverse reaction incidence rate of 35.7% (in a Phase I/II clinical study conducted in Japan, the adverse reaction incidence rate was 54.2%). The most common adverse drug reactions observed (more than 10 cases observed) of the 365 cases reported were cerebral edema (124 cases, 22.2%), seizure (43 cases, 7.7%), fever (21 cases, 3.8%), hemiplegia (17 cases, 3.0%), poor recovery (14 cases, 2.5%) and epilepsy (11 cases, 2.0%). In addition, 138 of the 365 adverse reactions were classified as CTCAE (Common Terminology Criteria for Adverse Events) Grade 3 or higher, with 5 cases or more observed of cerebral edema (38 cases), poor recovery (12 cases), seizure (9 cases), hydrocephalus (7 cases), meningitis (6 cases), hemiplegia (6 cases) and epilepsy (5 cases).

Regarding efficacy, using the Kaplan-Meier method on 536 patients included for analysis, the 1-year estimated survival rate following implantation of the agent was 72.5%, and when separated into newly diagnosed and recurrent cases, the 1-year estimated survival rate was 79.1% for newly diagnosed cases and 61.6% for recurrent cases. The efficacy data obtained from this survey for either patients with newly diagnosed malignant glioma or patients with recurrent glioblastoma does not differ greatly from the data submitted at the time of approval.