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Eisai Co., Ltd.

Ministry Of Health, Labour and Welfare Grants Orphan Drug Designation in Japan to Anticancer Agent Tazemetostat for Unresectable INI1-Negative Epithelioid Sarcoma

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced today that it has received orphan drug designation for anticancer agent the EZH2[*1] inhibitor tazemetostat hydrobromide (generic name, product name "Tazverik® Tablets 200 mg", "tazemetostat") for unresectable INI1[*2]-negative epithelioid sarcoma that has progressed after chemotherapy, from the Ministry of Health, Labour and Welfare (MHLW).

Epithelioid sarcoma is a type of soft tissue sarcoma that is a rare cancer estimated to account for about 1% of all soft tissue sarcoma.[1] Only 174 cases were registered from major hospitals across Japan over a 10-year period from 2006 to 2015.[2] Loss of INI1,which is a negative regulator of EZH2, is observed in over 90% of epithelioid sarcoma cases,[3] leading to EZH2 activation that is believed to drive tumor onset and malignant progression. Treatment options are limited, resulting in an extremely high unmet medical need.

Tazemetostat was approved in Japan in June 2021 for relapsed or refractory *EZH2* gene mutation-positive follicular lymphoma (only when standard treatment is not applicable). For INI1-negative unresectable epithelioid sarcoma that has progressed after chemotherapy, a Phase II investigator-initiated trial of tazemetostat (A Phase II Trial of Tazemetostat for Patients with Unresectable or Metastatic Epithelioid Sarcoma: TAZETTA trial), led by the National Cancer Center Hospital, is currently underway.

Eisai identifies oncology as one of its priority areas and strives to develop groundbreaking new therapies aimed at curing cancer. We remain committed to meeting the diverse needs of cancer patients worldwide, their families, and healthcare professionals, and to enhancing the benefits delivered to them.

*1 A type of histone methyl group elongation enzyme, it is a protein that controls gene expression by methylating the 27th lysine residue of histone H3 (H3K27).
*2 One of the proteins that make up the SWI/SNF chromatin complex (a protein complex that modifies chromatin structure to regulate gene function), it is involved in regulating gene expression.

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[Notes to editors]

1. About tazemetostat hydrobromide (generic name, product name "Tazverik Tablets 200 mg")

Tazemetostat is a first-in-class, oral small molecule inhibitor that targets EZH2 that was jointly researched and developed under the alliance agreement between Eisai and Epizyme, Inc., an Ipsen company, utilizing Epizyme, Inc.'s proprietary product platform. This agent selectively inhibits EZH2 in a competitive matter with S-adenosylmethionine (a methyl group donor) to suppress methylation of H3K27.[4] Eisai was granted exclusive rights for development and commercialization of this agent in Japan, where the drug was approved in June 2021 for the indication of "relapsed or refractory *EZH2* gene mutation-positive follicular lymphoma (only when standard treatment is not applicable)". Epizyme, Inc. continues to develop this agent and currently commercializes it in the United States, where accelerated approval was granted for in January 2020 with the indication of "adults and pediatric patients aged 16 years and older with metastatic or locally advanced epithelioid sarcoma not eligible for complete resection". In June of the same year, the accelerated approval was granted for this agent with the indication of "adult relapsed / refractory follicular lymphoma who had at least 2 regimens of prior treatment and whose tumors are positive for an *EZH2* mutation as detected by an FDA-approved test", and of "adult relapsed / refractory follicular lymphoma for which there are no satisfactory alternative treatment options". Recently in March 2025, this agent was also conditionally approved in Mainland China for the treatment of adult patients with relapsed or refractory (R/R) follicular lymphoma (FL) whose tumors are positive for an *EZH2* mutation and who have received at least 2 prior systemic therapies.

[1] Asano N et al. Prognostic Value of Relevant Clinicopathologic Variables in Epithelioid Sarcoma: A Multi-Institutional Retrospective Study of 44 Patients. *Ann Surg Oncol*. 2015;22(8):2624–32.
https://link.springer.com/content/pdf/10.1245/s10434-014-4294-1.pdf.

[2] National Cancer Center Japan website: Launch of a nationwide, four-site, investigator-initiated Phase II trial of the EZH2 inhibitor (E7438) in patients with epithelioid sarcoma (Japanese only).
https://www.ncc.go.jp/jp/information/pr_release/2023/0622/index.html. Last accessed: July 2025.

[3] Hornick JL et al. Loss of INI1 expression is characteristic of both conventional and proximal-type epithelioid sarcoma. *Am J Surg Pathol*. 2009 Apr;33(4):542–50.
https://journals.lww.com/ajsp/abstract/2009/04000/loss_of_ini1_expression_is_characteristic_of_both.8.aspx.

[4] Sarah K. Knutson, Satoshi Kawano, Yukinori Minoshima, et al. Selective Inhibition of EZH2 by EPZ-6438 Leads to Potent Antitumor Activity in EZH2-Mutant Non-Hodgkin Lymphoma. *Molecular Cancer Therapeutics.* 2014 Apr; 13(4):842–854.
https://aacrjournals.org/mct/article/13/4/842/91698/Selective-Inhibition-of-EZH2-by-EPZ-6438-Leads-to.

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