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To whom it may concern:

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Notice regarding acquisition of approval to add indications, etc. for "Kytril® injections and intravenous infusion bags" that act as 5-HT3 receptor antagonists

TAIYO HOLDINGS CO., LTD. (hereinafter, "TAIYO HOLDINGS") hereby announces that today, its consolidated subsidiary TAIYO Pharma Co., Ltd. (hereinafter, "TAIYO Pharma") obtained approval from the Ministry of Health, Labour and Welfare to add indications, dosages and administrations pertaining to "postoperative gastrointestinal symptoms (nausea, vomiting)" for "Kytril® injection 1mg," "Kytril® injection 3mg," "Kytril® intravenous infusion bag 3mg/50mL" and "Kytril® intravenous infusion bag 3mg/100mL" (generic name: granisetron hydrochloride) (hereinafter, collectively "Kytril® injections and intravenous infusion bags"), which act as 5-HT3 receptor antagonists.

1. Circumstances leading to acquisition of approval

After a request for the development of "Kytril® injection and intravenous infusion bag" was issued by the Japanese Society of Anesthesiologists, at the meeting of the "Committee on Unapproved or Off-labeled Drugs with High Medical Needs" that convened on July 12, 2021, [1)] "Kytril® injection and intravenous infusion bag" are publicly known in medical and pharmacological sciences for "postoperative gastrointestinal symptoms (nausea, vomiting)." Furthermore, at the meeting of the First Committee on Drugs under the Pharmaceutical Affairs Council that convened on August 30, 2021, it was concluded that there would be no issue with filing a public knowledge-based application[2)] for that purpose. Based on the above, on September 22, 2021, TAIYO Pharma filed a public knowledge-based application to add indications, dosages and administrations, which resulted in it obtaining the approval in question.

In addition to causing patients distress, Postoperative Nausea and Vomiting (hereinafter, "PONV") is also a factor that delays their postoperative recovery. Indications pertaining to PONV in adults have been approved for granisetron hydrochloride injections in Europe, the United States and other countries and regions. In textbooks and clinical guidelines within and outside of Japan, the drugs have been positioned as a standard therapeutic agent in the prevention and treatment of PONV in adults.

Going forward, in addition to its endeavors to facilitate contributions by "Kytril® injection and intravenous infusion bag" as new therapeutic agents for "postoperative gastrointestinal symptoms (nausea, vomiting)," TAIYO Pharma will continue to do its part for the provision of pharmaceutical products that address feedback from the medical frontlines.

1) The *Committee on Unapproved or Off-Labeled Drugs with High Medical Needs* was established with the aim of contributing to the promotion of the development of unapproved drugs and off-labeled drugs by pharmaceutical companies by assessing the medical need for drugs and indications that are approved for use in Europe and the United States but not approved in Japan, and by evaluating the relevance of these drugs for public knowledge-based application and confirming the appropriateness of the tests that need to be performed additionally for application for approval.
2) Public knowledge-based application refers to an application for approval made without conducting all or part of clinical trials on the basis that the drug has already been approved for relevant indications in a foreign country and the efficacy and safety of the drug are medically known.

2. Product overview

Brand name	Kytril® injection 1mg Kytril® injection 3mg Kytril® intravenous infusion bag 3mg/50mL Kytril® intravenous infusion bag 3mg/100mL
Generic name	Granisetron hydrochloride
Indications	Gastrointestinal symptoms (nausea, vomiting) associated with the administration of antineoplastic agents (cisplatin, etc.) and irradiation Postoperative gastrointestinal symptoms (nausea, vomiting)
Dosages and administrations	**Gastrointestinal symptoms (nausea, vomiting) associated with the administration of antineoplastic agents (cisplatin, etc.)** Adults: Typically, adults are administered one 40μg/kg dose per day as a granisetron via intravenous injection or drip. Note that the dose is increased or decreased as appropriate depending on the patient's age and symptoms. In cases where symptoms do not improve, a single additional 40μg/kg dose may be administered. Children: Typically, children are administered one 40μg/kg dose per day as a granisetron via intravenous drip. Note that the dose is increased or decreased as appropriate depending on the patient's age and symptoms. In cases where symptoms do not improve, a single additional 40μg/kg dose may be administered. **Gastrointestinal symptoms (nausea, vomiting) associated with irradiation** Typically, adults are administered a single 40μg/kg dose as a granisetron via intravenous drip. Note that the dose is increased or decreased as appropriate depending on the patient's age and symptoms. However, the maximum number of doses per day is two. **Postoperative gastrointestinal symptoms (nausea, vomiting)** Typically, adults are administered a single 1mg dose as a granisetron via intravenous injection or drip. Note that the dose is increased or decreased as appropriate depending on the patient's age and symptoms. However,

	the maximum dose per day is 3mg.
Precautions regarding dosages and administrations	(Universal for pharmaceutical formulation) When using for gastrointestinal symptoms associated with irradiation, administer via intravenous drip prior to irradiation. Note that when using for gastrointestinal symptoms associated with Total Body Irradiation (TBI) upon pretreatment for hematopoietic stem cell transplantation, the administration period should ideally be four days. When using for postoperative gastrointestinal symptoms, administer with appropriate timing before and after operation after taking the patient's background, the operative method, etc. into consideration.

*The underlined areas have been added.

3. Future outlook

The impact of this matter, including that on the consolidated business results of TAIYO HOLDINGS for the fiscal year ending March 31, 2022, will be minute. However, TAIYO HOLDINGS will promptly provide notification of any matters that merit disclosure should they arise.

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