WINSTON & STRAWN LLP

CLIENT ALERT

Updates on Drug Regulations in Japan – Reducing Barriers to Entry for Drug Companies Entering the Japanese Market

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As the global market for drug therapies continues to evolve, stakeholders in the life sciences industry must continue to expand their understanding of the varying regulatory-approval mechanisms across the key international markets. In the aftermath of the COVID-19 pandemic and the ensuing supply chain challenges, government authorities and public-health leaders on a country-by-country basis are prudently investing more in revisiting their respective nonemergency-drug approval criteria. The Japanese government is no exception, as discussed further below.

As of March 2023, 143 products approved in the United States or European Union are not approved in Japan. Of these, 86 items have not yet been developed domestically. The Japanese government is concerned about this "drug lag." The Ministry of Health, Labor, and Welfare of Japan (MHLW) is planning and implementing several measures to solve the drug lag. In other words, these measures will expand opportunities for foreign pharmaceutical companies to market their products in Japan.

MULTIREGIONAL CLINICAL TRIALS (MRCTS)

The necessity of phase I study in the Japanese population might have been a burden for foreign companies to develop a new drug in Japan. "Basic Principles for Conducting Phase I Trials in the Japanese Population Prior to Global Clinical Trials," an administrative notice published by the MHLW on October 27, 2014, explained that if, at the point of initiating a multiregional clinical trial (MRCT), tolerability in humans has not been sufficiently confirmed or the safety risk is likely to be high in the Japanese population, a phase I study should be required in the Japanese before participating in the MRCT.

However, the MHLW abolished this administrative notice and published a new administrative notice ("Basic principles for conducting phase 1 studies in Japanese prior to initiating multi-regional clinical trials including Japan for drugs in which early clinical development is preceding outside Japan") on December 25, 2023 (English translation is on pages 8 to 10). In the new notice, the MHLW changed the former concept of the necessity of phase I study and announced that, in principle, an additional phase I study in Japanese people is not needed unless it is deemed necessary after assessing whether the safety/tolerability of the dosage to be evaluated in the MRCTs in Japanese participants can be explained and the safety is clinically acceptable/manageable based on the data available prior to Japan's participation. The new notice also provides an example of decisions for individual products, such as orphan

drugs and pediatric drugs. As a result, it can be said that the necessity of phase I study has become clearer than before.

As a side note, according to the new notice, prior to marketing-authorization applications, the differences in pharmacokinetics (PK) and/or pharmacodynamics (PD) between Japanese and non-Japanese should be assessed through measures such as collecting PK and/or PD data in Japanese people in MRCTs regardless of conducting a phase I study in the Japanese population.

PMDA SETTING UP AN OFFICE IN THE UNITED STATES

The MHLW plans to open a U.S. office of the Pharmaceutical and Medical Device Agency (PMDA, equivalent to the FDA in the United States) in 2024. The purpose is to encourage small and medium-sized foreign biotech companies to develop and apply for marketing authorization in Japan. The PMDA U.S. office will disseminate information on drug regulations in Japan and provide complimentary advice on drug regulations. In particular, it will focus on products publicly solicited for development and provide regulatory consultation on matters such as implementing clinical trials in Japan. It also aims to collaborate with the FDA in MRCTs. The office location is not disclosed yet, but as of June 2023, a board member of the PMDA mentioned that they planned to set up an office in Washington, DC.

DRUG PRICING

In Japan, based on the National Health Insurance system, the MHLW determines the drug price standards and revises the standards every year. In 2024, a new evaluation item (*Jinsoku donyu kasan*, "premium for rapid introduction") will be added to the drug price standards for rapidly introducing innovative new drugs into Japan in order to resolve drug lag.

The requirements to get the premium are:

- products developed through MRCTs (limited to cases where clinical trials are being conducted in Japan), or products developed through clinical trials conducted in Japan at the same time or prior to conducting in countries other than Japan;
- products subject to priority review pursuant to the Pharmaceutical and Medical Device Act of Japan;
- products whose market authorization was applied earlier than in the United States and Europe, or within six months of the earliest application in the United States or Europe (in the same indications); and
- products approved earlier than in the United States and Europe, or within six months of the earliest approval in the United States or Europe (in the same indications).

If all requirements are satisfied, the product can obtain 5–10% of the premium for rapid introduction.

The MHLW is continuously considering measures to eliminate drug lag. It might be best for foreign pharmaceutical companies to keep an eye on up-to-date regulatory information from Japan.

Winston & Strawn LLP is engaged in the Japanese life sciences market and is closely monitoring industry and regulatory developments to enable us to provide timely strategic advice to our clients.
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