Basic Knowledge of Pharmaceuticals

What are pharmaceuticals?

Pharmaceuticals are used to diagnose, treat or prevent illness in a form that matches each purpose, such as internal use, external use, and injection. There are three types of pharmaceuticals: "ethical drugs" and "over-the-counter drugs," which can be purchased at pharmacies, drug stores, and online, and "drugs that require instruction" that must be sold in person to the user.

We research and develop, manufacture and sell ethical drugs called "new drugs (original drugs)," which are usually produced over a period of 10 or more years and substantial R&D investment. To provide effective and safe drugs, numerous regulations have been established, from research and development to drug launch, and we are required to verify their quality, efficacy and safety for a certain period of time (reexamination period) even after launch.

➡ See page 113 for details about our value chain initiatives.

Research and development and approval of new drugs

The efficacy and safety of new drugs are studied through the process of basic research, non-clinical study, and clinical study. Subsequently, after approval by the Minister of Health, Labor and Welfare and the listing of NHI drug prices, the drug is covered by insurance and can be prescribed to patients. The approval system varies by country, and the materials that each country's system requires must be submitted.

New drugs created through drug discovery are useful not only to treat and prevent disease, but also to promote cutting-edge research in various fields including medicine and pharmacology through drug discovery activities, leading to the advancement of science.

Pharmaceuticals and intellectual property

Research and development of a new drug takes a long time, and the probability of successfully launching a new drug is extremely low at 1 out of 22,407 possible outcomes. Furthermore, enormous R&D expenses are required (please see the ratio of R&D expenses to sales of the Company on page 9).

Without the proper protection of the intellectual property of the developed drug, pharmaceutical companies will have a difficult time continuing to research and develop new drugs. Therefore, since pharmaceutical companies have the exclusive right to manufacture and sell new drugs for a certain period of time, they acquire and protect their intellectual property, mainly the patent rights.

A patent right is the right to protect an invention and is valid for 20 years from the patent's filing date. Pharmaceuticals require approval for manufacturing and marketing based on the Pharmaceuticals, Medical Devices and Other Therapeutic Products Act, and because it takes a long time to obtain that approval, the patent period will be eroded, so in some cases, an extension of the patent's life of up to five years may be permitted.

Pharmaceutical-related patents include "substance patents" that exclusively protect the pharmaceutical itself with a patent for the substance, and "use patents" related to new indications/effects and the safety of specific substances. There are also "formulation patents" that are granted to new formulation innovations such as drug stabilization, and "process patents" that are granted if the process is different even for the exact same drug.

Generic name and product name

Pharmaceuticals have generic names and product names. The generic name is the "ingredient name" that indicates the ingredients of the drug itself, while the product name is the "brand name" registered as a trademark by the pharmaceutical company. Even if the product name is different, when the drug has the same active ingredients, the generic name is the same and is universally used.

Generic drug

When the reexamination period for verifying the efficacy and safety of a new drug and the term of its patent right have both expired, other pharmaceutical companies will be able to manufacture and sell drugs with the same active ingredients as the new drugs (original drugs) as generic drugs.

Originally, the drug's common name was called the generic name in English, so generic drugs that use the same active ingredients as the new drug are called generic drugs after the common name (generic name), which is the ingredient name.

Drug price system

In Japan, under its universal health insurance system, ethical drugs must not only obtain approval for their manufacture and marketing, but must also be listed in the "drug price standard." The "drug price standard" establishes the "product name" and "price" of pharmaceuticals that can be used for treatments that are covered by insurance, and is the official price (drug price) set by the Minister of Health, Labor and Welfare.

In the United States, since there is no universal public health insurance that covers all citizens, the market is characterized by the extremely large presence of private

health insurance companies. Moreover, based on market principles in operation between pharmaceutical companies, insurance companies and medical institutions, pharmaceutical companies can independently set drug prices.

Drug prices in Japan tend to be lower than in the United States, which uses a free price system.

National Health Insurance (NHI) drug price revision

The drug price standard in Japan is based on the premise that the actual purchase price reflects the official price of ethical drugs.

The Ministry of Health, Labor and Welfare reviews drug prices (drug price revisions) generally once every two years to ensure that market transaction prices are reflected in drug prices. In addition, in the year between the biannual drug price revisions, an "interim year revision" is supposed to be applied to products that substantially deviate from the drug price based on the idea that the actual market price will be reflected in the drug price in a timely manner so as to lower the financial burden on the public.

(Note) The Company has revised basic knowledge of pharmaceuticals based on "Textbook 2020-2021" published by the Japan Pharmaceutical Manufacturers Association.

Glossary

An explanation of terms used in the pharmaceutical industry.

> Unmet medical needs
Medical needs that have not yet been met, in other words, medical needs for which there are still no effective treatment.

> Key Opinion Leader (KOL)
An experienced physician who provides thought leadership in the diagnosis, treatment and research of a diseases.

> In-licensing
Acquisition of the right to sell or develop a drug or drug candidate compound from another company. Typically, a portion of the profit is continuously paid to the licensor, and the profit is less than that of products developed in-house.

> Pipeline
A compound that is a new drug candidate.

> First in class
Highly innovative pharmaceuticals. Notably, it is an original drug that is highly novel and effective and can substantially transform the conventional system of treatment.

> Blockbuster
A new drug with unprecedented efficacy, such as a product that generates profits that far exceed development costs. While having no clear definition in terms of sales, it often refers to products that achieve more than ¥100 billion or $1 billion annually in sales.

> Best in class
New drugs that have a clear advantage over the existing drugs.

> Modality
This refers to the material classification (category) of a drug, and specifically includes small molecule compounds, therapeutic antibodies, nucleic acid drugs, regenerative and cell therapy medicine, and gene therapy. The definition of modality tends to shift from "substance" to "means," and therapeutic applications other than pharmaceuticals can be called a modality.

> MR
Abbreviation for Medical Representative. Their main task is to collect, provide, and communicate information on the quality, efficacy, and safety of medicines to healthcare professionals such as doctors and pharmacists to ensure their proper use and dissemination.

> New Drug Application (NDA)
Abbreviation for New Drug Application, and refers to new drug applications in the United States.

> POC
Abbreviation for Proof of Concept, which is the confirmation of expected safety and efficacy in humans.

> Precision Medicine
High-precision healthcare through the understanding of pathophysiology and pathogenesis based on the latest science and technology, the stratification of patients using biomarkers, and the prediction of therapeutic effects.

> QOL
Abbreviation for Quality of Life.