Takeda's Position on the Impact of Pharmaceuticals in the Environment (PiE)

Summary

In keeping with our values of Takeda-ism - Integrity, Fairness, Honesty, and Perseverance, and as a science-driven company working towards our vision of discovering and delivering life-transforming treatments guided by our commitments to patients, people and the planet , Takeda believes that human health and the health of our planet are inextricably linked. As such, we:

- Recognize that active pharmaceuticals in the environment can have negative ecological impacts.
- Support efforts to better understand these impacts throughout the life cycle of a pharmaceutical compound, from development through disposal, to develop potential strategies for mitigation.
- Commit to assessing the environmental risk of our active pharmaceuticals in accordance with pharmaceutical drug regulatory approval processes as well as actively managing the environmental emissions of our manufacturing, including Takeda-developed drug products that are manufactured through contracts with third parties.

We believe that meaningful actions can be taken to ensure that emissions and resulting potential impacts are mitigated.

Background

The regulatory approval processes of agencies such as the European Medicines Agency and the U.S. Food and Drug Administration require considerable human health and environmental risk data. For this reason, the environmental effects of pharmaceuticals are generally better known than other traditional environmental contaminants. Based on cited research[1], the presence of pharmaceuticals in the environment is driven primarily

[1] BIO Intelligence Service. (2013, December 12). *Study on the environmental risks of medicinal products.*

by residues from patient use and excretion, to a lesser extent through the improper disposal of unused or expired medications, and to an even lesser extent by environmental emissions from drug manufacturing processes. Because of our limited ability to control the most significant emission pathways directly or completely, release of pharmaceuticals into the environment cannot be completely avoided with currently available technologies and practices. However, Takeda believes that meaningful steps can be taken to ensure that emissions and impacts are mitigated.

Many pharmaceutical and health care products such as vitamins, electrolytes, amino acids, peptides, proteins, carbohydrates, lipids, vaccines, biologics, plasma-derived therapies, and herbal products, are identical, or similar, to compounds that exist in nature. Accordingly, many of these compounds break down or biodegrade in wastewater treatment systems and/or in the ambient environment, thereby mitigating the hazardous or pharmacological effect on the environment.

The principal environmental concern is with regard to active pharmaceutical ingredients that may both persist in, and be hazardous in the environment, or have pharmacological effects. These active pharmaceuticals primarily end up in the aquatic environment and have been detected in surface and groundwaters at "part per billion" and "part per trillion" levels, leading to concerns around the impact on aquatic species, bioaccumulation in the food chain, drinking water quality and other potential human exposures.[2] While studies from the World Health Organization have concluded that "trace quantities of pharmaceuticals in drinking water are very unlikely to pose risks to human health because of the substantial margin of exposure or margin of safety between the concentrations detected and the concentrations likely to evoke a pharmacological effect,"[3] there is evidence of harm to certain aquatic species from long-term exposure to some active pharmaceuticals, notably hormone disruptors, antimicrobials and pain medications[4].

Takeda's Perspective

The following principles guide Takeda's strategic approach towards managing pharmaceuticals in the

https://ec.europa.eu/health/system/files/2016-11/study_environment_0.pdf

[2] Boxall, A. et al. (2012), *Pharmaceuticals and personal care products in the environment: what are the big questions?* Environmental Health Perspectives Vol. 120/9, pp 1221-1229, https://doi.org/10.1289/ehp.1104477

[3] World Health Organization (WHO). (2013, November 2013*). Information sheet: Pharmaceuticals in drinking-water.* https://www.who.int/publications/m/item/information-sheet-pharmaceuticals-in-drinking-water.

[4] aus der Beek, T. et al. (2016), *Pharmaceuticals in the environment-Global occurrences and perspectives*. Environmental Toxicology and Chemistry, Vol. 35/4, pp. 823-835, http://dx.doi.org/10.1002/etc.3339

environment:

- We support a collaborative approach to further mitigating risks so that industry, academia, relevant stakeholders, and regulatory agencies can determine action based on sound scientific evidence and appropriate risk-benefit analyses. Current evidence indicates that the benefits derived from the use of pharmaceuticals to treat patients far outweigh the risks arising from their presence in trace amounts in the environment. A collaborative approach to further mitigating risks is the best path.
- We support continued research into potential environmental effects of active pharmaceuticals, especially on aquatic organisms and those associated with exposure to mixtures of active pharmaceuticals over a sustained period of time. We also partner with the European Federation of Pharmaceutical Industries and Associations (EFPIA) to improve methods to identify and quantify the environmental risks of pharmaceutical products.
- We recognize that we have the responsibility to study and better understand the potential environmental impacts of our pharmaceuticals throughout their product lifecycles. We remain committed to developing relevant data to use as a basis for risk assessments to ensure that the manufacturing, use and disposal of our pharmaceutical products does not adversely affect human health or the environment including using proven technologies to minimise exposure of active pharmaceutical ingredients from production of manufacturing waste water and thus public sewage streams; this includes Takeda-developed drug products that are manufactured through our contracts with third parties.
- We support and participate in pharmaceutical take-back programs in collaboration with relevant industry groups. We also support the education of our patients and end users to encourage safe return or disposal of unwanted or expired medicines and sharps.

Conclusion

The science focusing on the broader environmental impact of pharmaceuticals is complex considering the variety of aquatic species, chemicals, active pharmaceuticals, and the combinations thereof. Takeda believes that the benefits derived from the use of pharmaceuticals to treat patients far outweigh the risks arising from their presence in trace amounts in the environment. Takeda is also committed to ensuring that harmful emissions and impacts are mitigated.

About Takeda Pharmaceutical Company Limited

Takeda is a global, values-based, R&D-driven biopharmaceutical leader headquartered in Japan, committed to discover and deliver life-transforming treatments, guided by our commitment to patients, our people and the

planet. Takeda focuses its R&D efforts on four therapeutic areas: Oncology, Rare Genetics and Hematology, Neuroscience, and Gastroenterology (GI). We also make targeted R&D investments in Plasma-Derived Therapies and Vaccines.

July 2022