独立行政法人 医薬品医療機器総合機構
Pharmaceuticals and Medical Devices Agency

Regulatory Experience and Considerations to Date from PMDA

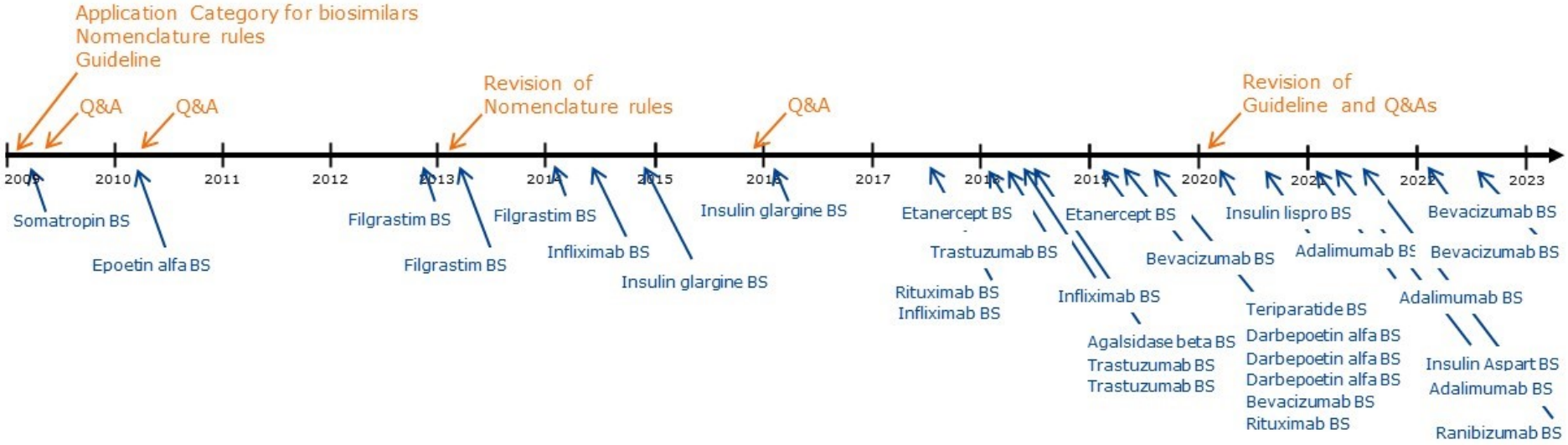
Ryosuke KURIBAYASHI, Ph.D.
Deputy Review Director
Office of Cellular and Tissue-based Products
Pharmaceuticals and Medical Devices Agency

The views and opinions expressed in this presentation are those of the presenter and should not necessarily represent the views and opinions of the PMDA.

Outline

- Approved biosimilars in Japan
- Approved biosimilar programs which included a comparative efficacy study (CES) , summary of learnings
- Approved biosimilar programs which did not include a CES and why one was not requested
- Any post-marketing/real-world learnings

Approved biosimilars in Japan



32 biosimilars have been approved during the period 2009–2022.

18: mAbs/Fusion proteins
3: Cytokines
6: Hormones
1: Enzymes
4: ESAs

Approved biosimilar programs which included a CES, summary of learnings

- 23 biosimilars were approved based on comparative analytical studies, a comparative PK study and a CES.
- 7 biosimilars were approved based on comparative analytical studies and a comparative PK/PD study (i.e., without CES).
  3 biosimilars were filgrastim, 4 biosimilars were insulin analogues.
- 1 biosimilar was approved based on comparative analytical studies, a comparative PK study, and a PD study. (i.e., without CES)
  Agalsidase beta BS
- 1 biosimilar was approved based on comparative analytical studies and a CES. (i.e., without comparative PK study)
  Ranibizumab BS

Approved biosimilar programs which included a CES, summary of learnings

- Japanese Biosimilar Guideline

6 Clinical trails

In general, it will be difficult to demonstrate the comparability of a biosimilar with the reference product only based on the data on quality attributes and the results of nonclinical studies. Therefore, the sponsor should evaluate the comparability of a biosimilar through clinical trials. ……. Where pharmacokinetic (PK) and/or pharmacodynamic (PD) studies are sufficient to assure comparability in the clinical endpoint of interest, the afore-mentioned, additional clinical studies to evaluate efficacy might be omitted.

Approved biosimilar programs which did not include a CES and why one was not requested

- 7 biosimilars were approved based on comparative analytical studies and a comparative PK/PD study (i.e., without CES).
  Filgrastim BS, insulin analogues BS

Because PD marker that is a validated surrogate marker for clinical efficacy are available for these products.

Approved biosimilar programs which did not include a CES and why one was not requested

- 1 biosimilar was approved based on comparative analytical studies, a comparative PK study, and a PD study. (i.e., without CES)
  Agalsidase beta BS

Because a biosimilar of agalsidase beta is used against the patients of Fabry disease which was a rare disease.

A sponsor didn't conduct a CES and also a 2 arms comparative parallel-designed PD study due to feasibility, disease property, and mechanism of action (i.e., enzyme replacement therapy).

The study design of PD is single-arm switched therapy from originator to BS (not parallel design).

Mol Genet Metab. 2020;130(3):215-224.

Any post-marketing/real-world learnings

BS is required the implementation of RMP as the “Approval condition: The applicant is required to develop and appropriately implement a risk management plan” based on the domestic notification.

Teriparatide BS SC injection [Mochida] and Infliximab BS IV infusion [NK] were evaluated the safety and efficacy in post marketing surveillance. Approval condition of these two products was removed in 2023.

No safety concern more than originators is found through PMS of BSs so far.

Thank you for your attention!

Ryosuke KURIBAYASHI
Office of Cellular and Tissue-based Products
Pharmaceuticals and Medical Devices Agency