Electronic Supplementary Material

Regulation of biosimilar medicines and current perspectives on interchangeability and policy

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Table S1: Regulatory explanations of the term 'biosimilar'

European Medicines Agency[1]	A biosimilar is a biological medicinal product that contains a version of the active substance of an already authorised original biological medicinal product (reference medicinal product) in the EEA. Similarity to the reference medicinal product in terms of quality characteristics, biological activity, safety and efficacy based on a comprehensive comparability exercise needs to be established.
U.S. Food & Drug Administration [2]	Biosimilar or biosimilarity means that 'the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components' and that 'there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product'.

EEA- European Economic Area

[1] European Medicines Agency (2014) Guideline on similar biological medicinal products

[2] Section 7002(b) (3) of the Affordable Care Act, adding section 351(i) (2) of the Public Health Services Act

Table S2: Comparability exercise to support major manufacturing process changes - details of clinical studies and extrapolated indications

Product name (Active substance)	**Approved indications**	**Nature of change**	**Clinical data**	**Extrapolated indication**	**Ref**
Herceptin® (Trastuzumab)	Early breast cancer Metastatic breast cancer	New formulation for subcutaneous administration	Clinical trials in HER2+ early breast cancer patients	Extrapolation to metastatic setting	*[1]*
Aranesp® (Darbepoetin alfa)	Anaemia associated with chronic kidney failure Anaemia in adult cancer patients receiving chemotherapy	New master cell bank and new manufacturing technology	Clinical trials in chronic kidney failure patients	Extrapolation to cancer indication	[1]
Avonex® (Interferon beta-1a)	Multiple sclerosis	Changes to master cell bank and manufacturing process after pivotal phase III trials	PK data	MS indication approved without new clinical efficacy trial	[2, 3]

PK; pharmacokinetic, MS; multiple sclerosis

Table S3: Substitution of biological medicines in Australia - Details of reference biological medicines and their biosimilars listed on the Australian Pharmaceutical Benefits Scheme (August 2018)

Substance	**Products**	**Substitution permitted ('a' flag status granted by PBAC)*.**	**Reason 'a' flag status not granted**	**Ref**
Etanercept	Enbrel® Brenzys®	Yes	N/A	[4]
Epoetin alfa Epoetin lambda	Eprex® Novicrit®	No	At time of authorisation Novicrit has restricted route of administration when compared to Eprex	[4, 5]
Filgrastim	Neupogen® Nivestim®	No	Absence of TGA statement that supports 'a' flagging	[4, 6]
Follitropin Alfa	Gonal-f® Bemfola®	No	Substitution difficult from a practical perspective owing to differences in strengths, number of pens per pack and maximum quantities per brand	[4, 7]
Infliximab	Remicade® Inflectra® Renflexis®	Yes	N/A	[4]
Pegfilgrastim	Neulasta®** Ristempa®**	Yes*	N/A	[4]
Somatropin	Genotropin® Omnitrope®	No	No details provided on PBAC website	[4]

**'Brand equivalents are accompanied by an 'a' flag on the Pharmaceutical Benefits Schedule. An 'a' flagged medicine may be substituted by a pharmacist at the point of dispensing.*

***Neulasta and Ristempa are not biosimilars but are the same products with different brand names*

PBAC, Pharmaceutical Benefits Advisory Committee; TGA, Therapeutic Goods Administration

References

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