Health Canada | Santé Canada
Health Products and Food Branch | Direction générale des produits de santé et des aliments

Biologics and Genetic
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10-116885 - 569

Re: Interchangeability / Substitutability of Subsequent Entry Biologics (SEBs)

Dear Provincial/Territorial Drug Plan Directors:

This letter is intended to bring to your attention Health Canada's responses to inquiries regarding SEBs and interchangeability/substitutability.

Health Canada has recently finalised a guidance document that is expected to facilitate the federal drug regulatory approval process for subsequent entry biologics (SEBs). An SEB is a biologic drug that enters the market subsequent to a version previously authorized in Canada, and with demonstrated similarity to a reference biologic drug. It relies in part on prior information regarding safety and efficacy that is deemed relevant due to the demonstration of similarity to the reference biologic drug and which influences the amount and type of original data required.

Throughout the SEB policy development process Health Canada has been asked by external stakeholders whether an SEB can be used interchangeably with its reference biologic drug; whether an SEB is automatically substitutable with its reference biologic drug; and whether an SEB is therapeutically substitutable with its reference biologic drug.

In response to these stakeholder inquires, Health Canada has stated the following:

- SEBs are not "generic" biologics. Authorization of an SEB is not a declaration of pharmaceutical or therapeutic equivalence to the reference biologic drug.

Stakeholders have also recommended that, as the federal regulator of drug products, Health Canada should review data that supports therapeutic interchangeability and make a recommendation as to whether this can be done safely and effectively by physicians.

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In response to this recommendation, Health Canada has stated the following:

- Specialized clinical studies can be used to support therapeutic interchangeability, however, these studies are not usually done and their relevance may not be long-lasting. Over time, as sponsors of the SEB and the reference biologic drug make their own independent manufacturing changes, differences could be introduced that affect the drug products. For this reason, Health Canada does not support automatic substitution of a SEB for its reference biologic drug and recommends that physicians make only well-informed decisions regarding therapeutic interchange.

If you have questions or concerns regarding Health Canada's position as it has been expressed here, please contact us at:

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For more information about SEBs please refer to the following documents (available on the Health Canada website):

- *Guidance for Sponsors: Information and Submission Requirements for Subsequent Entry Biologics (SEBs)*
- *Questions & Answers To Accompany the Final "Guidance for Sponsors: Information and Submission Requirements for Subsequent Entry Biologics (SEBs)"*

Yours sincerely,

Dr. Elwyn Griffiths
Director General

Cc: Federal/Provincial Relations Division, Strategic Policy Branch, Health Canada
Office of Pharmaceuticals Management Strategies, Strategic Policy Branch, Health Canada