Biosimilars : State of knowledge and recommendations from the Programme de gestion thérapeutique des médicaments

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Programme de GESTION THÉRAPEUTIQUE des médicaments

Le pGTm est une initiative des cinq centres hospitaliers universitaires du Québec

Introduction

- Biosimilars have been gradually making their way to the Canadian market.
- Since 2014, Health Canada has granted marketing authorization for 6 biosimilars
- Omnitrope™ (somatropin) has been available since 2009.
- Quebec and Canadian regulatory and assessment agencies have not published their position on substituting biosimilars for reference biologic drugs (RBDs) or on their interchangeability.

Objectives

- To summarize the state of knowledge needed to understand the issues concerning biosimilars.
- To make recommendations for determining their role and their main conditions of use in Quebec's five university teaching hospitals (UTHs).

Methodology

- Literature review
- Consultation of the websites of Quebec, Canadian, American and European regulatory and assessment agencies.
- Literature search:
  - Clinical issues
  - Similarity studies
  - Substitution studies
- Identification of the elements to consider when adopting a position.

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Results

Elements to consider

- Biosimilars are **heterogeneous**. Substituting all biosimilars and RBDs in all situations cannot be recommended because of differences in terms of:
  - The properties of the different biosimilars (e.g., immunogenic properties)
  - Patient characteristics, the stage of the disease being treated
  - The features of the diseases to be treated with a biosimilar
  - The quality and quantity of the published data
- **Interchangeability** between biosimilars and RBDs in all situations cannot be recommended because of a lack of evidence for evaluating the effects of alternation.
- Observational studies evaluating **single** substitution show a **tendency towards broadly comparable efficacies and safety profiles**. Few unexpected adverse effects are being reported at this time, but rare differences have been reported.
- The estimate of the actual impact of substitution is limited (number of patients and duration of observation). **The occurrence of unexpected effects** (e.g., immunological effects with little long-term impact) cannot be ruled out.
- The **official indications** for a given biosimilar may differ from those for the RBD.
- No clinician can be completely abreast of the current state of knowledge because biosimilars are an **emerging phenomenon in Quebec**. Clinical experience is still limited.
- The UTHs should consider the products used in **outpatients** for listing in their formularies to ensure the continuity of the treatments and to avoid alternation when necessary.

Activities in progress

- Clinical intervention model
- Individual evaluations by pharmacy and therapeutics committees
- Decision-making tool
- Linkages with third-party payers and purchasing groups

BIOSIMILAIRES - TABLEAU DÉCISIONNEL

Générique Commercial	PBR ou biosimilaire	Niveau canadien	Niveau québécois	
			RAMQ-INESSS-PGTM	CHU-1 Comité de pharmacologie Prescription – Service
Etanercept				
Enbrel	PBR	2005 – AMM Indications adultes : Polyarthrite rhumatoïde, rhumatisme psoriasique (arthrite psoriasique), spondylite ankylosante, psoriasis en plaques Indications pédiatriques : Enfants 4-17 ans : psoriasis en plaques, arthrite juvénile idiopathique polyarticulaire	Médicament d'exception Adulte Arthrite psoriasis et psoriasis en plaques (Remboursement de Enbrel[RC] (serngue) et de Enbrel[RC] Pédiatrie : Adulte et pédiatrie : PGTM non évalué	Statut local : HF
Brenzys	Biosimilaire d'Enbrel	2016 – AMM Indications adultes : Indications pédiatriques : Données pour clientèle pédiatrique :	2017/08/18 Médicament d'exception Adulte Pédiatrie: Non évalué. PGTM non évalué	Statut local : HFP avec ce produit et recevant de façon régulière à domicile pour éviter l'alternance Substitution automatique : NON Substitution unique : NON Interchangeabilité (alternance) : NON

*PBR : produit biologique de référence – AMM : autorisation de mise en marché – HF : non inscrit sur la liste (hors formulaire) - HFP : HF avec particularité (usage restreint)
* RAMQ : Régie de l'assurance maladie du Québec – INESSS : Institut national d'excellence en santé et en services sociaux –
* PGTM : Programme de gestion thérapeutique de médicaments

Point of view: substitution and interchangeability

Health Canada: Marketing authorization does not constitute a declaration of therapeutic or pharmaceutical equivalence with the RBD. Demonstrating similarity therefore does not mean that the biosimilar and the RBD are automatically interchangeable or substitutable.

Ordre des pharmaciens du Québec: A pharmacist can substitute for a prescribed drug a drug with the same generic name. Pharmaceutical, pharmacological, therapeutic and clinical considerations should be taken into account. (Definition drafted in the context of generic drugs).

Food and Drug Administration: Interchangeability criteria: Biosimilarity must be demonstrated. The biosimilar must produce the same clinical effect as the reference biologic drug in any patient. When a biosimilar is administered more than once to a given patient, the risks in terms of safety and loss of efficacy in the event of alternation with or substitution for the RBD must not be greater than those associated with using the RBD with no alternation or substitution.

The FDA maintains a list of drugs recognized as being biosimilar. FDA intends to add drugs recognized as being interchangeable. As at January 2018, no drugs were added.
Purple Book : Lists of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations

Recommendations

1) The Pharmacy and Therapeutics Committees should individually assess each biosimilar with regard to the advisability of listing it in the formularies, its substitution and its interchangeability.
2) Substitution can be considered on the basis of the following criteria:
   - Treatment-naïve patient,
   - Interchangeability recognized by a regulatory agency,
   - Weak immunogenic profile,
   - Existence of an objective efficacy measure.
3) A plan for reducing the risks associated with alternation should be put in place. The UTHs should assess potential situations involving alternating between an RBD and its biosimilar when selecting listed products for different patient populations.
4) The UTHs should make joint decisions.

Conclusion

The Programme de gestion thérapeutique des médicaments has adopted four recommendations concerning the use of biosimilars in the UTHs.

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