SUBSEQUENT ENTRY BIOLOGICS

The term subsequent entry biologic (SEB) refers to new drugs that are similar but not identical to an originator's biologic drug (the reference biologic). Biologics are a class of drugs manufactured from living organisms that cannot be synthesized and the complexities of the manufacturing process mean that every biologic product is unique.

Canadians have long been familiar with generic drugs and the routine substitution by pharmacists for a generic product instead of the brand name product. This is not the case with biologics, indeed Health Canada clearly states that an SEB is not interchangeable with the originator's product.

As patents expire on the first generation of biologics, subsequent entry biologics have started to enter the market. Health Canada operates under a guidance document,[1] not a regulation, which describes the submission and review process for SEBs. The SEB will be given the same chemical name, the International Nonproprietary Name (INN) as the original biologic; the brand name will differ but the INN for both biologics will be the same. This implies much more than similarity and has the potential to create confusion.

Quebec recently approved provincial funding for an SEB that is similar to Remicade (infliximab) and used in rheumatoid arthritis, spondylitis, psoriatic arthritis and chronic plaque psoriasis. Of note is that Remicade also has approved uses for other diseases but those are not included in the approved uses for the "new" infliximab (Inflectra). That is a notable detail since Health Canada's guidance document shows that extrapolation of indications will be considered for any SEB and could occur in the absence of rigorous clinical trials or substantive evidence of effectiveness.[1] Health Canada could permit any approved use of the original biologic to be assigned to the SEB, based on evidence that the SEB is similar enough to probably deliver similar outcomes in all the other indications. That evidence does not have to include clinical trials for the other indications. Indeed, stakeholders have pointed out that the limited clinical trials conducted for SEBs tend to be shorter, with earlier endpoints, since the objective is to demonstrate similarity, not equivalence or improvement in patient outcomes. This point alone is greatly disturbing to clinicians who expect very high standard of scientific evidence in drug approvals and who know that biologics cannot be perfectly replicated.

In Quebec, the December 2014 decision to permit – and require – pharmacists to substitute an SEB for an original biologic carries with it the requirement that patients be notified and if they choose the more expensive brand of infliximab the patient may pay the extra money to receive it. That encounter appears to be the only opportunity for choice, whether by the patient, the prescriber or the pharmacist. The prescriber can write "no substitution" on the prescription but must demonstrate "recognized therapeutic concerns" to prevent substitution. Effectively, the Quebec drug plan has created a status of interchangeability that is not recommended by Health Canada and will have unknown impact on patients. As all the provinces start to review SEBs and make decisions about how/if to fund them, the potential for this amount of substitution – for therapeutic equivalence – can become a significant challenge.

Among the concerns raised by stakeholders, such as BioteCanada, is a fear that Canadian physicians, pharmacists and patients are not well informed about SEBs and are ill-equipped to make the decisions they will face. BioteCanada recently released survey results of 427 prescribers from Alberta, British Columbia, Ontario and Quebec in which 41 per cent admitted they either had never heard of SEBs or could not define them. When these physicians were asked what message they receive from the fact that two products have the same non-proprietary name:

- 64 per cent believed the medicines are structurally identical,
- 62 per cent believed that either product would deliver the same results for a patient,
- 49 per cent believed the patient could be safely switched from one product to the other during the course of treatment,
- and 76 per cent believed the medicines are approved for the same indications.

Those responses hint at the complexity of the task ahead, to educate patients and health professionals, to seek more detail, rigor and transparency from regulators about the evidence for SEBs, and to offer choice to prescribers and patients.

References

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