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7 September 2017

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Dear Sir/Madam

TGA Consultation Regarding Nomenclature for Biologic Medicines

The Australian Rheumatology Association thanks the TGA for the opportunity to comment on nomenclature for biosimilar medicines.

Biosimilar medicines are already in use in Australia. The issue of nomenclature has become more urgent given the listing of several drugs which are used in ambulatory care settings, especially in the rheumatology therapeutic area.

In Australia now, there are three versions of infliximab available- Remicade (originator- Janssen), Inflectra (biosimilar- Pfizer), and Renflexis (biosimilar- MSD). All three are known by the INN infliximab, and all are 'a'-flagged, meaning they are substitutable at the pharmacy counter. These agents are given intravenously, at hospitals or infusion centres. Two versions of etanercept are available - Enbrel (originator- Pfizer) and Brenzys (biosimilar- MSD). The latter is given by the consumer him/her self in a subcutaneous injection, and is also subject to substitution at the pharmacy level.

Biologic medicines are complex and microheterogeneous. Biosimilar copies cannot be viewed as generics because their different manufacturing processes result in post-translational changes (eg glycosylation). Emergent evidence suggests transition from the originator is safe and effective, but the evidence around repeated switches is more limited. There is also no clinical evidence around multiple switches involving more than one biosimilar. 'a'-flagging means that repeated substitution between originators and their biosimilar/s is more likely, and there is a lack of evidence around the outcomes of this practice.

Likewise, none of the clinical trials for the originators, biosimilars or switch studies are powered to detect rarer but significant adverse events eg cancer, which carries the added confounder of long latency from exposure to event. Loss of response with repeated switches may also be an issue. Post-marketing surveillance and pharmacovigilance becomes critically important in this setting. The system in place relies on spontaneous reporting of adverse events and carries risks of both under-reporting and incorrect attribution.

Unique identifiers will permit better traceability in the case of an adverse event, whether related to the drug itself or the device, which may differ significantly between brands. It will support the choice of the prescriber and the patient and limit accidental switches, though identification may still be delayed.

An ideal naming system would be and simple and consistent across the world.

The ARA would like to see improvements in electronic prescribing, streamlined authority application for all biologics, and links with the PBS and pharmacies which would allow the prescriber to be notified in real-time of what the patient is actually dispensed. Brands already have unique codes for pharmacy reimbursement, and the building of appropriate interfaces could allow this data to be available to prescribers, facilitating reporting adverse events, and to registries, such as the Australian Rheumatology Association Database (ARAD). ARAD was established to determine the long-term effectiveness, safety and cost-effectiveness of biologic therapy for inflammatory arthritis. Registry data will be critical in following the performance of these agents in the real world, both in terms of long-term safety and response.

Option 1. Status Quo
We believe it is important to be able to identify the exact medication prescribed in order to permit accurate attribution of adverse events. At present the originator and its biosimilars are all identified by the same approved biological name. If an adverse event occurs, it will be difficult for the patient and the prescriber to identify and report it correctly, a further impediment to a voluntary notification system which does not mandate collection of trade names.

Option 2. Status quo with activities which increase public reporting of adverse events with the inclusion of the product's trade name, AUST R and batch number
This option is not likely to be successful. It relies on someone recording the batch number of each item dispensed to the individual month to month. While this may be practical for vaccines, which are administered as one-off items, it will not be feasible for medications which are regularly self-injected for an indefinite period. Adverse events with biologic agents may not appear immediately, and incorrect attribution may occur if there is not a record of every batch number of the medicine which has been dispensed throughout the period of treatment, perhaps for years. It would be cumbersome and costly to record this information; who would be responsible for that, and how would it be communicated to the prescriber? The recording, collection and interpretation of this information would be a further disincentive to report adverse events.

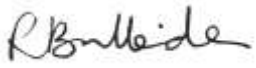
Option 3. Barcode system, similar to EU
This option offers a possible solution, but only if combined with improvements in IT systems to enable notification of prescribers about what is dispensed in real time, as the pharmacist is submitting this exact information to the PBS. This could be designed in a way to interface with practice management software, or via PRODA email notifications on a daily basis. It could also be usefully recorded in registries. If the barcode, with its associated information were embedded in the patient's electronic record (either at a practice or myHealth record), there would be the potential for adverse events to be reported more easily and more systematic and complete pharmacovigilance to be in place.

Option 4. Introduction of suffixes to the naming of biologic medicines
In many ways, this is the ideal solution, particularly if it were possible to adopt an international standard, as has been suggested by the WHO. However, there has been significant delay in progress of the Biologic Qualifier (BQ). There is a meeting in October 2017 to discuss this further, but it would seem unlikely that there will be a rapid agreement or implementation of this system. Meanwhile the FDA has mandated and executed a naming system as outlined in the document. There are potential issues with this, including the naming of a biosimilar which is approved in Australia before it is available in the US.

None of the options is ideal. Option 4 is preferred, but presents significant challenges in the international context with a reliance on the WHO progressing the BQ option in a timely manner. Option 3 does offer promising capacity for data collection and accurate matching of adverse events to the causative agent. We do not support Options 1 or 2. We agree that education will be needed regardless of the option selected, to encourage reporting of adverse events. Loss of response is also an important consideration and will be difficult to identify without collection of accurate data, including dispensing information, into registries.

The ARA supports the introduction of biosimilars to the Australian market, and would see the adoption of a unique identifier as a confidence-builder, rather than as a barrier. The most likely outcome of a failure to adopt a naming convention will be under-reporting and inaccurate attribution of adverse events and a failure to recognise any loss of therapeutic response in the setting of repeated substitutions.

Yours sincerely



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