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17 June 2015

Dear Chair and Members
Senate Economics Legislation Committee
economics.sen@aph.gov.au

Re: National Health Amendment (Pharmaceutical Benefits) Bill

We would like to raise our serious concerns about the potential impact on patient safety of certain provisions of the National Health Amendment (Pharmaceutical Benefits) Bill 2015 (the Bill) which facilitate the substitution of biosimilars for biologic medications at the pharmacy level.

We represent the largest patient group that will be affected by these provisions because biologic medications play an important role in the management of a range of auto-immune forms of arthritis, including rheumatoid arthritis and juvenile arthritis. If a safety issue arises as a result of measures in this package, it will be the people living with these serious and often disabling conditions that will have to live every day with the potentially severe consequences.

Consequently we were disappointed that we were not consulted about the potential impact on people with arthritis in any of the negotiations around the provisions of the PBS Access and Sustainability package.

Our position is that we welcome the introduction of biosimilars because they offer the potential to reduce health system costs and increase patient access and choice to effective biologic medications. However, at present there is not enough evidence to support the safety and efficacy of substituting biosimilars for biologics in people who are stable on the originator product. Consequently we are strongly opposed to current moves to allow substitution at the pharmacy level, including provisions in the Bill and recent advice from the PBAC that it will consider, as its default position, allowing substitution to occur.

Until more evidence is available, we strongly urge the government to proceed with caution to ensure measures to encourage the uptake of biosimilars do not compromise patient safety in any way.

A letter we have written recently to the Minister for Health outlining our concerns about the substitution of biosimilars is attached. We have also written in similar terms to the PBAC.

The specific provisions of the Bill that we are concerned about are the amendments relating to PBS listing for bioequivalent and biosimilar medicines and treating brands as Schedule equivalent. These are:

- Schedule 1, Clause 3, which provides for a brand or pharmaceutical item that is biosimilar or bioequivalent to a listed item, to be taken to have the same drug.

- Schedule 2, Clause 1, which provides for the Minister to determine, having regard to any advice from the PBAC, that a brand of pharmaceutical item is to be treated as equivalent to one or more other brands of pharmaceutical items.

These clauses would allow biosimilars to be treated in the same way as generic medications. However, a biosimilar is not a generic biological medication.[i] Biologic medications are extremely complex molecules grown using living organisms and it is virtually impossible to replicate them exactly. Minor variations in the manufacturing process can have a major impact on efficacy and patient safety. Consequently it cannot be assumed that a biosimilar can be used interchangeably with its biologic reference product.

We are also concerned that the legislation gives the responsibility of advising the Minister as to whether a biosimilar is to be treated as equivalent to its reference product to the PBAC. While we respect the skills of the PBAC members, the PBAC's role is to evaluate products for cost-effectiveness and reimbursement. The bioequivalence of a biosimilar is an issue of quality, safety and efficacy which should be determined by the TGA which is responsible for registering pharmaceuticals in Australia. The TGA's view is that it is not currently possible 'to determine a degree of similarity, between a biosimilar and an already registered biological medicine sufficient to support a designation by the TGA of 'bioequivalence'.[ii] Consequently we recommend that Clause 1 in Schedule 2 be amended to read '… having regard to advice from the TGA and the PBAC…'

We would be pleased to provide any additional information to the Committee that you may require.

Yours sincerely,

Ainslie Cahill
Chief Executive Officer

About Arthritis Australia

Arthritis Australia is the peak arthritis consumer organisation in Australia, representing more than three million people living with over 100 forms of arthritis. We provide support and information to people with arthritis as well as their families and friends and advocate on behalf of consumers to leaders in business, industry and government. We also the largest non-government funder of arthritis research in Australia.

[i] Therapeutic Goods Administration https://www.tga.gov.au/book/what-biosimilar viewed 16 June 2015.

[ii] https://www.tga.gov.au/book/labels-product-information-pi-and-consumer-medicine-information-cmi-biosimilars v*iewed* 16 June 2015

Arthritis AUSTRALIA

Australian Rheumatology Association

9 June 2015

The Hon Sussan Ley
Minister for Health
PO Box 6022
House of Representatives
Parliament House
Canberra ACT 2600

Dear Minister,

We request an urgent meeting to discuss with you our serious concerns that allowing biosimilars to be substituted for biologic medications at the pharmacy level may compromise patient safety. Biologics play an important role in treating a number of auto-immune forms of arthritis such as rheumatoid arthritis and juvenile arthritis.

Arthritis Australia and the Australian Rheumatology Association strongly recommend that measures be put in place to protect patient safety with respect to the usage of biosimilars in Australia;

- People already receiving a biologic medication should not be switched to the biosimilar version without the informed mutual decision of the prescriber and the consumer.
- New patients or patients moving to a new biologic therapy could be started on a biosimilar.
- Complex biosimilars of the biologic disease modifying anti-rhematic drugs (bDMARDs) used to treat auto-immune conditions should not be 'a' flagged by the PBAC until further clinical evidence supporting the safety and efficacy of switching between the biosimilar and its originator product is available.
- A clear naming convention for biosimilars should be adopted to facilitate tracking and reporting of adverse events.
- Enhanced post-marketing pharmacovigilance and adverse events monitoring should be put in place to monitor the clinical efficacy and safety of biosimilars in the Australian market.
- Education programs for consumers, prescribers and pharmacists in relation to biosimilars should include a strong focus on protecting patient safety and should be developed in consultation and collaboration with consumers, clinicians and other stakeholders.

The rationale for our position is as follows.

Patient safety may be compromised by allowing substitution

Biosimilars are not generics. Biologic medications are extremely complex molecules grown using living organisms and it is virtually impossible to replicate them exactly. Consequently it cannot be assumed that a biosimilar can be used interchangeably with its biologic reference product.

The risk of inducing an immune response, known as immunogenicity, is an important efficacy and safety concern for all biologics, including biosimilars. Small differences in the materials, manufacturing process, distribution and route of administration of biologics can have a major impact on immunogenicity. For example a minor change in manufacturing of the biologic

erythropoietin a decade ago led to a sharp increase in an incurable form of severe antibody-induced anaemia. It took years to determine and address the cause.[1]

The bDMARDs used to treat auto-immune arthritis carry an increased risk of immunogenicity both because the molecules are more complex than other biologics and because they are used over long periods for chronic conditions.[2]

The first biosimilar of a bDMARD (infliximab) is currently being considered by the TGA and the PBAC for use in Australia.

More evidence is required to support the efficacy and safety of substitution

There is widespread concern that switching between a biologic and its biosimilar may increase the risk of immunogenicity.[3] [4] [5]

International approval processes for biosimilars do not require clinical data on the safety and efficacy of switching between the biologic and its biosimilar. The only exception is the FDA which requires this additional evidence for biosimilars to determine interchangeability.[6]

Clinical evidence to support the safety of switching to biosimilars in people who are stable on the originator product, especially infliximab, is sparse.[7] In the absence of this data, Norway is funding a study into the safety and efficacy of switching from Remicade (infliximab originator) to the biosimilar treatment Remsima. This study is due for completion in May 2016.[8]

Leading experts and regulatory authorities do not support substitution

Regulation of biosimilars is still an evolving field. Notably, leading clinical experts and regulatory authorities do not support substitution of biosimilars for biologics at the point of dispensing. These include regulatory authorities in the UK,[9] Canada,[10] and most European countries,[2] as well as the American[11] and British Colleges of Rheumatology[12] and the Council of Australian Therapeutic Advisory Groups,[13] which provides guidance on drug use in Australian hospitals.

The PBAC's advice that it will consider 'a' flagging of biosimilars as suitable for substitution at the pharmacy level is in contrast to the weight of opinion internationally. Of particular concern is the PBAC's advice that it would consider 'absence of data to suggest significant differences in clinical effectiveness or safety' when considering 'a' flagging.[14] This is inappropriate as absence of evidence is not the same as evidence of absence.

'A' flagging will lead to inadvertent substitution at the pharmacy level without the knowledge, understanding or agreement of the consumer and/or prescriber. While both can veto substitution, consumers may not understand that biosimilars are not generics and busy doctors may forget to prescribe by brand name or to specify that substitution is not permitted.

Safety monitoring may be compromised

Substitution at the pharmacy level can create confusion when reporting adverse events. Effective safety monitoring needs doctors and consumers to know exactly which medicine is being taken.

Immune reactions can also occur after a patient has been using a biologic for a long time, so if medications have been switched it can be difficult to tell which product is responsible for any adverse event.

In Thailand, a number of cases of immune reactions to a biologic medication (epoetin alfa) were recorded between 2004 and 2007. The market included a number of biosimilars of this product and hospitals and pharmacists frequently switched patients between products, often with incomplete documentation. Despite intensive investigation, it was not clear which product or products had caused the problem.[15]

Disease control may be compromised

Achieving adequate disease control or remission for people with auto-immune forms of arthritis can be challenging and may take many attempts using different combinations and doses of various medications, including different bDMARDs. This process can take years.

Eligibility criteria for access to biologic medications on the PBS are also strict and require patients to fail other therapies before these medications can be prescribed or changed.

In rheumatology, clinical trials of biosimilars have been of new users only, with no trial of direct substitution. In the absence of data from such trials, substitution which may jeopardise hard-won disease control should not be allowed.

A safety issue would be a major setback to the introduction of biosimilars

Biosimilars offer the welcome potential to reduce health system costs and increase patient access to effective biologic medications. However it is essential to proceed with caution to ensure measures to encourage their uptake do not compromise patient safety in any way. Aside from the impact on individuals, if a safety issue does arise, it would be a significant set-back for the future adoption of biosimilars and hence the potential to realise the benefits they may offer.

We look forward to discussing our concerns with you at your earliest convenience.

Yours sincerely

Ms Ainslie Cahill
CEO
Arthritis Australia

Dr Mona Marabani
President
Australian Rheumatology Association

For further information contact:

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About us

Arthritis Australia is the peak arthritis consumer organisation in Australia, providing support and information to people with arthritis as well as their families and friends and advocating on behalf of consumers to leaders in business, industry and government.

The Australian Rheumatology Association is the professional association of rheumatologists in Australia. Rheumatologists are specialist physicians who diagnose and treat diseases affecting joints, muscles and bones. Rheumatologists are one of only two prescriber groups who can prescribe bDMARDs for rheumatic conditions under the PBS.

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