Agenda Item 6

BIOSIMILARS REIMBURSEMENT

1 Purpose of Item

1.1 The Minister (delegate) requests the Pharmaceutical Benefits Advisory Committee (PBAC) provide advice on the following matter(s) under section 101(3) of *the National Health Act, 1953* (the Act):

The PBAC review a summary of the Department's proposal to implement new measures for the reimbursement of biosimilar medicines on the Pharmaceutical Benefits Scheme (PBS). Further, the delegate requests that the PBAC consider the appropriateness of the proposed measures, s38

2 Background and Current Situation

Biologics and Biosimilars on the PBS

2.1 There are over 65 biological medicines currently funded through the PBS. Expenditure on biologics has increased dramatically over the last five years, from approximately $1 billion in 2009-10 to around $2.3 billion in 2013-14; an increase of 130 per cent. Of the ten most expensive PBS medicines in 2013-14, five were biologics with a combined cost to government of $860 million in 2013-14. A number of biologics are coming off-patent in the next five years (see Attachment A), and biosimilar versions offer comparable health benefits for less cost.

2.2 Current arrangements for PBS listing of biosimilars do not appear to be achieving the savings originally expected of these products. Currently only a modest portion of biosimilars available overseas (in particular Europe) are on the market in Australia.

2.3 Any PBS drug must have an "a" flag on its listing to enable substitution by the pharmacist. None of the biosimilars currently on the PBS have an a-flag (due to the evolving nature of the policies in this space both in Australia and internationally). Without an "a" flag, pharmacists cannot dispense biosimilars in place of the originator as they ordinarily would for a generic. This has been a key factor inhibiting biosimilar uptake.

2.4 Current PBS pricing policy already ensures at least a 16% price reduction is achieved through movement to the F2 formulary, when a new biosimilar enters the market. However, the inability for the pharmacist to substitute these products is restricting competition and limiting the effectiveness of existing pricing mechanisms (price disclosure) to drive the level of savings that are being achieved internationally (around 30 per cent in Europe). If further savings are to be achieved we need to look beyond these existing mechanisms.

2.5 There are currently three biosimilar drugs listed on the PBS (Nivestim, Zarzio and Tevagrastim), all three are brands of filgrastim. A fourth drug, Novicrit (epoetin

lambda), was approved by TGA as a biosimilar of Eprex (epoetin alfa), but it is not a biosimilar for the purposes of the *National Health Act 1953*. PBAC instead recommended listing of the Novicrit at its July 2010 meeting on the basis of cost-minimisation to other erythropoietin-containing products. As such, Novicrit and its originator Eprex remain in F1, whereas Neupogen and the three biosimilar brands of filgrastim took the statutory price reduction and moved to the F2 formulary, when they were listed.

2.6 In Australia currently biosimilar price reductions are driven more effectively by hospital tendering, than PBS pricing policy. For example, in Western Australia (which publishes the prices of medicines paid in public hospitals), the biosimilar of filgrastim is almost 400 percent cheaper than the originator brand Neupogen. This suggests that widespread substitution of biosimilar filgrastim is common practice in Australia within the hospital system.

2.7 s38

2.8 TGA has indicated that an application to register a biosimilar infliximab product is currently under evaluation.

3 Proposal and Rationale

3.1 The proposal currently being developed for consideration by Government aims to increase the listing and uptake of less expensive biosimilar drugs as alternatives to existing, more expensive originator biologics on the Pharmaceutical Benefits Scheme (PBS). The key features of this proposal are:

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3.2 s38

Stakeholder Engagement

3.3 Recent consultations between the Department and over 20 PBS stakeholders groups which included the Generic Medicines Industry Association (GMiA), Medicines Australia (MA), the Consumers Health Forum and the Pharmacy Guild of Australia, has enabled the development of this draft proposal for consideration by Government.

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International Experience

3.4 International experience with biosimilars indicates that although regulatory agencies may not make recommendations on substitutability of biosimilars that health agencies around the world are looking at ways to drive utilisation as a means of obtaining better value for biologics.

3.5 In France, when prescribing a biological, physicians are required to specify on the prescription whether this is the first time the biological is prescribed and if so pharmacists are allowed to substitute this for a biosimilar providing that the biosimilar belongs to the same group as the prescribed product, known as a 'similar biologic group' (which should consist of the reference biologic and its authorized biosimilars, however these lists must still be drafted by the French regulator ANSM (Agence Nationale de Sécurité du Médicament) and on the proviso that the prescribing physician has not explicitly marked the prescription as 'non-substitutable'. If the pharmacist substitutes a biosimilar for the prescribed biological, they must write both the name of the dispensed product on the prescription and inform the prescribing physician. If the treatment is continued and the prescription is renewed, the same (substituted) medicine should be dispensed.

3.6 Germany, which has the highest use of biosimilars in Europe (around 50% volume uptake) have 17 "physician based regions" in Germany, the majority of which have implemented biosimilar quotas for Epoetin (EPO), resulting in increased uptake. They have an active role of prescription utilization management (KV) to track physicians' budgets. Payer education activities such as "dear doctor" letters address potential safety concerns and "reinforce biosimilar concept", which has had a significant impact on uptake. Biosimilar EPO uptake is around 60%, with cumulative savings to Germany between 2007-2011 estimated to be €551m (around $A807m). Germany, amongst other European countries are also considering tendering some biosimilars because of the existence of parallel traders in Europe.

3.7 Several reviews of the experience in Europe (including a recent assessment by the European Commission) have concluded that availability of biosimilar drugs has not resulted in any spike in apparent safety issues such as immunogenicity.

3.8 Although few biosimilars are yet on the market in North America, the United States of America has started to embrace savings with biosimilars with some private health insurance companies charging patients lesser copayment amounts for choosing a biosimilar over the biologic. Health Canada does not designate interchangeability or substitution between biologic and biosimilars, however each province has the authority to decide whether it will allow substitution in its provincial reimbursement plans or allow pharmacists to substitute for patients with private insurance.

4 Suggested action

4.1 That the PBAC consider the proposed measures in relation to biosimilar medicines, outlined above, and provide their view in relation to the proposal, including any concerns.

4.2 In the context of the proposed measures and to complement them, would the PBAC also please consider and advise, on the appropriateness of:

4.2.1 s38 s38

4.2.2 s38

Further Information:

1. Attachment A – Biologics on the PBS – Patent Expiry dates
2. Attachment B – Filgrastim Current PBS Utilisation

Attachment A

Biologics on the PBS – Patent Expiry dates

INN NAME	Patent Expiry
Interferon Alfa-2b	05-May-02
Interferon Alfa-2a	31-Jul-02
Heparin	02-Jan-06
Chorionic Gonadotrophin	09-Feb-06
Interferon Beta-1a	01-Apr-06
Dalteparin	12-Mar-06
Insulin Isophane	12-Mar-06
Epoetin Alfa	24-Apr-06
Epoetin Beta	24-Apr-06
Enoxaparin	13-May-06
Filgrastim	22-Aug-06
Insulin Neutral-Insulin Isophane	01-Oct-06
Somatropin	25-Oct-06
Interferon Gamma-1b	14-Oct-07
Interferon Beta-1b	12-Oct-08
Lenograstim	19-Nov-08
Follitropin Alfa	28-Oct-09
Dornase Alfa	20-Dec-09
Abciximab	01-Mar-10
Insulin Lispro / + Protamine Suspension	13-Jun-11
Follitropin Beta	23-Aug-11
Insulin Aspart /+ Protamine Suspension	29-Aug-11
Bacillus Calmette-Guerin (BCG) Tice strain	17-Oct-11
Tenecteplase	09-Nov-12
Reteplase	15-Jan-13
Rituximab	12-Nov-13
Botulinum Toxin Type A Purified Neurotoxin Complex	28-Nov-13
Tocilizumab	21-May-14
Insulin glargine	06-Nov-14
Botulinum Type A Toxin-Haemagglutinin Complex	06-Nov-14
Etanercept	17-Jul-15
Infliximab	02-Aug-15
Natalizumab	31-Aug-15
Trastuzumab	14-Sep-15
Thyrotropin alfa	04-Jan-16
Pneumococcal vaccine	21-Feb-16
Darbepoetin alfa	13-Jul-16
Abatacept	16-Jun-17
Omalizumab	13-Jun-17
Pegfilgrastim	26-Sep-17
Ribavirin + Peginterferon alfa-2a	16-Oct-17
Ribavirin + Peginterferon alfa-2b	16-Oct-17

Ranibizumab	03-Apr-18
Peginterferon Alfa-2a	28-May-18
Choriogonadotropin Alfa	17-Sep-18
Adalimumab	10-Dec-18
Insulin detemir	30-Jun-19
Bevacizumab	24-Feb-20
Insulin glulisine	21-Apr-20
Diphtheria and tetanus vaccine	02-May-21
Cetuximab	14-Feb-22
Denosumab	22-Dec-22
Corifollitropin alfa	14-Jan-23
Panitumumab	05-May-23
Romiplostim	08-Aug-23
Epoetin lambda	18-Jun-24
Methoxy polyethylene glycol- epoetin beta	28-Jul-24
Ustekinumab	28-Jul-24
Bacillus Calmette-Guerin (BCG) Connaught strain	25-Jul-24
Golimumab	13-Nov-24
Certolizumab pegol	20-Jan-25
Aflibercept	23-May-25
Ipilimumab	24-Aug-25
Insulin neutral	17-Sep-25

Attachment B

Filgrastim Current PBS Utilisation

Filgrastim brands dominate the biosimilars on the PBS. Although the extent of inpatient utilisation is not known, it seems reasonable to assume that uptake and market share observed in PBS scripts is a rough reflection of hospital inpatient use. Based on script volumes for the 12 months to May 2014, utilisation of all filgrastim products on the PBS (including the originator Neupogen, but not pegfilgrastim)is in the table below.

	Private	%	Public	%	Total	%	Listing Date
Neupogen	2,958	82.88%	5,191	64.14%	8,149	69.88%	September 1993
Nivestim	537	15.05%	1,933	23.88%	2,470	21.18%	1 April 2011
Tevagrastim	68	1.91%	949	11.73%	1,017	8.72%	1 March 2012
Zarzio	6	0.17%	20	0.25%	26	0.22%	1 September 2013
TOTAL	**3,569**	**100.00%**	**8,093**	**100.00%**	**11,662**	**100.00%**	--

Neupogen has 70% of PBS utilisation (with biosimilars making up the remainder). Individual proportions reflect the order of market entry in Australia. Each of the listed filgrastim products is priced the same per mg on the PBS, thus use of the biosimilar offers no cost advantage per se compared with Neupogen.

There is also a difference in market share between private vs. public hospital scripts. One explanation is that hospital specialists prefer to prescribe Neupogen if possible, whereas in public hospitals prescribing of a particular brand is constrained by hospital formulary policy.

Once pegfilgrastim (Neulasta) scripts are added for the same period (below), it can be seen that the longer acting molecule overwhelmingly dominates colony-stimulating factor use with more than three quarters of use being pegfilgrastim in any setting.

	Private	%	Public	%	Total	%	Price per tx course
Neupogen	2,958	12.71%	5,191	15.16%	8,149	14.17%	
Nivestim	537	2.31%	1,933	5.64%	2,470	4.29%	For all filgrastim brands:
Tevagrastim	68	0.29%	949	2.77%	1,017	1.77%	
Zarzio	6	0.03%	20	0.06%	26	0.05%	~$1,460
Neulasta	19,701	84.66%	26,153	76.37%	45,854	**79.72%**	For Neulasta: ~$1,945
TOTAL	23,270	100.00%	34,246	100.00%	57,516	100.00%	---

A modest reduction in the price of the biosimilars would make little difference to the overall cost of peg/filgrastim use as the biosimilars constitute a little over 5% of the total colony-stimulating factor use. The price per average treatment course for pegfilgrastim (1 dose per course) and is also about 25% more expensive per course than filgrastim (11.5 doses per course, on average). Introduction of a biosimilar pegfilgrastim would be expected to make a far greater impact in terms of PBS savings.