5.11 PEGFILGRASTIM
Injection 6 mg in 0.6 mL single use pre-filled syringe, Pelgraz®, Accord Healthcare Pty Ltd

1 Purpose of Application

1.1 The minor submission sought a Section 100 Highly Specialised Drugs (HSD) program listing for a new biosimilar brand of pegfilgrastim (Pelgraz®) for all indications for which the reference brand (Neulasta®) is currently PBS listed.

2 Requested listing

2.1 The submission requested the same listings for Pelgraz as the reference product, Neulasta.

2.2 Suggestions and additions proposed by the Secretariat to the requested listings are in italics, and deletions are in strikethrough.

Name, Restriction, Manner of administration and form	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Proprietary Name and Manufacturer	
PEGFILGRASTIM 6 mg/0.6 mL injection, 0.6 mL syringe	9514R (Public) 6363X (Private)	1	1	11	Pelgraz®	Accord Healthcare Pty Ltd

Restriction Summary [new] / Treatment of Concept: [new]

Concept ID	
	Category / Program: Section 100 – Highly Specialised Drugs Program – Public/Private
	Prescriber type: ☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
	Restriction Level / Method: ☐Unrestricted benefit ☐Restricted benefit ☐Authority Required – In Writing ☐Authority Required – Telephone/Electronic/Emergency ☒Authority Required - Streamlined
New	**Administrative Advice:** ***Biosimilar prescribing policy*** *Prescribing of the biosimilar brand PELGRAZ® is encouraged for treatment naïve patients. Encouraging biosimilar prescribing for treatment naïve patients is Government policy. A viable biosimilar market is expected to result in reduced costs for biological medicines, allowing the Government to reinvest in new treatments. Further information can be found on the Biosimilar Awareness Initiative webpage (www.health.gov.au/biosimilars).*
New	**Administrative Advice:** *Prescribers must include the proprietary name (brand) on the prescription to ensure the appropriate item is approved.*
N/A	**Episodicity:** ~~Administered once per chemotherapy cycle~~
16253	**Condition:** Chemotherapy-induced neutropenia
	Indication: Chemotherapy-induced neutropenia
	Clinical criteria:
22299	Patient must be receiving chemotherapy with the intention of achieving a cure or a substantial remission,
	AND
21993	Patient must be at greater than 20% risk of developing febrile neutropenia;
	OR

21994	Patient must be at substantial risk (greater than 20%) of prolonged severe neutropenia for more than or equal to seven days.

Name, Restriction, Manner of administration and form	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Proprietary Name and Manufacturer	
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Restriction Summary [new] / Treatment of Concept: [new]

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New	**Administrative Advice:** *Prescribers must include the proprietary name (brand) on the prescription to ensure the appropriate item is approved.*
N/A	**Episodicity:** ~~Administered once per chemotherapy cycle~~
16253	**Condition:** Chemotherapy-induced neutropenia
	Indication: Chemotherapy-induced neutropenia
	Clinical criteria:
22299	Patient must be receiving chemotherapy with the intention of achieving a cure or a substantial remission,
	AND
22003	Patient must have had a prior episode of febrile neutropenia;
	OR
22310	Patient must have had a prior episode of prolonged severe neutropenia for more than or equal to seven days.

For more detail on PBAC's view, see section 6 PBAC outcome.

3 Background

3.1 Pegfilgrastim is currently listed on the Section 100 HSD program as an Authority Required (STREAMLINED) listing for chemotherapy-induced neutropenia.

3.2 There are two 'a' flagged generic brands of pegfilgrastim, Ristempa and Tezmota. Ristempa and Tezmota have the same Sponsor as Neulasta (Juno Pharmaceuticals). Generic brands have the same active ingredient and are bioequivalent to the originator brand

3.3 There is one 'a' flagged biosimilar brand of pegfilgrastim, Ziextenzo. Biosimilar brands usually contain biotechnology-derived proteins as the active substance and have similar core characteristics to the reference brand, such as physicochemical, biological, immunological, efficacy and safety characteristics.

Registration status

3.4 The Lapelga® brand of pegfilgrastim pre-filled syringe was listed on the Australian Register of Therapeutic Goods (ARTG) on 19 August 2019 with the same indication as the reference brand, Neulasta: for the treatment of cancer patients following chemotherapy, to decrease the duration of severe neutropenia and so reduce the incidence of infections, as manifested by febrile neutropenia. Lapelga was later rebranded to Pelgraz.

3.5 The submission also requested PBS-listing of a new dose form of pegfilgrastim: 6 mg in 0.6 mL single use pre-filled injector (i.e. pen device). The PBAC Secretariat did not accept this part of the submission because the dose form was still being evaluated by the Therapeutic Goods Administration (TGA) and was pending approval. Minor submissions can only be made for dose forms that are TGA registered or have a positive TGA Delegate's overview at the time of submission.

Previous PBAC consideration

3.6 Pelgraz has not been considered by the PBAC previously.

3.7 The PBAC has previously recommended two biosimilar pegfilgrastim brands for listing on the PBS: Fulphila (November 2018) and Ziextenzo (November 2019). Ziextenzo was listed on the PBS on 1 March 2020. At the time of the March 2020 PBAC meeting, Fulphila had yet to be listed on the PBS. For more detail on PBAC's view, see section 6 PBAC outcome.

4 Comparator

4.1 The minor submission nominated the reference brand of pegfilgrastim, Neulasta, as the main comparator, which was appropriate.

5 Consideration of the evidence

5.1 As a minor submission, no evaluation of the clinical evidence was undertaken and the financial estimates have not been independently evaluated.

Sponsor hearing

5.2 There was no hearing for this item as it was a minor submission.

Consumer comments

5.3 The PBAC noted that no consumer comments were received for this item

Clinical trials

5.4 The minor submission presented two studies to support its claim of biosimilarity, and equivalent efficacy and safety of Pelgraz compared to Neulasta.

5.5 Details of the trials presented in the submission are provided in the table below.

Table 1: Trials and associated reports presented in the submission

Trial ID	Protocol	Publication citation
Direct randomised trial(s)		
APO-Peg-02	A comparative Phase 1 pharmacokinetic (PK)/ pharmacodynamic (PD) study, inclusive of immunogenicity endpoints, was conducted in healthy subjects and similarity in PK and PD between Pelgraz and Neulasta was demonstrated.	Clinical Study Report APO-Peg-02: Comparative, randomized, single-dose, assessor-blinded, 2-way crossover pharmacokinetic and pharmacodynamic study of subcutaneously administered Pegylated ApoFilgrastim (Apotex Inc.) and Neulasta® (Amgen Inc.) (USA) in healthy volunteer subjects. Apotex Inc. 2016a. Revision #0003: December 19, 2016.
APO-Peg-03	A Phase III study of comparative efficacy, safety and immunogenicity assessments for Pelgraz and Neulasta in was conducted in breast cancer patients, demonstrating that there are no clinically meaningful differences between the biosimilar and the reference biologic drug.	Clinical Study Report APO-Peg-03: A phase III, randomized, active controlled, assessor-blinded study of safety and efficacy of Pegylated Apo-Filgrastim versus US and EU licensed Neulasta® in subjects with stage IIa, IIb or IIIa breast cancer receiving TAC anticancer chemotherapy in adjuvant setting. Apotex Inc. 2016b. Version 3.0/Dec 20, 2016, Amendment 2.

Source: pg. 21 pf the Submission

Comparative effectiveness

5.6 In the first trial (APO-Peg-02), the prespecified criteria for equivalence of Pelgraz and Neulasta for the pharmacokinetic (PK) and pharmacodynamics (PD) primary endpoints were met. The equivalence results were supportive of the PK similarity of Pelgraz and Neulasta.

5.7 In the second trial (APO-Peg-03), the primary efficacy endpoint was the duration of severe neutropenia (DSN) in Cycle 1. The TGA Delegate considered the equivalence data satisfactory to show clinical similarity and interchangeability.

Comparative harms

5.8 In the second trial, no new adverse events (AEs) were observed compared with the known profile for Neulasta. No unexpected serious AEs were reported. The TGA Delegate considered that the safety profile of Pelgraz and Neulasta were similar.

Clinical claim

5.9 The submission claimed non-inferior comparative effectiveness and non-inferior comparative safety of Pelgraz compared with Neulasta. The TGA Delegate was satisfied that the data for Pelgraz demonstrated an equivalent level of efficacy and safety for the desired indication as the comparator drug.

5.10 The PBAC considered that the claim of non-inferior comparative effectiveness was reasonably supported by the data.

5.11 The PBAC considered that the claim of non-inferior comparative safety was reasonably supported by the data.

Economic analysis

5.12 The minor submission presented a cost-minimisation analysis of Pelgraz compared with Neulasta. The equi-effective doses were estimated as 6 mg of Pelgraz is equal to 6 mg of Neulasta for the same frequency and duration of therapy.

5.13 The Sponsor noted the price reductions applied to pegfilgrastim in 2017 following listing of the Ristempa brand, and in 2018 following the broadening of the restriction as recommended by the PBAC in March 2018 with a price reduction to ensure a cost-effective listing in the expanded population. The minor submission requested an ex-manufacturer price for Pelgraz equivalent to that of Neulasta at the time of listing.

5.14 The Secretariat noted that Neulasta received a price reduction when the Ristempa brand of pegfilgrastim was PBS listed. Accordingly, there would not be a statutory price reduction following the listing of the first biosimilar brand of pegfilgrastim (whether that is Pelgraz, Ziextenzo or Fulphila) on the PBS.

Estimated PBS usage & financial implications

5.15 The submission assumed that Pelgraz would be listed at the same price as Neulasta (and other brands of pegfilgrastim) and would result in no net cost to the Government.

5.16 The submission claimed that the listing of Pelgraz is not expected to cause market growth of pegfilgrastim, because no increase in the market occurred when other new brands of pegfilgrastim were listed. The submission stated that there was predictable growth in the pegfilgrastim market in August 2018, related to the broadening of the restriction for pegfilgrastim that was recommended at the March 2018 PBAC meeting.

For more detail on PBAC's view, see section 6 PBAC outcome.

6 PBAC Outcome

6.1 The PBAC recommended the listing of the biosimilar brand of pegfilgrastim, Pelgraz, on the basis that it should only be available under special arrangements under Section 100 (Highly Specialised Drugs program) for all indications for which the reference brand (Neulasta) is currently PBS-listed.

6.2 The PBAC recommended listing Pelgraz on a cost-minimisation basis to the Neulasta brand of pegfilgrastim, and noted that this would result in no net cost to the Government because the listing of Pelgraz is not expected to grow the market.

6.3 The PBAC noted the TGA Delegate's conclusion that the biosimilarity between Pelgraz and Neulasta was well supported by the chemistry, pre-clinical and clinical data, which supported registration of Pelgraz as a biosimilar product to Neulasta.

6.4 The PBAC advised, under Section 101 (4AACD) of the National Health Act 1953, that the Pelgraz, Neulasta, Ziextenzo, Ristempa, Tezmota and Fulphila brands of pegfilgrastim should be considered equivalent for the purposes of substitution (i.e. 'a' flagged).

6.5 The PBAC recommended the current administrative note about biosimilar prescribing policy continue to apply, but with updates to reflect that there will be more than one biosimilar brand.

6.6 The PBAC noted that pegfilgrastim is not included on the list of PBS medicines suitable for nurse practitioner prescribing.

6.7 The PBAC noted that the Early Supply Rule does not apply to pegfilgrastim.

6.8 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because Pelgraz® is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity over Neulasta®, or not expected to address a high and urgent unmet clinical need given the presence of an alternative therapy, the criteria prescribed by the National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2009 for Pricing Pathway A were not met.

6.9 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:
Recommended

7 Recommended listing

7.1 Add new pegfilgrastim trade product pack (Pelgraz®) to the available brands:

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Category / Program: Section 100 – Highly Specialised Drugs Program – Public/Private
Prescriber type: ☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Restriction Level / Method: ☒Authority Required – Streamlined (7822)
Administrative Advice: **Biosimilar prescribing policy** Prescribing of the biosimilar brand Pelgraz, Fulphila or Ziextenzo is encouraged for treatment naïve patients. Encouraging biosimilar prescribing for treatment naïve patients is Government policy. A viable biosimilar market is expected to result in reduced costs for biological medicines, allowing the Government to reinvest in new treatments. Further information can be found on the Biosimilar Awareness Initiative webpage (www.health.gov.au/biosimilars).
Indication: Chemotherapy-induced neutropenia
Clinical criteria:
Patient must be receiving chemotherapy with the intention of achieving a cure or a substantial remission,

AND
Patient must be at greater than 20% risk of developing febrile neutropenia; or
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Patient must have had a prior episode of prolonged severe neutropenia for more than or equal to seven days.

This restriction may be subject to further review. Should there be any changes made to the restriction the Sponsor will be informed.

8 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

9 Sponsor's Comment

The sponsor had no comment.