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CADTH Biosimilar Summary Dossier

PEGFILGRASTIM (LAPELGA)

(Apobiologix, a division of Apotex Inc.)

Indication: Febrile neutropenia, prevention or treatment

Service Line:	CADTH Common Drug Review
Version:	Final
Publication Date:	May 2018
Report Length:	13 Pages

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Section 1: Biosimilar Product Information

Biosimilar (Brand Name)	Lapelga
Active Pharmaceutical Ingredient	Pegfilgrastim
Manufacturer	Apobiologix, a division of Apotex Inc.
Strength(s) / Dosage Form(s) / Route of Administration(s)	6 mg/0.6 mL (10 mg/mL) / Sterile preservative-free solution for injection / Subcutaneous
Health Canada-Approved Indication(s)	To decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-neoplastic drugs.
Health Canada–Approved Reference Product Indications Not Being Sought by the Manufacturer (if applicable)	Not applicable
NOC date(s)[a]	April 5, 2018

[a] Please provide NOC date(s) according to indication.
NOC = notice of compliance.

Section 2: Reference Product Information

Reference Product (Brand Name)	Neulasta
Active Pharmaceutical Ingredient	Pegfilgrastim
Manufacturer	Amgen
Strength(s) / Dosage form(s) / Route of Administration(s)	6 mg/0.6 mL (10 mg/mL) / Sterile preservative-free solution for injection / Subcutaneous
Health Canada-Approved Indication(s)	To decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-neoplastic drugs.

Section 3: Manufacturer's Reimbursement Request

Manufacturer's Reimbursement Request	Be listed as the preferred pegfilgrastim product to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-neoplastic drugs.

Section 4: Health Canada's Assessment of Lapelga for Market Authorization

4.1 Authorized Indications

LAPELGA (pegfilgrastim) is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-neoplastic drugs.

Indications: Indications have been granted on the basis of similarity between Lapelga and the reference biologic drug, Neulasta. Further details can be found in the Health Canada-approved product monographs for Lapelga and Neulasta:

- Lapelga: https://pdf.hres.ca/dpd_pm/00044614.PDF
- Neulasta: https://pdf.hres.ca/dpd_pm/00039226.PDF

4.2 Summary of Comparative Clinical Trials (Section 15 of the Health Canada-approved Product Monograph for Lapelga)

4.2.1 Comparative Trial Design and Study Demographics

The clinical development program to support similarity between Lapelga and the reference biologic drug (Neulasta) is based on a Phase 1 study (APO-Peg-02) in healthy subjects and a Phase 3 study (APO-Peg-03) in the adjuvant breast cancer setting. An overview of the study designs and subject demographic characteristics of subjects or patients enrolled in each clinical study are presented in Table 1.

Table 1: Comparative Clinical Trial Design and Patient Demographics

Study Number	Trial Design	Dosage, Route of Administration, and Duration	Number of Subjects or Patients	Median Age (range)	Sex n (%)
APO-Peg-02	Single-dose, randomized two-way crossover, assessor-blinded, active-controlled, PK/PD study in healthy subjects	**Test Product:** Lapelga (Apotex Inc.); Single dose (6 mg/0.6 mL); Subcutaneous administration **Reference Biologic Drug:** US-licensed Neulasta (Amgen Inc.); Single dose (6 mg/0.6 mL); Subcutaneous administration 28 days in each period with at least 8 weeks washout between treatment administrations	66 subjects were randomized (56 subjects completed dosing)	41 (20-55) years old	Male: 49 (74%) Female: 17 (26%)
APO-Peg-03	Randomized, active-controlled, assessor-blinded, safety and efficacy trial conducted in breast cancer patients (stage IIa, IIb or IIIa) receiving TAC (docetaxel, doxorubicin, cyclophosphamide)	**Test Product:** Lapelga (Apotex Inc.) **Reference Biologic Drug:** US-licensed Neulasta (Amgen Inc.); EU-approved Neulasta (Amgen Europe B.V.)	595 female patients, 589 patients were dosed (Lapelga: 294, US-licensed Neulasta: 148, EU-approved Neulasta: 147)	52 (22-80) years old	Female: 595 (100%)

Study Number	Trial Design	Dosage, Route of Administration, and Duration	Number of Subjects or Patients	Median Age (range)	Sex n (%)
APO-Peg-03	anticancer chemotherapy. Patients were randomized to either Lapelga or US-licensed Neulasta or EU-approved Neulasta in a 2:1:1 ratio.	6 mg fixed dose (6mg/0.6mL), administered once per chemotherapy cycle for 6 cycles; subcutaneous The study consisted of 3 periods: 1. **Screening** (up to 3 weeks). 2. **Active treatment period** (6 cycles each of 3 weeks i.e. a total of 18 weeks). 3. **Safety follow-up period** (up to 30 weeks following the completion of TAC regimen).			

PD = pharmacodynamics; PK = pharmacokinetic; TAC = docetaxel, doxorubicin, cyclophosphamide

4.2.2 Comparative Clinical Trial Results

Study APO-Peg-02

APO-Peg-02 was a comparative Phase 1, randomized, single-dose, assessor-blinded, 2-way crossover pharmacokinetics and pharmacodynamics study of subcutaneously administered Lapelga and US-licensed Neulasta (US-Neulasta) conducted in healthy subjects (N = 66).

Of the 66 subjects who were dosed, 56 subjects who completed both periods of the study were included in the PK and PD populations for the assessment of similarity. Ten subjects (15.15%) were excluded from the statistical analysis because of adverse events in 3 subjects, noncompliance with study drug in 4 subjects, administration of intravenously infused fluids which could potentially impact PK/PD measures in 2 subjects and voluntary withdrawal of consent for 1 subject.

Pharmacokinetic Results

Table 2 shows the PK results following the administration of Lapelga and US-Neulasta. The ratios of the geometric means for the test/reference (Lapelga/Neulasta) were within the pre-defined acceptance range of 80 – 125% for AUCt, AUCinf and Cmax. In addition, the 90% confidence interval of the geometric mean ratio for AUCinf was also contained within this acceptance range whereas the upper bound of the AUCt ratio was 125.5%. The marginally high upper bound is a consequence of a smaller drug content in the US-Neulasta dose (less than 95% of the label claim) administered during the study, as supported by the results from the potency corrected data in Table 3 below.

Table 2: Mean (CV %) Pharmacokinetic Parameters Following a Fixed Single Subcutaneous Injection of 6 mg Lapelga or US- Neulasta to Healthy Subjects (PK Population) – Measured Data

Pegfilgrastim (6 mg) Geometric Mean Arithmetic Mean (CV %)				
Endpoint	**Lapelga * (N = 56)**	**US-Neulasta [t] (N = 56)**	**Ratio of Means [%] [b]**	**90% Confidence Interval [%]**
AUC_t [ng*h/mL]	6725 8282 (64)	6027 7622 (74)	111.6	99.2 − 125.5

Pegfilgrastim (6 mg) Geometric Mean Arithmetic Mean (CV %)				
AUC_{inf} [a] [ng*h/mL]	6741 8224 (67)	6186 7890 (72)	109.0	95.5 – 124.3
C_{max} [ng/mL]	159 193 (60)	150 183 (66)	105.7	
T_{max} [h] [§]	25.82 (31)	24.18 (38)	105.2	
$T_{1/2}$ [a] [h] [§]	58.03 (39)	55.09 (30)	103.2	

AUCt = The area under the curve (AUC - calculated by the linear trapezoidal rule) from time zero up to the sampling time for which the last non-zero concentration;
AUCinf = The AUC from time zero to infinity;
Cmax = The maximum observed concentration of pegfilgrastim over the sampling interval;
Tmax = Time at which Cmax is observed; T1/2 = Terminal elimination half-life.
* 6 mg/0.6 mL (Apotex Inc.) – measured concentration 6.1 mg/0.6 mL
t 6 mg/0.6 mL (Amgen Inc. USA) – measured concentration 5.7 mg/0.6 mL
§ Expressed as the arithmetic mean (CV %) only
a T1/2 and AUCinf were not determined in subjects if the log-linear terminal phase was not clearly defined. N = 50 for Lapelga and N = 53 for Neulasta.
b Based on the least square estimates of the geometric means of AUCt, Cmax, AUCinf. Based on the least square estimates of the arithmetic means for Tmax and T1/2.
Source: Lapelga Product Monograph, Table 6

Table 3 shows results from the potency corrected pegfilgrastim concentration data for both Lapelga and US-Neulasta. For the primary pharmacokinetic endpoint of AUCt, the 90% confidence interval of the Lapelga/Neulasta ratio of geometric means was contained within the acceptance range of 80 - 125%.

Table 3: Mean (CV %) Pharmacokinetic Parameters Following a Fixed Single Subcutaneous Injection of 6 mg Lapelga or US-Neulasta to Healthy Subjects (PK Population) – Potency Corrected Data

Pegfilgrastim (6 mg) Geometric Mean Arithmetic Mean (CV %)				
Endpoint	**Lapelga * (N = 56)**	**US-Neulasta [t] (N = 56)**	**Ratio of Means [%] [b]**	**90% Confidence Interval [%]**
AUC_t [ng*h/mL]	6631 8166 (64)	6425 8126 (74)	103.2	91.7 – 116.1
AUC_{inf} [a] [ng*h/mL]	6647 8109 (67)	6595 8410 (72)	100.8	88.3 – 115.0
C_{max} [ng/mL]	157 190 (60)	160 195 (66)	97.7	
T_{max} [h] [§]	25.82 (31)	24.18 (38)	105.2	
$T_{1/2}$ [a] [h] [§]	58.03 (39)	55.09 (30)	103.2	

AUCt = The area under the curve (AUC - calculated by the linear trapezoidal rule) from time zero up to the sampling time for which the last non-zero concentration;
AUCinf = The AUC from time zero to infinity;
Cmax = The maximum observed concentration of pegfilgrastim over the sampling interval;
Tmax = Time at which Cmax is observed;
T1/2 = Terminal elimination half-life.
* 6 mg/0.6 mL (Apotex Inc.)
t 6 mg/0.6 mL (Amgen Inc. USA)
§ Expressed as the arithmetic mean (CV%) only
a T1/2 and AUCinf were not determined in subjects if the log-linear terminal phase was not clearly defined. N = 50 for Lapelga and N = 53 for Neulasta.
b Based on the least square estimates of the geometric means of AUCt, Cmax, AUCinf. Based on the least square estimates of the arithmetic means for Tmax and T1/2.
Source: Lapelga Product Monograph, Table 7

Pharmacodynamic Results

As demonstrated by the PD results in Table 4, the 95% CI of the ratio (Lapelga/Neulasta) of geometric means of the primary PD endpoint parameter for Absolute Neutrophil Count (ANC), AUECt was fully contained within the pre-defined acceptance margins of 80-125%. In addition, the Emax and Tmax of the two products are similar.

Table 4: Mean (SD) Pharmacodynamic Parameters (Absolute Neutrophil Count [ANC]) following a Fixed Single Subcutaneous Administration of 6 mg/0.6 mL Lapelga or Neulasta to Healthy Subjects (PD Population)

Endpoint		Lapelga (N = 56)	US-Neulasta (N = 56)	Ratio of Geometric Means [%]	95% CI [%]
$AUEC_t$ (cells x 10^9*h/L)	Mean (SD)	4749.85 (1247.09)	4817.55 (1314.54)	98.8	96.0 – 101.6
E_{max} (cells x 10^9/L)	Mean (SD)	29.75 (7.99)	30.94 (8.72)	96.3	
T_{max} (h)	Mean (SD)	63.43 (16.54)	60.86 (18.94)	103.8	

SD = Standard Deviation; CI = Confidence interval
$AUEC_t$ = the area under the effect curve from time zero measured up to the last sampling time;
E_{max} = the maximum effect on ANC observed over the sampling interval;
T_{max} = The sampling time at which E_{max} occurred.
Source: Lapelga Product Monograph, Table 8

Comparative Safety

Safety

The safety and immunogenicity comparisons of Lapelga and Neulasta were studied in APO-Peg-03, a Phase 3, randomized, assessor blinded, active controlled study of subcutaneously administered Lapelga, US-licensed or EU-approved Neulasta in patients with early breast cancer receiving TAC (docetaxel, doxorubicin, cyclophosphamide) anticancer chemotherapy in an adjuvant setting. The study was conducted in 11 countries in Central and Eastern Europe.

There were 595 patients enrolled and randomized. Of these randomized patients, 589 were dosed (294 in the Lapelga, 148 in the US-Neulasta, and 147 in the EU-Neulasta treatment arms). Of the patients dosed, 547 (92.9%) patients completed the treatment phase of the study for all 6 cycles (single dose per cycle); 268 (91.2%) in Lapelga, 142 (95.9%) in US-Neulasta and 137 (93.2%) in EU-Neulasta treatment arms.

The types, frequency and severity of adverse events were comparable between Lapelga and Neulasta.

Immunogenicity Results

In the APO-Peg-03 study, samples were tested in an assay using a multi-tiered approach to first screen, then confirm and provide a relative anti-pegfilgrastim Anti-drug Antibody (ADA) concentration (titre). Any confirmed positive samples were then further characterized to determine if the anti-pegfilgrastim antibodies present in a sample were specific for the protein moiety (GCSF) or PEG moiety by competition with Apo-Filgrastim (GCSF) and PEG, respectively. Lastly, the assay was also used to determine whether the confirmed antipegfilgrastim antibodies bind to the endogenous counterpart of the drug. The confirmed positive samples were also tested in a neutralizing antibody assay.

In the APO-Peg-03 study, 18 of 589 (3.1%) patients assessed for immunogenicity were confirmed to be positive for ADA at one or more time points. Incidence of treatment-emergent induced ADA was low and similar between the three treatment groups: 1.0% (3/294) in the Lapelga arm, 0.7% (1/148) in the US-Neulasta arm and 0.7% (1/147) in the EU-Neulasta arm. The samples from the 18 patients with confirmed ADA positive results were tested in the cell based assay to evaluate the presence of antibodies with neutralizing activity.

Neutralizing activity could have been specific to pegfilgrastim or rhuGCSF. Neither Lapelga nor Neulasta exposure resulted in the induction of neutralizing antibodies to pegfilgrastim. Neutralizing antibodies to endogenous rhuGCSF were detected in 3 patients (0.5%). Two of these patients were positive at the screening visit, of which one was negative at all post-dosing time points and one was only positive for rhuGCSF neutralizing antibodies at one other time point (Week 20). The third patient was positive for rhuGCSF neutralizing antibodies at two post-treatment time points. The rhuGCSF neutralizing antibodies were transient and all 3 patients were negative for neutralizing antibodies at their last time points tested.

Section 5: Cost Overview

5.1 Cost Comparison

The Lapelga 6 mg/0.6 mL PFS drug product is being submitted at a 25% lower price ($1,878.7300) relative to the currently listed ADBL price of Neulasta 6 mg/0.6 mL PFS, which is at $2,504.9700. Consequently, the 25% cost differential equates to $626.24 savings per 6 mg PFS.

Some provincial drug plans (e.g. AB) fund both pegfilgrastim (reference biologic Neulasta) and filgrastim (reference biologic Neupogen, biosimilar Grastofil). Since some patients who are candidates for G-CSF therapy can be treated with either pegfilgrastim or filgrastim, filgrastim can also be considered as a (indirect) comparator for the pegfilgrastim indication (as it relates to provincial funding decisions in some provinces). The comparative pricing information for filgrastim is provided in the table below.

It should be noted that for filgrastim products, the full contents of vials or PFSs might not be used depending on patients' weight. However, as both Grastofil and Neupogen are single use only, the number of vials or PFSs was rounded up to calculate the "Average Drug Cost".

Table 5: Cost Comparison of Biosimilar and the Reference Product for Febrile Neutropenia, Prevention or Treatment

Drug / Comparator	Strength	Dosage Form	Price ($)[a]	Recommended Dose	Average Drug Cost[d] ($)
Canadian Costs					
Lapelga	6 mg/0.6 mL PFS	Sterile solution for injection	$1,878.7300	6 mg[b]	$9,393.6500
Neulasta			$2,504.9700		$12,524.8500
Indirect Comparators (Filgrastim)					
Grastofil	300 µg/0.5 mL PFS	Sterile solution for injection	$144.3135	5 µg/kg/day[c]	$5,772.54[e]
	480 µg/0.8 mL PFS		$230.9017		$9,236.07[f]
Neupogen	300 µg/1 mL vial		$173.1890		$6,927.56[e]
	480 µg/1.6 mL vial		$277.1020		$11,084.08

[a] Alberta Health Formulary, February 13, 2018. Alberta prices were used since it was the only CDR-participating jurisdiction with publicly-available pricing for Neulasta, Grastofil, and Neupogen. The price for Neupogen 480 µg/1.6 mL vial was obtained from the Ontario Drug Benefit Formulary, February 21, 2018 (the price of the Neupogen 300 µg/1 mL vial is also the same between ODB and AHF).
[b] Lapelga and Neulasta product monograph. Lapelga and the reference product Neulasta both have fixed dosing schedule (i.e. a single 6 mg injection per chemotherapy cycle).
[c] Grastofil and Neupogen product monograph. Grastofil and the reference product Neupogen both have weight-based dosing schedule (i.e. 5 µg/kg/day until absolute neutrophil count surpasses 10 x 10^9/L after the ANC nadir has occurred, or for up to 2 weeks, during each chemotherapy cycle).
[d] For a patient receiving 5 chemotherapy cycles (1 injection per cycle for Lapelga/Neulasta and 8 injections per cycle for Grastofil/Neupogen)
[e] As *Alberta's Criteria for Special Authorization of Select Drug Products* or the *FILGRASTIM / PEGFILGRASTIM / PLERIXAFOR SPECIAL AUTHORIZATION REQUEST FORM* do not provide reimbursement criteria by patient weight, ODB's reimbursement criteria for a patient weighing less than 90kg (the maximum reimbursement coverage is 300 µg per day) was used.
[f] As *Alberta's Criteria for Special Authorization of Select Drug Products* or the *FILGRASTIM / PEGFILGRASTIM / PLERIXAFOR SPECIAL AUTHORIZATION REQUEST FORM* do not provide reimbursement criteria by patient weight, ODB's reimbursement criteria for a patient weighing more than or equal to 90kg, the maximum reimbursement coverage is 480 µg per day) was used.

5.2 CADTH CDR Comment on Cost Comparison

Summary of Manufacturer's Analysis

The pegfilgrastim biosimilar (Lapelga) is available as a 6 mg/0.6 mL pre-filled syringe for subcutaneous injection at a manufacturer-submitted price of $1,878.73 per 6 mg/0.6 mL injection. The manufacturer conducted a cost comparison of Lapelga with its reference biologic (Neulasta), as well as a supplemental comparison with filgrastim (Grastofil and Neupogen), for the indication of febrile neutropenia treatment. As part of the submitted cost comparison, the manufacturer considered a single injection per cycle of chemotherapy for both Lapelga and Neulasta, whereas Grastofil and Neupogen require eight injections per cycle of chemotherapy. The manufacturer's assessment assumed five chemotherapy cycles. The manufacturer reported that Lapelga is 25% less costly ($1,878.73 per 6 mg/0.6 mL injection) than the primary comparator Neulasta ($2,504.97 per 6 mg/0.6 mL injection).

CADTH CDR Assessment

- The methods used by the manufacturer for the cost comparison of Lapelga and Neulasta were found to be acceptable by the CADTH Common Drug Review (CDR). The manufacturer's supplemental cost comparison with Grastofil and Neupogen was noted with interest but not considered appropriate given the lack of comparative clinical information.

Issues for Consideration

- The reference biologic (Neulausta) was reviewed by CADTH in 2004, with the recommendation to list for patients with non-myeloid cancer who are receiving chemotherapy and have a high risk of developing prolonged neutropenia. Grastofil was reviewed by CADTH, receiving a recommendation to list in a similar manner to Neupogen.
- Neulasta is not reimbursed in the majority of participating drug plans. CADTH CDR could identify only two jurisdictions, Alberta and Manitoba (on a case-by-case basis), that currently reimburse Neulasta. Plans that list Neulasta have some variability in pricing: $2,504.97 in Alberta and $2,454.41 in Manitoba. Eight provinces reimburse at least one dosing scheme of Grastofil. Six provinces reimburse at least one dosing scheme of Neupogen. Depending on the dosing scheme, the price of Grastofil ranges from $144.31 to $230.92 per pre-filled syringe across jurisdictions, whereas Neupogen ranges from $173.19 to $277.11 per vial (compared with $1,878.73 per pre-filled syringe for Lapelga).[1]

Conclusion

At the submitted price, the drug cost of Lapelga is 23% to 25% less than the publicly available price of Neulasta.

CADTH cannot conclude or comment on the comparative clinical effectiveness of pegfilgrastim versus filgrastim, or the cost-effectiveness of Lapelga in jurisdictions that currently do not list Neulasta.

Section 6: Implementation Considerations

6.1 Patient and Provider Support Programs

Will a patient support program be made available by the manufacturer? ☒ Yes or ☐ No

Will a health care provider support program be made available by the manufacturer? ☐ Yes or ☒ No

6.2 Summary of Patient Input

This section is intended to be a summary of patient input based on the perspectives of patient groups providing input on this submission. The original patient input submissions are shared with the pan-Canadian Pharmaceutical Alliance (pCPA) and participating drug plans, and are published on CADTH's website.

No patient input was received for this submission.

6.3 Summary of Jurisdictional Input

Jurisdictional input on biosimilars is provided by the Drug Policy Advisory Committee Formulary Working Group (FWG), which includes representatives from the federal, provincial, and territorial publicly funded drug plans. The FWG provides advice to CADTH on pharmaceutical issues and identifies operational and implementation considerations for drugs being reviewed through the CADTH CDR process. The input provided in this summary is intended to help inform product negotiations by the pCPA.

From the perspective of the public drugs, biosimilars have the potential to provide long-term cost reductions. These can be reinvested to help ensure the sustainability of drug funding and provide reimbursement for new drugs where there is currently an unmet therapeutic need. The following are some of the considerations that were highlighted as relevant to take into account when the pCPA and the drug plans determine whether or not Lapelga should be reimbursed, and the appropriate conditions for reimbursement:

Treatment initiation	• patient perspectives regarding the biosimilar under review (as specified in the patient group input provided to CADTH, if available) • identification of the patient population for whom treatment with the biosimilar under review would be most appropriate • setting where treatment with the drug is likely to be initiated (e.g., community versus hospital setting)
Reimbursement status	• current reimbursement status of the reference product and/other biosimilar products across the participating drug plans
Cost-savings	• magnitude of cost-savings offered by the biosimilar under review relative to the reference product and/or other biosimilar products
Patient support programs	• availability of a patient support program for the biosimilar under review • characteristics of any patient support programs for the biosimilar under review relative to those offered for the reference product and/or other biosimilar products
Switching to the biosimilar	• evidence regarding the safety and effectiveness of switching a patient from the reference product, or another biosimilar, to the biosimilar under review • patient perspectives regarding switching from the reference product, and/or other biosimilar products, to the biosimilar under review • jurisdictional policies regarding switching from the reference product or another biosimilar, to the biosimilar under review

Section 7: Reimbursement Status for Reference Product and Other Biosimilars

For each indication that is approved by Health Canada for the biosimilar (or likely to be approved, in the case of a submission filed on a pre-NOC basis), please provide the publicly available reimbursement status and criteria for the reference product and other biosimilars, if applicable. CADTH may update the information provided by the manufacturer with new information provided by the participating jurisdictions, as required.

Step 1: Use the following abbreviations to complete the table. Use a separate row for each indication and add more rows if necessary.

Abbreviation	Description
EX	Exception item for which coverage is determined on a case-by-case basis
FB	Full benefit
NB	Not a benefit
RES	Restricted benefit with specified criteria (e.g., special authorization, exception drug status, limited use benefit)
UR	Under review
–	Information not available

Listing Status for Neulasta

Indication(s)	CDR-Participating Drug Plans													
	BC	**AB**	**SK**	**MB**	**ON**	**NB**	**NS**	**PE**	**NL**	**YK**	**NT**	**NIHB**	**DND**	**VAC**
Decreasing incidence of infection as manifested by febrile neutropenia	NB	RES	NB	EX	NB	NB	NB	NB	NB	RES	RES	RES	RES	RES

AB = Alberta, BC = British Columbia, DND = Department of National Defence; MN = Manitoba; NIHB = Non-Insured Health Benefits Program; NL = Newfoundland and Labrador; NS = Nova Scotia; NT = Northwest Territories; ON = Ontario; PE = Prince Edward Island; SK = Saskatchewan; VAC =Veterans Affairs Canada; YK = Yukon.

Listing Status for (name of other biosimilar) – NOT APPLICABLE (NONE)

Indication(s)	CDR-Participating Drug Plans													
	BC	AB	SK	MB	ON	NB	NS	PE	NL	YK	NT	NIHB	DND	VAC
Indication 1														
Indication 2														
Indication 3														
Indication 4														

AB = Alberta, BC = British Columbia, DND = Department of National Defence; MN = Manitoba; NIHB = Non-Insured Health Benefits Program; NL = Newfoundland and Labrador; NS = Nova Scotia; NT = Northwest Territories; ON = Ontario; PE = Prince Edward Island; SK = Saskatchewan; VAC =Veterans Affairs Canada; YK = Yukon.

Step 2: For all restricted benefit entries (RES), please state the criteria used by each drug plan. Use a separate table for each indication and add or delete rows as necessary.

Restricted Benefit Criteria for Neulasta for Febrile Neutropenia, Prevention or Treatment

Drug Plan	Criteria for Restricted Benefit
BC	Not a benefit
AB	"In patients with non-myeloid malignancies, receiving myelosuppressive anti-neoplastic drugs with curative intent, to decrease the incidence of infection, as manifested by febrile neutropenia." Please note: coverage cannot be considered for palliative patients.
SK	Not a benefit
MB	Case-by-case via CancerCare Manitoba
ON	Not a benefit
NB	Not a benefit
NS	Not a benefit
PE	Not a benefit
NL	Not a benefit
YK	For secondary prophylaxis of febrile neutropenia in cancer patients receiving potentially curative myelosuppressive chemotherapy. For the rescue of prolonged febrile neutropenia following chemotherapy. For cancer patients undergoing peripheral blood progenitor cell (PBPC) collection & therapy. For post-Bone Marrow Transplant patients to stimulate bone marrow engraftment (start greater than or equal to d+1) For post-Bone Marrow Transplant patients requiring rescue of failure to engraft (start greater than or equal to d+14) For patients with chronic benign cyclical neutropenia or myeloblastic disorders or aplastic anemia who are awaiting bone marrow transplantation. Approval for 6 months
NT	Criteria same as those for NIHB via Extended Health Benefits
NIHB	**Chemotherapy Support** • Primary Prophylaxis ○ For use in previously untreated patients receiving a moderate to severely myelosuppressive chemotherapy regimen (i.e. ≥40% incidence of febrile neutropenia). Febrile neutropenia is defined as a temperature ≥38.5°C or >38.0°C three times in a 24 hour period and neutropenia with an absolute neutrophil count (ANC) <0.5 x 10^9/L. • Secondary Prophylaxis ○ For use in patients receiving myelosuppressive chemotherapy who have experienced an episode of febrile neutropenic sepsis or profound neutropenia in a previous cycle of chemotherapy; OR ○ For use in patients who have experienced a dose reduction or treatment delay longer than one week, due to neutropenia. The recommended dosage of pegfilgrastim is a single subcutaneous injection of 6 mg, administered once per cycle of chemotherapy. Pegfilgrastim should be administered no sooner than 24 hours after the administration of cytotoxic

Drug Plan	Criteria for Restricted Benefit
	chemotherapy.
DND	SA Criteria not listed
VAC	SA Criteria not listed

Restricted Benefit Criteria for (name of other biosimilar) for the treatment of (state the indication) – NOT APPLICABLE (NONE)

Drug Plan	Criteria for Restricted Benefit
Add name	State the exact criteria
Add name	State the exact criteria
Add name	State the exact criteria

References

CADTH References

1. DeltaPA [database on Internet]. [Ottawa]: IQVIA; 2018 [cited 2018 Apr 5]. Available from: https://www.iqvia.com/ Subscription required.