MINISTRY OF HEALTH
DECISION BRIEFING NOTE

Cliff # 1044777

PREPARED FOR: Eric Lun, Excutive Director - **FOR DECISION**

TITLE: Drug Review Listing Decision for infliximab (Inflectra™) for Rheumatoid Arthritis, Ankylosing Spondylitis, Plaque Psoriasis, and Psoriatic Arthritis

PURPOSE: To make a drug review listing decision for infliximab (Inflectra™) for rheumatoid arthritis, ankylosing spondylitis, plaque psoriasis, and psoriatic arthritis.

BACKGROUND:

- Infliximab (Inflectra™), marketed by Hospira Healthcare Corporation, was submitted to the Ministry of Health (the Ministry) requesting PharmaCare coverage in a similar manner to infliximab (Remicade®), for the treatment of rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriatic arthritis (PsA) and plaque psoriasis (PsO). Subsequently, Hospira was acquired by Pfizer Canada Inc.
- Inflectra™ is a subsequent entry biologic (SEB) based on the innovator product, infliximab (Remicade®).
- On December 14, 2014, the Canadian Drug Expert Committee (CDEC) recommended that infliximab (Inflectra™) be listed in accordance with the Health Canada–approved indications for the treatment of RA, AS, PsA and PsO, with conditions. (Please see Appendix 1)
- On January 12, 2015, the Drug Benefit Council (DBC) recommended that Inflectra™ be listed for the treatment of RA, AS, PsA and PsO:
    a. in patients for whom infliximab is considered to be the most appropriate treatment option;
    b. in a manner similar to infliximab (Remicade®);
    c. Inflectra™ should be the first option for treatment-naïve infliximab patients.
    - The DBC will review clinical data for patients switching from Remicade® to Inflectra™ when it becomes available and provide a recommendation at that time (see Appendix 2).
- Infliximab (Remicade®) is a Limited Coverage benefit for the treatment of RA, PsA, AS, severe psoriasis and Crohn's disease when prescribed by a specialist and according to the criteria in corresponding Special Authority forms.
- Infliximab (Inflectra™) is not indicated for the treatment of ulcerative colitis or Crohn's disease in Canada and the manufacturer is in the process of seeking Health Canada approval for these indications.

DISCUSSION:

- In their review, the DBC considered the final review completed by the Common Drug Review (CDR), which included clinical and pharmacoeconomic evidence review material and the recommendation from CDEC. The DBC also considered Clinical Practice Reviews from two specialists, as well as a Budget Impact Assessment (BIA) and patient input from three patients, and three patient groups.
- Two randomized controlled trials demonstrated that Inflectra™ has a similar efficacy, safety and pharmacokinetic profile to Remicade® in patients with RA and AS and, by extrapolation, in patients with PsA and PsO.

- Based on the DBC's recommendation, at the submitted price, Inflectra™ is less costly than Remicade® for treatment of RA, AS, PsA, and PsO, but is more expensive than most other biologics indicated for these conditions.

FINANCIAL IMPLICATIONS:

- s.13,s.17

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	Jan to Mar 2016	2016/17	2017/18	2018/19	2019/20	2020/21	5-Year Total
If the current Remicade PLA is terminated	s.13,s.17						
If the current Remicade PLA is kept							

OPTIONS:

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Option 2: Effective February 19, 2016, list infliximab (Inflectra™) as a Limited Coverage benefit for the treatment of RA, PsA, AS, and PsO, for infliximab naïve patients (Appendix 4).

Pro: Consistent with CDEC and DBC recommendations. The Ministry and the public will benefit from lower transparent price and long-term savings.

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RECOMMENDATION: Option 2.

Original Signed By February 19, 2016

Approved Date Signed

Eric Lun, Executive Director

Drug Intelligence & Optimization

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In contrast to Remicade, Inflectra is not approved for the treatment of Crohn disease or ulcerative colitis.

Summary of CDEC Considerations:

CDEC considered the following information prepared by the CADTH Common Drug Review
(CDR): a review of manufacturer-provided information on the clinical efficacy, biosimilarity, and extrapolation of data for Inflectra; a critique of the manufacturer's pharmacoeconomic evaluation; and patient group–submitted information about outcomes and issues important to patients.

Patient Input Information

The following is a summary of key information provided by six patient groups that responded to the CDR call for patient input:

☐ Therapeutic options are required for patients who live with arthritis, and SEBs offer another biologic drug therapy that may be effective for patients who are biologic-naive or who have failed on other biologic drugs. Many patients are uncertain, however, about whether an SEB actually offers an additional therapeutic option.

☐ Some patients expect that Inflectra will be considerably less costly than the reference product and will therefore lower health care costs and potentially increase access to treatment.

☐ Patients expressed concern about the following:

☐ Patient support programs are an important part of biologic therapies and patient groups are unclear whether manufacturers of SEBs will offer them.

☐ Inflectra and Remicade have the same non-proprietary name (i.e., infliximab) and patients are concerned about being inadvertently exposed to the wrong drug or being "switched" to the SEB without their knowledge or consent.

☐ Some patient groups were uncertain whether the SEB will work as well as the reference product, whether it was tested as rigorously, and whether it was or will be manufactured as carefully.

Clinical Trials

The manufacturer provided efficacy data from two pivotal clinical trials:

☐ PLANET-RA (N = 606) was a phase 3, randomized, double-blind, multi-centre, multinational, parallel-group clinical equivalence study designed to compare the efficacy and safety of Inflectra with Remicade, in patients with active rheumatoid arthritis who had an inadequate response to treatment with methotrexate. The primary end point was the proportion of patients with an American College of Rheumatology (ACR) 20 response at week 30. Therapeutic equivalence of clinical response according to ACR20 criteria would be demonstrated if the 95% confidence interval (CI) for the treatment difference was within ± 15%.

☐ PLANET-AS (N = 250) was a phase 1, randomized, double-blind, multi-centre, multinational, parallel-group study designed to compare the PK, safety, and efficacy of Inflectra and Remicade, in patients with active ankylosing spondylitis. The primary end point was to demonstrate PK equivalence at a steady state of area under the concentration-time curve and observed maximum steady state serum concentration between Inflectra and Remicade between weeks 22 and 30. Equivalence was demonstrated if the 90% CIs lay within the equivalence margin of 80% to 125%.

Outcomes

CDEC discussed the following outcomes:

Appendix 1

CDEC FINAL RECOMMENDATION

INFLIXIMAB

(Inflectra — Hospira Healthcare Corporation)

Indications: Rheumatoid Arthritis, Ankylosing Spondylitis, Psoriatic Arthritis, Plaque Psoriasis

Recommendation:

The Canadian Drug Expert Committee (CDEC) recommends that Inflectra (infliximab subsequent entry biologic [SEB]) be listed in accordance with the Health Canada–approved indications for the treatment of rheumatoid arthritis, ankylosing spondylitis, plaque psoriasis, and psoriatic arthritis, if the following conditions are met:

Conditions:

☐ For use in patients for whom infliximab is considered to be the most appropriate treatment option.

☐ List in a manner similar to Remicade.

Reasons for the Recommendation:

1. Two randomized controlled trials (RCTs) demonstrated that Inflectra and Remicade have similar efficacy, safety, and pharmacokinetic (PK) profiles in patients with rheumatoid arthritis (PLANET-RA; N = 606) and ankylosing spondylitis (PLANET-AS; N = 250).
2. Extrapolation of the data from rheumatoid arthritis and ankylosing spondylitis to psoriatic arthritis and psoriatic plaques is supported by the similar pathophysiology of these conditions and the identical dosage regimen for infliximab for these indications.
3. At the submitted price ($650.00 per 100 mg vial), Inflectra is less costly than Remicade ($987.56 per 100 mg vial) for the treatment of rheumatoid arthritis, ankylosing spondylitis, psoriatic plaques, and psoriatic arthritis.

Of Note:

CDEC noted that several comparators used for the treatment of rheumatoid arthritis, ankylosing spondylitis, plaque psoriasis, and psoriatic arthritis are less costly than Inflectra.

Background:

Inflectra is an infliximab SEB based on Remicade as a reference product. It has been approved in Canada for the following indications:

☐ Use in combination with methotrexate for reduction in signs and symptoms, inhibition of the progression of structural damage, and improvement in physical function in adult patients with moderately to severely active rheumatoid arthritis.

☐ Reduction of signs and symptoms and improvement in physical function in patients with active ankylosing spondylitis who have responded inadequately, or are intolerant to, conventional therapies.

☐ Reduction of signs and symptoms, induction of majorclinical response, and inhibition of the progression of structural damage of active arthritis, and improvement in physical function in patients with psoriatic arthritis.

☐ Treatment of adult patients with chronic moderate to severe plaque psoriasis who are candidates for systemic therapy. For patients with chronic moderate plaque psoriasis, Inflectra should be used after phototherapy has been shown to be ineffective or inappropriate.

☐ ACR 20 response rate— defined as the proportion of patients achieving 20% improvement in tender and swollen joint counts and 20% improvement in three of the five remaining ACR core set measures: patient pain assessment (measured by visual analogue scale [VAS]), patient global assessment (measured by VAS), physician global assessment (measured by VAS), patient self-assessed disability (measured by Health Assessment Questionnaire), and acute-phase reactant (erythrocyte sedimentation rate [ESR] or C-reactive protein [CRP]).
☐ ACR 50 and ACR 70— similar to the ACR 20, but with improvements of 50% and 70%.
☐ Disease Activity Score 28 (DAS 28)— a measure or disease activity that takes into consideration the 28-joint counts of tenderness and swelling, plus the ESR or CRP, and a general health assessment scored on a VAS. Scores of less than 2.6 are considered to be remission, and a score greater than 5.1 is considered to be high disease activity.
☐ European League Against Rheumatism (EULAR) response criteria— classification of disease state based on the DAS 28 scale.
☐ ASAS 20 response— defined as an improvement of at least 20% and an absolute improvement of at least 10 units on a 0 to 100 scale, or 1 unit on a 0 to 10 scale from baseline in at least three of the following domains: patient global assessment of disease status; patient assessment of spinal pain; function according to the Bath Ankylosing Spondylitis Functional Index; morning stiffness determined using the last two questions of the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI). Additionally, ASAS 20 responders should not have deterioration (worsening of at least 20% and an absolute worsening of at least 10 units on a 0 to 100 scale or 1 unit on a 0 to 10 scale) of the remaining assessment domain relative to baseline.
☐ ASAS 40 response — defined as an improvement of at least 40% and an absolute improvement of at least 2 units on a 0 to 10 scale from baseline in at least three of the four domains of the ASAS 20, with no deterioration from baseline in the remaining domain.
☐ Serious adverse events, total adverse events, and withdrawals due to adverse events.

Efficacy

Rheumatoid Arthritis (PLANET-RA)

☐ The proportion of patients achieving an ACR 20 response at week 30 was similar in the Inflectra group (60.9%) and the Remicade group (58.6%). The difference of proportions between the groups was 2% (95% CI, –6% to 10%) in the intention-to-treat (ITT) analysis and 4% (95% CI, –4% to 12%) in the per-protocol (PP) analysis. The 95% CIs for the treatment difference were contained within the pre-determined equivalence range of ± 15% for both ITT and PP analyses.
☐ The proportion of patients who demonstrated ACR50 and ACR70 responses was similar between the Inflectra and Remicade groups, with treatment differences reported as follows:
☐ ACR 50: 2% (95% CI, –6% to 9%) at week 30 and week 54.
☐ ACR 70: 1% (95% CI, –5% to 7%) at week 30 and week 54.
☐ The changes in DAS28 scores were similar between the Inflectra and Remicade groups regardless of whether the measure included CRP or ESR. The least square mean difference between Inflectra and Remicade was reported as follows:
☐ DAS 28 (ESR): s.21

s.21

☐ DAS 28 (CRP): s.21
s.21

☐ There were no statistically significant differences between the Inflectra and Remicade groups for the proportion of patients achieving moderate or good responses for both EULAR (ESR) and EULAR (CRP) measures. The odds ratios for achieving moderate or good responses were as follows:

☐ EULAR (ESR): s.21
s.21

☐ EULAR (CRP): s.21
s.21

Ankylosing Spondylitis (PLANET-AS)

☐ A similar proportion of patients in the Inflectra and Remicade groups demonstrated ASAS 20 and ASAS 40 responses at weeks 14, 30, and 54. There were no statistically significant differences between the two treatment groups, with odds ratios reported as follows:

☐ ASAS 20: 0.91 (95% CI, 0.53 to 1.54) at week 14; 0.91 (95% CI, 0.51 to 1.62) at week 30; and 0.89 (95% CI, 0.50 to 1.59) at week 54.

☐ ASAS 40: 0.85 (95% CI, 0.51 to 1.42) at week 14; 1.19 (95% CI, 0.70 to 200) at week 30; and 1.26 (95% CI, 0.73 to 2.15) at week 54.

Harms (Safety and Tolerability)

☐ The proportion of patients who reported at least one serious adverse event was:
☐ PLANET-RA: 13.9% with Inflectra and 10.0% with Remicade.
☐ PLANET-AS s.21 % with Inflectra and s.2 % with Remicade.
☐ The proportion of patients who reported at least one adverse event was:
☐ PLANET-RA: 70.2% with Inflectra and 70.3% with Remicade.
☐ PLANET-AS: 72.7% with Inflectra and 67.2% with Remicade.
☐ The proportion of patients with at least one infection was:
☐ PLANET-RA: s.21 % with Inflectra and s.21 % with Remicade.
☐ PLANET-AS: % with Inflectra and % with Remicade.

Common Drug Review

☐ The proportion of patients who withdrew as a result of adverse events was:
☐ PLANET-RA: s.21 % with Inflectra and s.21 % with Remicade.
☐ PLANET-AS: with Inflectra and s.2 % with Remicade.

Extrapolation

Health Canada granted the extrapolation of data from the manufacturer's studies in rheumatoid arthritis (PLANET-RA) and ankylosing spondylitis (PLANET-AS) to the indications of plaque psoriasis and psoriatic arthritis. Health Canada stated that the indications for psoriatic arthritis and plaque psoriasis were granted on the basis of similarity and the absence of meaningful differences between Inflectra and Remicade with respect to quality, mechanism of action, disease pathophysiology, safety, dosage regimen, and on clinical experience with the reference product (i.e., Remicade). The manufacturer had also requested extrapolation to Crohn disease and ulcerative colitis; however, Health Canada did not grant those indications for Inflectra, noting that the differences between Inflectra and Remicade could have an impact on the clinical safety and efficacy in those patient populations.

Cost and Cost-Effectiveness

The manufacturer submitted a cost comparison of Inflectra with Remicade for the four indications under review: rheumatoid arthritis, ankylosing spondylitis, plaque psoriasis,

and psoriatic arthritis. The cost of Inflectra ($650 per 100 mg vial) is 34.2% less costly than Remicade when using the Ontario Exceptional Access Program (EAP) price of Remicade ($987.56 per 100 mg vial).

CDR identified the following issues for consideration:

☐ Inflectra can be used either for patients who would otherwise have initiated Remicade or other biologic disease-modifying antirheumatoid drugs (bDMARDs). Compared with other, less expensive bDMARDs, Inflectra would result in an incremental cost.

☐ Some drug plans have a lower list price than Ontario EAP for Remicade and, as such, the expected savings with Inflectra may vary across the CDR-participating drug plans. Furthermore, the projected savings do not account for any product listing agreements for Remicade.

☐ For patients who have an incomplete response with infliximab, consideration may be given to adjusting the dose up to 10 mg/kg and/or treating as often as every four weeks. Dose escalation would affect both Inflectra and Remicade, not affecting the relative cost difference. However, this would have a considerable impact when comparing the cost of Inflectra with other bDMARDs.

☐ The dosage of infliximab is based on a patient's body weight, and the manufacturer's comparisons for rheumatology indications were based on an average weight of 70 kg. Inflectra and Remicade share the same dosing strategies, and variations in body weight would not affect the relative cost difference between the two; however, this would have an impact when Inflectra is compared with other bDMARDs.

☐ The indications under review are chronic in nature. The relative cost of Inflectra compared with Remicade is not expected to vary with a longer time horizon, but this would affect the comparison with other bDMARDs, due to the loading doses used in the first year for some biologic therapies.

In addition to the issues above, the recommended dose for each indication will also affect the relative cost of Inflectra compared with Remicade and other bDMARDs:

☐ For rheumatoid arthritis, for the first year of treatment, assuming a weight of 70 kg, Inflectra (3 mg/kg, $15,600) is less costly than Remicade (3 mg/kg, $23,701) and all other bDMARDs (range: $15,680 to $20,207), except for low-dose intravenous tocilizumab 4 mg/kg ($8,153) and subcutaneous tocilizumab every other week ($10,014). If the dose of infliximab is increased to 5 mg/kg or 10 mg/kg, or the frequency of injection is increased to every four weeks during the first year, Inflectra may become more costly than most other bDMARDs.

☐ For ankylosing spondylitis, for the first year of treatment, Inflectra (5 mg/kg, $20,800) is less costly than Remicade (5 mg/kg, $31,601) but more costly than all other bDMARDs (range: $18,243 to $20,207).

☐ For psoriatic arthritis, for the first year of treatment, Inflectra (5 mg/kg, $20,800) is less costly than Remicade (5 mg/kg, $31,601) and ustekinumab ($22,966), but more costly than all other bDMARDs (range: $18,243 to $20,207).

☐ For plaque psoriasis, for the first year of treatment (using Saskatchewan Formulary costs, as Ontario EAP does not routinely reimburse bDMARDs for this indication), Inflectra (5 mg/kg, $20,800) is less costly than Remicade (5 mg/kg, $31,232), etanercept ($25,001 to $25,008), and ustekinumab ($22,966), but is more costly than adalimumab ($20,730).

Other Discussion Points:

☐ At the submitted price, Inflectra is less costly than Remicade; however, it is more costly than other bDMARDs approved for use in the same indications.

☐ Listing status for Remicade varies across the CDR-participating drug plans.

Research Gaps:

☐ There are no controlled clinical trials evaluating the safety and efficacy of Inflectra in the treatment of plaque psoriasis or psoriatic arthritis.

☐ There are limited data regarding the long-term efficacy and safety of Inflectra in any of the indicated patient populations.

CDEC Members:

Dr. Lindsay Nicolle (Chair), Dr. James Silvius (Vice-Chair), Dr. Silvia Alessi-Severini, Dr. Ahmed Bayoumi, Dr. Bruce Carleton, Mr. Frank Gavin, Dr. Peter Jamieson, Mr. Allen Lefebvre, Dr. Kerry Mansell, Dr. Irvin Mayers, Dr. Yvonne Shevchuk, and Dr. Adil Virani.

November 19, 2014 Meeting

Regrets:

None

Conflicts of Interest:

None

About This Document:

CDEC provides formulary listing recommendations or advice to CDR-participating drug plans.

CDR clinical and pharmacoeconomic reviews are based on published and unpublished information available up to the time that CDEC deliberated on a review and made a recommendation or issued a record of advice. Patient information submitted by Canadian patient groups is included in the CDR reviews and used in the CDEC deliberations.

The manufacturer has reviewed this document and has/has not requested the removal of confidential information. CADTH has redacted the requested confidential information in accordance with the CDR Confidentiality Guidelines.

The CDEC recommendation or record of advice neither takes the place of a medical professional providing care to a particular patient nor is it intended to replace professional advice.

CADTH is not legally responsible for any damages arising from the use or misuse of any information contained in or implied by the contents of this document.

The statements, conclusions, and views expressed herein do not necessarily represent

Appendix 2

Drug Benefit Council (DBC) Recommendation and Reasons for Recommendation

FINAL

Infliximab (Inflectra™)
Hospira Healthcare Corporation

Description:

Drug review of **infliximab (Inflectra™) Subsequent Entry Biologic (SEB)** for the following Health Canada approved indications:

> For the treatment of ankylosing spondylitis, plaque psoriasis, psoriatic arthritis, and rheumatoid arthritis.

In their review, the DBC considered the following: final review completed by the Common Drug Review (CDR) on December 19, 2014, which included clinical and pharmacoeconomic evidence review material and the recommendation from the Canadian Drug Expert Committee (CDEC). The DBC also considered Patient Input Questionnaire responses from 3 patients and 3 Patient Groups, Clinical Practice Reviews from two specialists, as well as a Budget Impact Assessment.

Dosage Forms:

Inflectra™ is available as infliximab 100 mg vial for IV infusion according to weight-based dosing.

Recommendations:

- The Drug Benefit Council (DBC) recommends that **infliximab (Inflectra™)** be listed for the treatment of rheumatoid arthritis, ankylosing spondylitis, plaque psoriasis, and psoriatic arthritis:
    a. in patients for whom infliximab is considered to be the most appropriate treatment option;
    b. in a manner similar to infliximab (Remicade®)
    c. Inflectra™ should be the first option for treatment-naïve infliximab patients

- The DBC will review clinical data for patients switching from Remicade® to Inflectra™ when it becomes available and provide a recommendation at that time.

Reasons for the Recommendation:

1. Summary

- Two randomized controlled trials (RCTs) demonstrated Inflectra™ has a similar efficacy, safety and pharmacokinetic (PK) profile to Remicade® in patients with rheumatoid arthritis (RA) and ankylosing spondylitis (AS) and, by extrapolation, in patients with psoriatic arthritis and plaque psoriasis.
- At the submitted price, Inflectra™ is less costly than Remicade® for treatment of RA, AS, plaque psoriasis, and psoriatic arthritis, but is more expensive than most other biologics indicated for these conditions.

2. Clinical Efficacy

- The DBC considered the CDR systematic review of Inflectra™, which found two clinical trials evaluating the efficacy and safety of CT-P13 (Inflectra™) against Remicade® (PLANET-RA and PLANET-AS).
- PLANET-RA was a phase 3, randomized, double-blind, multi-centre, multinational, parallel-group clinical equivalence study designed to compare the efficacy and safety of Inflectra™ with Remicade®, in patients with active RA who had an inadequate response to treatment with methotrexate.
- The proportion of patients achieving the primary end point, an American College of Rheumatology (ACR 20) response at week 30, was similar in the Inflectra™ group and the Remicade® group. The proportion of patients who demonstrated ACR50 and ACR70 responses was also similar between the Inflectra™ and Remicade® groups.
- The changes in Disease Activity Score (DAS28, a measure of disease activity that records the 28-joint counts of tenderness and swelling) were similar between the Inflectra™ and Remicade® groups. There were also no statistically significant differences between the Inflectra™ and Remicade® groups for the proportion of patients achieving moderate or good responses for both European League Against Rheumatism (EULAR) ESR and CRP measures.
- PLANET-AS was a phase 1, randomized, double-blind, multi-centre, multinational, parallel-group study designed to compare the PK, safety, and efficacy of Inflectra™ and Remicade®, in patients with active AS. The primary end point was to demonstrate PK equivalence at a steady state of area under the concentration-time curve and observed maximum steady state serum concentration between Inflectra™ and Remicade® between weeks 22 and 30.
- A similar proportion of patients in the Inflectra™ and Remicade® groups demonstrated ASAS 20 and ASAS 40 responses at weeks 14, 30, and 54.
- The available data for PLANET-RA and PLANET-AS are consistent with the conclusion that Inflectra™ and Remicade® have similar efficacy and safety profiles in patients with RA and with AS, respectively.
- The CDR extrapolated the data from rheumatoid arthritis and ankylosing spondylitis to psoriatic arthritis and psoriatic plaques, reasoning that this extrapolation is supported by the similar pathophysiology of these conditions and the identical dosage regimen for infliximab for these indications.

3. Safety

- The proportion of patients who reported at least one serious adverse event, at least one adverse event, at least one infection, or who withdrew as a result of adverse events was similar between Inflectra™ and Remicade® groups in the clinical trials.

- Health Canada did not recommend extrapolation of the efficacy and safety data to the indications of Crohn's disease and ulcerative colitis due to differences between the mechanism of action of Inflectra™ and Remicade® in these diseases.

4. Economic Considerations

- At the submitted price Inflectra™ is less costly than Remicade® for the treatment of RA, AS, plaque psoriatic, and psoriatic arthritis, but is not less expensive than other biologics indicated for these conditions.

5. Of Note

- Patient Input Questionnaire responses from 3 patients and 3 Patient Groups indicated that RA is a chronic condition that can result in pain, inflammation, and inability to function at work or as a parent. According to a survey from one of the Patient Groups, of patients suffering from more severe disease, almost half relied heavily on caregiver assistance to accomplish daily activities. RA and related conditions can have substantial impacts on personal, physical, social, and emotional aspects of life.
- No patients had tried Inflectra™. Patients felt that ongoing monitoring was appropriate, and expressed concern that switching from Remicade® to Inflectra™ should only occur as a result of physician consultation with patients.

Appendix 3
Infliximab SEB (Inflectra™) Budget Impact Summary –February 1st, 2015

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Page 13 to/à Page 14

Withheld pursuant to/removed as

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Appendix 4

Limited Coverage Drugs – Infliximab (Inflectra™)

Generic Name	infliximab (Inflectra™)
Strength	100 mg vial
Form	Vial for infusion

Special Authority Criteria	Approval Period
1. Treatment of Rheumatoid Arthritis according to established criteria* when prescribed by a rheumatologist.	First approval: 1 year Renewal: 1 year to indefinite
2. Treatment of Psoriatic Arthritis according to established criteria* when prescribed by a rheumatologist.	First approval: 1 year Renewal: 1 year to indefinite
3. Treatment of Ankylosing Spondylitis according to established criteria* when prescribed by a rheumatologist.	First approval: 1 year Renewal: 1 year to indefinite
4. Treatment of moderate to severe plaque psoriasis, according to established criteria*, when prescribed by a dermatologist.	First approval: induction 3 doses Renewal: 1 year

* Click on the appropriate Special Authority Form below for full criteria.

Practitioner Exemptions

Special Notes

- All **NEW** infliximab patients for the above indications will be covered for Inflectra™ brand only.
- For coverage, the maximum allowable supply of infliximab is 56 days per fill. One infusion (dose) usually provides treatment for 56 days or less.

Special Authority Request Form(s)

Rheumatoid Arthritis

- 5345 - Biologics for Rheumatoid Arthritis – Initial /Switch (PDF, 333KB)
- 5354 - Biologics for Rheumatoid Arthritis - Renewal (PDF, 315KB)
- 5383 - Health Assessment Questionnaire (HAQ) (PDF, 526KB)

Psoriatic Arthritis

- 5360 - Biologics for Psoriatic Arthritis – Initial /Switch (PDF, 222KB)
- 5361 - Biologics for Psoriatic Arthritis - Renewal (PDF, 188KB)
- 5364 - Bath Ankylosing Spondylitis - Disease Activity Index (BASDAI) (PDF, 72KB)
- 5383 - Health Assessment Questionnaire (HAQ) (PDF, 526KB)

Ankylosing Spondylitis:

- 5365 - Biologics for Ankylosing Spondylitis – Initial /Switch (PDF, 223KB)
- 5366 - Biologics for Ankylosing Spondylitis - Renewal (PDF, 225KB)
- 5364 - Bath Ankylosing Spondylitis - Disease Activity Index (BASDAI) (PDF, 72KB)

Plaque Psoriasis

- 5380 - Biologics for Moderate to Severe Psoriasis (PDF, 181KB)
- 5379 - Psoriasis Area and Severity Index (PASI) Worksheet (PDF, 529KB)

BRITISH COLUMBIA | Ministry of Health

Drug Coverage Decision for B.C. PharmaCare

About PharmaCare B.C. PharmaCare is a government-funded drug plan. It helps British Columbians with the cost of eligible prescription drugs and specific medical supplies.

Details of Drug Reviewed

Drug	**infliximab**
Brand Name	Inflectra™
Dosage Form(s)	100 mg vial
Manufacturer	Pfizer Canada Inc.
Submission Review	**New Submission**
Use Reviewed	Rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriatic arthritis (PsA) and plaque psoriasis (PsO).
Common Drug Review (CDR)	Yes, CDR recommended: **to List with criteria**. Visit the CDR website for more details: www.cadth.ca/sites/default/files/cdr/complete/cdr_complete_SE0384_Inflectra_Dec-23-14.pdf.
Drug Benefit Council (DBC)	DBC met on January 12, 2015. DBC considered various inputs including: final review completed by the CDR on December 19, 2014, which included clinical and pharmacoeconomic evidence review material and the recommendation from the Canadian Drug Expert Committee (CDEC). The DBC also considered Clinical Practice Reviews from two specialists, as well as a Budget Impact Assessment (BIA) and patient input from three patients and three patient groups.
Drug Coverage Decision	**Limited Coverage Benefit.** Access the infliximab (Inflectra™) criteria from **www.gov.bc.ca/pharmacarespecialauthority**
Date	February 19, 2016
Reason(s)	Drug coverage decision is consistent with the CDEC and DBC recommendations. • Inflectra™ is a subsequent entry biologic (SEB) or "biosimilar" version of infliximab based upon the reference product Remicade®. It was approved by Health Canada and supported by the CDR for RA, AS, PsA and PsO based upon data demonstrating similarity and no meaningful differences compared to the reference product. • Based on the available evidence, Inflectra™ is similar to Remicade with respect to efficacy, safety and pharmacokinetics profile in patients with RA and AS and, by extrapolation, in patients with PsA and PsO. • At the submitted price, the cost of Inflectra is lower than the cost of Remicade®. • Pan-Canadian Pharmaceutical Alliance negotiated a lower transparent price that is available to all, public and private payers.
Other Information	None

The Drug Review Process in B.C.

A manufacturer submits a request to the Ministry of Health (Ministry).

An independent group called the Drug Benefit Council (DBC) gives advice to the Ministry. The DBC looks at:

- advice from a national group called the Common Drug Review
- whether the drug is safe and effective
- whether it is a good value for the people of B.C.
- the ethics of covering or not covering the drug
- input from physicians, patients, caregivers, patient groups and drug submission sponsors

The Ministry makes a decision based on many factors, including:

- advice from the DBC
- drugs used to treat similar medical conditions that B.C. PharmaCare already covers
- the overall cost of covering the drug

Visit the B.C. Drug Review Process and PharmaCare program for more information.

This document is intended for information only.
It does not take the place of advice from a physician or other qualified health care provider.

February 19, 2016 1040359

Dear Prescriber:

Re: PharmaCare coverage of infliximab (Inflectra™) for the treatment of rheumatology and dermatology indications; certolizumab (Cimzia®) for ankylosing spondylitis and psoriatic arthritis; and subcutaneous tocilizumab (Actemra®) for rheumatoid arthritis.

Effective **February 19, 2016**, PharmaCare is pleased to announce that it will cover infliximab (Inflectra™) for the treatment of eligible rheumatology and dermatology indications according to the existing Limited Coverage criteria.

Inflectra™ is a subsequent entry biologic (SEB) or "biosimilar" version of infliximab based upon the reference product Remicade®. It was approved by Health Canada and supported by the national Common Drug Review for the indications stated below based upon data demonstrating similarity and no meaningful differences compared to the reference product. In FY 14/15, the total spending on Remicade in B.C. by all payers for all indications was approximately $105 million, making it B.C.'s top drug expenditure. Through national price negotiations, public drug plans also negotiated a significantly lower public list price for Inflectra which is available for all payers, public and private, where savings can be invested into other priorities.

On or after February 19, 2016, all initial Special Authority (SA) requests for coverage of infliximab for ankylosing spondylitis, psoriatic arthritis, plaque psoriasis and rheumatoid arthritis received will be approved for the Inflectra brand of infliximab only. The Remicade brand of infliximab will not be approved for new infliximab starts for patients with these conditions as of this date.

Coverage of the Remicade brand of infliximab will continue for patients previously approved for PharmaCare coverage of Remicade; they will also be eligible for PharmaCare coverage of the Inflectra brand should they choose to switch.

When the Inflectra brand is desired, please specify "Inflectra" on the prescription to allow the pharmacy to dispense this specific formulation.

If you have questions about how Inflectra can be obtained, infusion sites or the patient support program for Inflectra, please contact:

Carol Honeyman (Navigator for B.C.)
Mobile: 604-340-2981
Email: choneyman@innomar-strategies.com

INFLECTRA Patient Assistance Program
1 844 466-6627 to enroll patients.
M-F 8:00 am- 8:00 pm EST.

…2

For information on PharmaCare's coverage decision, please see the Drug Decision Summary available at https://fmdb.hlth.gov.bc.ca.

For information on Health Canada's decision, please see the Summary Basis of Decision available at http://www.hc-sc.gc.ca/dhp-mps/prodpharma/sbd-smd/drug-med/sbd_smd_2014_inflectra_159493-eng.php.

For Common Drug Review's review and recommendation, please see https://www.cadth.ca/infliximab-18.

Rheumatology specialists may be interested to learn that as of February 19, 2016, PharmaCare will also offer Limited Coverage for the subcutaneous formulation of tocilizumab (Actemra®) for eligible patients with rheumatoid arthritis through the SA Program. Patients currently approved for intravenous tocilizumab can be switched to the subcutaneous formulation without submission of a separate SA request.

Furthermore, certolizumab (Cimzia®) will become an eligible Limited Coverage PharmaCare benefit for the treatment ankylosing spondylitis and psoriatic arthritis on February 19, 2016. Limited Coverage criteria will be the same as for existing biologic medications for these conditions.

For the updated SA forms, visit www.gov.bc.ca/pharmacarespecialauthority and select the drug name from the list of drugs provided.

Coverage of these medications is subject to the rules of a patient's PharmaCare plan, including any annual deductible requirement. PharmaCare policy does not allow retroactive coverage. Prescriptions that are filled prior to having a SA approval in place, or after SA coverage expires, are not eligible for coverage.

Sincerely,

Eric Lun, PharmD
Executive Director, Drug Intelligence & Optimization Branch
Medical Beneficiary and Pharmaceutical Services Division, Ministry of Health

BC PharmaCare Newsletter

February 19, 2016 Edition 16-001

Published by the Medical Beneficiary and Pharmaceutical Services Division to provide information for British Columbia's health care providers

QuickLinks

LOW COST ALTERNATIVE/REFERENCE DRUG PROGRAM—REIMBURSEMENT CHANGES FOR 2016/17

On **April 1, 2016**, changes to reimbursement limits for Low Cost Alternative(LCA)/Reference Drug Program (RDP) drugs will take effect. These include changes to maximum PharmaCare reimbursement for drugs in the:

- Low Cost Alternative (LCA) Program
- Reference Drug Program (RDP)
- Pan-Canadian Competitive Value Price Initiative for Generic Drugs

For information on all drugs affected by the price changes detailed below
see "Upcoming LCA/RDP Data Files" at www.gov.bc.ca/pharmacarecostalternativeprogram.

All PharmaCare reimbursement changes are effective April 1, 2016.

Continued…

BRITISH COLUMBIA | Ministry of Health

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Low Cost Alternative (LCA) Program

Under the LCA Program, PharmaCare targets a maximum amount it will reimburse for each drug in an LCA category. The LCA price is set at the maximum price that manufacturers can charge (the Maximum Accepted List Price or "MALP") plus 8%[1].

In 2010, PharmaCare began a phased decrease in the reimbursement for generic drugs. In this latest phase (**April 1, 2016—March 31, 2017**), the target MALP that manufacturers can charge for generic LCA drugs will continue to be:

- 20% of the equivalent brand product's list price for oral solids
- 35% of the equivalent brand product's list price for drugs available in other forms
- 18% of the equivalent brand product's list price for drugs subject to Pan-Canadian pricing (see **Generic Drugs Subject to Pan-Canadian Pricing** on page 3)

PharmaCare coverage under the new price targets

Normally, PharmaCare covers only the generic drugs priced at or below the LCA Price stated in the **LCA Spreadsheet**. The April 1 reimbursement limits for LCA drugs are published in the "Max Price" column of the **upcoming** LCA Spreadsheet.

Note: PharmaCare covers some generic drugs at a higher price on a "provisional basis." Coverage for these higher-priced generic drugs may be discontinued if a product becomes available at a better price.

Drugs becoming non-benefits

A list of the drugs that will no longer be covered as of April 1, 2016, is available in the upcoming removal spreadsheet.

Note: For LCA/RDP drugs, manufacturers will reflect the new pricing at **start of day March 1, 2016** (30 days before the new pricing takes effect).

Reference Drug Program (RDP)

The Reference Drug Program encourages cost-effective first-line prescribing for common medical conditions. Under the RDP, PharmaCare coverage is based on the cost of the reference drug or drugs in a therapeutic category. This is the drug(s) considered to be equally efficacious and the most cost effective in that category.

If an RDP drug is also an LCA drug, the reimbursement limit for drugs in that RDP category is the lower of the RDP or LCA Price.

The current list of RDP drugs and RDP prices is provided in the RDP Spreadsheet.

Continued…

[1] 5% markup for LCA drugs subject to the High-Cost Drugs.

Generic Drugs Subject to Pan-Canadian Pricing

In January 2013, under the Pan-Canadian Competitive Value Price Initiative for Generic Drugs, the Council of the Federation announced that, to achieve better value for generic drugs, its member provinces and territories would establish price points for the most common generic drugs.

Currently, the price for the following generic drugs is set at 18% of the equivalent brand product list price:

- **Atorvastatin**—used to treat high cholesterol
- **Ramipril**—used to treat elevated blood pressure and other cardiovascular conditions
- **Venlafaxine**—used to treat mental health conditions such as depression, anxiety, panic disorder
- **Amlodipine**—used to treat elevated blood pressure, chest pain and other cardiovascular conditions
- **Omeprazole**—used to treat a variety of gastrointestinal conditions
- **Rabeprazole**—used to treat a variety of gastrointestinal conditions
- **Rosuvastatin** —used to treat high cholesterol
- **Citalopram**—used to treat mental health conditions such as depression
- **Simvastatin**—used to treat high cholesterol
- **Pantoprazole**—used to treat a variety of gastrointestinal conditions including reflux
- **Clopidogrel** —used to treat cardiovascular conditions
- **Olanzapine**—used to treat mental health conditions such as schizophrenia or other psychosis
- **Metformin**—used to treat diabetes
- **Gabapentin**—used to treat epilepsy

Effective **April 1, 2016**, the following three generic drugs will also be priced at 18% of brand:

- **Quetiapine**—used to treat mental health conditions such as schizophrenia, depression, bipolar disorder
- **Donepezil**—used to treat Alzheimer's Disease
- **Zopiclone**—used to treat insomnia

The Pan-Canadian prices are included in the April 1, 2016, upcoming LCA Spreadsheet. Drugs subject to Pan-Canadian pricing are flagged with a "**Y**" in the **Pan-Canadian** column.

Below is a summary of the changes that will occur in Pan-Canadian pricing leading up to April 1, 2016:

Pan-Canadian Generic Drug	**Manufacturer price changes and PharmaCare coverage effective as of:**	
	March 1, 2016	**April 1, 2016**
Atorvastatin, ramipril, venlafaxine, amplodipine, omeprazole, rabeprazole, rosuvastatin, simvastatin, pantoprazole, citalopram, metformin, clopidogrel, olanzapine, and gabapentin	PharmaCare continues to reimburse up to 18% of the equivalent brand name drug plus an 8% markup.	
Quetiapine and donepezil	Manufacturers do not reduce pricing on March 1. PharmaCare continues to reimburse at the current manufacturer list price plus an 8% markup until March 31, 2016.	Manufacturers reduce pricing to Pan-Canadian levels. PharmaCare reimburses up to 18% of brand plus an 8% markup.
Zopiclone	Exception: Select zopiclone products. Some manufacturers reduce pricing from 25% to 20% of the equivalent brand name drug. PharmaCare continues to reimburse up to 25% of brand plus an 8% markup.	Manufacturers further reduce the price from 20% to Pan-Canadian levels of 18%. PharmaCare reimbursement drops to the Pan-Canadian price plus an 8% markup.

RECORD-KEEPING REQUIREMENTS—UPDATE

Audits are regularly performed by the Ministry of Health to ensure providers—and claims for drugs, medical supplies, and services for which PharmaCare reimburses providers—are in compliance with the terms of the *Pharmaceutical Services Act*, related regulations, and policies.

Documentation for Frequency of Dispensing, Medication Review and Smoking Cessation

During an audit, all Frequent Dispensing Authorizations* (HLTH 5378), Medication Review forms, and Smoking Cessation Declaration and Notification forms (HLTH 5464) must be available to the auditors **immediately upon their arrival**.

We strongly recommend that each type of form be kept in a separate binder or folder for each year (e.g., all Medication Review forms can be kept in a single binder/folder). Within the binder, the forms should be filed alphabetically by patient's name, then chronologically.

NOTES:

- Claims without the necessary, and fully completed, forms are subject to recovery.
- Frequent Dispensing Authorization forms must be faxed to the prescribers **before** medication is dispensed; claims associated with forms created after the fact are subject to recovery.

Methadone for Maintenance

Before dispensing a methadone prescription, the patient and pharmacist must acknowledge receipt by signing a patient/prescription-specific log. To ensure that the complete dispensing history is accessible, the properly signed patient/prescription-specific log and all other relevant information (including all correspondence with the prescriber) **must be attached to the original Controlled Prescription Program form**.

Each Controlled Prescription Program form with its relevant information attached should be filed sequentially by the first prescription or transaction number assigned to the prescription.

Please refer to Provider Regulation section 13(2) for details regarding additional methadone maintenance services records that pharmacy providers must keep.

ENTERING CLAIMS THAT EXCEED THE PHARMANET $9,999.99 MAXIMUM

PharmaNet currently limits claims to a maximum of $9,999.99. With drug claims exceeding this amount becoming more common, we would like to clarify the procedures for entering them in PharmaNet.

To ensure correct adjudication of claims exceeding $9,999.99, pharmacists are required to following procedures:

- Split the claim and submit as separate claims of less than $9,999.99;
- Accurately divide the drug cost in proportion to the dispensed quantity entered for each claim;
- Pro-rate the days' supply between the claims in proportion to the dispensed quantity entered for each claim (see example below);
- Do not split the dispensing fee; include it in only one of the claims. Enter a $0 dispensing fee on the remaining claims; and
- Enter the intervention code **MP** for all but the first claim.

Sample of submission of a claim in excess of $9,999.99

Claims for a 28-day supply of a drug with a dispensed quantity of 28 and drug cost of $24,000			
Field	**Claim 1**	**Claim 2**	**Claim 3**
Dispensed quantity	10	10	8
Days' supply	10	10	8
Drug cost	$8,571.43	$8,571.43	$6,857.14
Dispensing fee	Yes (usual fee claimed)	No (zeroed out)	No (zeroed out)
Intervention code	n/a	MP	MP

Note: When you must submit multiple claims due to drug cost exceeding $9,999.99, you are required to ensure any portion of the days' supply claimed in excess of the PharmaCare maximum for the drug (i.e., 30 or 100 days, as applicable) is entered into PharmaNet with the intervention code **DE—Adjudicate to $0.00 as requested**.

PLAN G REGISTRATION—REVISED PROCESS

Please be aware that the computer system that allowed Mental Health Substance Use Centres (MHSUCs) and the Ministry of Children and Family Development (MCFD) to submit coverage data directly into PharmaNet has been discontinued. As a result MHSUCs must now fax Plan G eligibility to Health Insurance BC. Within 24 hours of receiving a complete application, Health Insurance BC will enter the patient's Plan G coverage into PharmaNet.

EXCHANGE RATE UPDATE

New U.S. Exchange Rate **$1.4257***

*Based on the Bank of Canada rate at the close of business on

January 12, 2016.

The price list for prosthetic components is adjusted, as needed, based on the U.S. Exchange Rate published by the Bank of Canada.

Rates are reviewed regularly and adjusted whenever the rate changes by more than five cents and remains at a variance of five cents or more for at least five working days.

BENEFITS

Special Authority Coverage of Infliximab (Inflectra™)

Inflectra™ is a subsequent entry biologic (SEB) or "biosimilar" version of infliximab based upon the reference product Remicade®. It was approved by Health Canada and supported by the national Common Drug Review for various rheumatoid conditions and plaque psoriasis based upon data demonstrating similarity and no meaningful differences compared to the reference product.

For information on Health Canada's decision, please see the Summary Basis of Decision available at www.hc-sc.gc.ca/dhp-mps/prodpharma/sbd-smd/drug-med/sbd_smd_2014_inflectra_159493-eng.php.

For Common Drug Review's review and recommendation, please see www.cadth.ca/infliximab-18.

In fiscal year 2014/15, the total spending on Remicade® in B.C. by all payers for all indications was approximately $105 million, making it B.C.'s top drug expenditure. Through the pan-Canadian Pharmacuetical Alliance, provincial and territorial public drug plans negotiated a significantly lower transparent list price for Inflectra™, enabling savings for both public and private payers that can be reinvested into other priorities.

Effective **February 19, 2016**, PharmaCare covers infliximab (Inflectra™) for the treatment of eligible rheumatology and dermatology indications according to existing Limited Coverage criteria as follows:

SPECIAL AUTHORITY CRITERIA	APPROVAL PERIOD
1. Treatment of Rheumatoid Arthritis according to established criteria when prescribed by a rheumatologist.	First approval: 1 year Renewal: 1 year to indefinite
2. Treatment of Psoriatic Arthritis according to established criteria when prescribed by a rheumatologist.	First approval: 1 year Renewal: 1 year to indefinite
3. Treatment of Ankylosing Spondylitis according to established criteria when prescribed by a rheumatologist.	First approval: 1 year Renewal: 1 year to indefinite
4. Treatment of moderate to severe plaque psoriasis, according to established criteria when prescribed by a dermatologist.	First approval: induction 3 doses Renewal: 1 year

All Special Authority (SA) requests for coverage of infliximab for infliximab-naïve patients requiring the drug for the above indications will be approved for the Inflectra brand of infliximab only. Patients whose initial Special Authority was received before February 19, 2016, will be eligible for coverage of Remicade®.

Coverage of these drugs is subject to the rules of a patient's PharmaCare plan, including any annual deductible requirement. Retroactive coverage cannot be provided for prescriptions filled before Special Authority approval is in place.

Limited Coverage Drug Program

The following products are eligible benefits under the Limited Coverage Program—by Special Authority only—for Fair PharmaCare and Plans B, C, and F and, if indicated, Plan G and/or Plan P.

For information on all Special Authority drugs, visit our Special Authority page.

For criteria and forms for a **specific** drug, click on the **drug name** below.

COVERAGE EFFECTIVE	February 19, 2016		
DRUG NAME	Cimzia® (certolizumab pegol)		
INDICATION	Ankylosing spondylitis and psoriatic arthritis		
DIN	02331675	400 mg/2 mL	
PLAN G BENEFIT?	No		
PLAN P BENEFIT?	No		

COVERAGE EFFECTIVE	February 19, 2016		
DRUG NAME	Actemra® (tocilizumab) subcutaneous injection		
INDICATION	Rheumatoid Arthritis		
DIN	02424770	162 mg/0.9 mL pre-filled syringe	
PLAN G BENEFIT?	No		
PLAN P BENEFIT?	No		

COVERAGE EFFECTIVE	February 19, 2016		
DRUG NAME	Inflectra™ (infliximab)		
INDICATION	Ankylosing spondylitis, plaque psoriasis, psoriatic arthritis, rheumatoid arthritis		
DIN	02419475	100 mg vial	
PLAN G BENEFIT?	No		
PLAN P BENEFIT?	No		

Non-Benefits

The following products have been reviewed and will not be added as benefits under PharmaCare.

DIN/NPN	DRUG NAME
02441829	insulin glargine (Toujeo™ SoloSTAR®) subcutaneous solution 300 U/ml (450IU) pre-filled pen
02415690	macitentan (Opsumit™) 10 mg tablet
80043158	vitamin B12 / cyanocobalamin (Beduzil 1500) 1500 mcg extended release tablet
02434334	apremilast (Otezla®) 30 mg tablet for plaque psoriasis
02434318	apremilast (Otezla®) 27-count starter pack for plaque psoriasis
02417170	linaclotide (Constella™) 290 mcg capsule

MINISTRY OF HEALTH
DECISION BRIEFING NOTE

Cliff # 1060702

PREPARED FOR: Eric Lun, Executive Director **- FOR DECISION**

TITLE: Drug Review Listing Decision for infliximab (Inflectra) biosimilar for Crohn's disease and ulcerative colitis.

PURPOSE: To make a drug review listing decision for the submission of infliximab (Inflectra) biosimilar for Crohn's disease and ulcerative colitis.

BACKGROUND:

- Infliximab (Inflectra®) is a biosimilar product based on the innovator product, infliximab (Remicade®).
- On June 10, 2016, Inflectra, marketed by Hospira HealthCare Corporation, a Pfizer Company, received Health Canada Notice of Compliance for the treatment of Crohn's disease (CD), fistulising CD, and ulcerative colitis (UC).
- Inflectra for the treatment of CD and UC was reviewed by the Common Drug Review (CDR) and on October 25, 2016, the Canadian Drug Expert Committee (CDEC) recommended that Inflectra be reimbursed in accordance with the Health Canada–approved indications for the treatment of CD, fistulising CD, and UC, if the following clinical criterion and conditions are met (Appendix 1):

  Clinical Criterion:
  - For use in patients for whom infliximab is considered to be the most appropriate treatment option.

  Conditions:
  - Reimburse in a manner similar to Remicade.
  - The cost of treatment with Inflectra should provide a significant cost savings for jurisdictions compared with the cost of treatment with Remicade.
- Inflectra was reviewed by the Ministry of Health (Ministry) for the treatment of rheumatoid arthritis (RA), ankylosing spondylitis (AS), plaque psoriasis and psoriatic arthritis (PsA) and as of February 19, 2016, is a Limited Coverage benefit for infliximab-naïve patients for these indications.
- Remicade is a Limited Coverage benefit for the treatment of RA, PsA, AS, plaque psoriasis for patients that received coverage prior to February 19, 2016. Remicade is also a Limited Coverage benefit for the treatment of CD.
- Remicade is considered for coverage on exceptional case-by-case basis for the treatment of UC, but no biologic treatment options are covered as PharmaCare benefits for the treatment of this condition.
- Inflectra was not reviewed by the Drug Benefit Council (DBC) for the treatment of infliximab-naïve patients for CD and UC because there are other similar drugs that were previously reviewed by the DBC. The DBC may review switching of patients from Remicade to Inflectra in the future.

DISCUSSION:

- In its review, the Ministry considered the final review completed by the CDR, which included clinical and pharmacoeconomic evidence review material and the recommendation from CDEC, Clinical Practice Reviews from three specialists and a patient input from one patient.

- Health Canada established similarity between Inflectra and Remicade from two clinical trials, one in patients with RA and the other in patients with AS.
- Extrapolation of the data from RA and AS to CD and UC was granted by Health Canada on the basis of similarity between Inflectra and Remicade in patients with RA and AS, and newly submitted physiochemical and biological data.
- Based on one ongoing phase IV, open-label, single arm, post-marketing surveillance study in patients with CD and UC, there appears to be no efficacy, safety nor tolerability concerns in patients treated with Inflectra.
- The Ministry stakeholder engagement for implementation of Inflectra coverage for treatment-naïve patients included three webinars for gastroenterologists, and information sharing with health authorities and a patient group.

FINANCIAL IMPLICATIONS:

- s.13,s.17
-
-
-

OPTIONS:

s.13

Option 2: Effective November 1, 2016, list infliximab (Inflectra) as a Limited Coverage benefit for the treatment of CD and UC for infliximab-naïve patients (Appendix 2).

Pro: Consistent with CDEC recommendation, provides a transparent PharmaCare coverage for the treatment of UC and budget savings to the Ministry.

RECOMMENDATION:

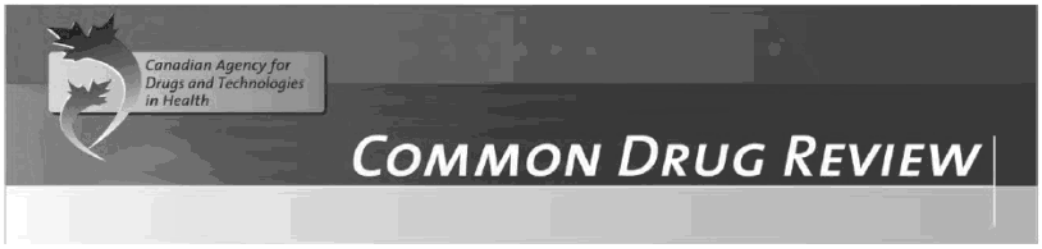
Option 2

Original Signed By
Approved
Eric Lun, Executive Director
Drug Intelligence & Optimization

November 1, 2016
Date Signed

Program ADM/Division: Barbara Walman, Assistant Deputy Minister
Telephone: 250-952-1705
Program Contact (for content): Eric Lun
Drafter: Tijana Fazlagic
Date: November 3, 2016
File Name with Path: P:\DIO-FM-Access Restricted\Drugs 70325-30\infliximab SEB\infliximab (Inflectra) CD-UC 3478 CDR\Decision Briefing Note\infliximab SEB (Inflectra) UC 3478 LCC DBN.docx

Appendix 1



CADTH CANADIAN DRUG EXPERT COMMITTEE FINAL RECOMMENDATION

INFLIXIMAB
(Inflectra — Hospira, a Pfizer Company)
Indications: Crohn Disease and Ulcerative Colitis

Please refer to the CADTH Canadian Drug Expert Committee (CDEC) recommendation dated December 19, 2014 for the reimbursement recommendation for Inflectra for the previously approved Health Canada indications — ankylosing spondylitis, rheumatoid arthritis, psoriatic arthritis, and plaque psoriasis.

Recommendation:
CDEC recommends that Inflectra (infliximab subsequent entry biologic [SEB]) be reimbursed in accordance with the Health Canada–approved indications for the treatment of Crohn disease (CD), fistulizing Crohn disease (FCD), and ulcerative colitis (UC), if the following clinical criterion and conditions are met:

Clinical Criterion:
- For use in patients for whom infliximab is considered to be the most appropriate treatment option.

Conditions:
- Reimburse in a manner similar to Remicade.
- The cost of treatment with Inflectra should provide a significant cost savings for jurisdictions compared with the cost of treatment with Remicade.

Reasons for the Recommendation:
1. Similarity between Inflectra and the reference product (Remicade) was established in two previously reviewed clinical trials in patients with rheumatoid arthritis (RA) and ankylosing spondylitis (AS) (PLANET-RA and PLANET-AS).
2. Extrapolation of the data from RA and AS to CD, FCD, and UC was granted by Health Canada on the basis of similarity between Inflectra and Remicade in patients with RA and AS, and newly submitted physiochemical and biological data.
3. The results of one ongoing phase IV, open-label, single arm, post-marketing surveillance study (CT-P13 PMS) suggested that there were no efficacy, safety, or tolerability concerns for patients with CD, FCD, and UC who were treated with Inflectra.

4. At the submitted price ($525.00 per 100 mg vial), Inflectra is less costly than Remicade ($987.56 per 100 mg vial) for use in accordance with the Health Canada–approved indications for the treatment CD, FCD, and UC.

Background:
Inflectra is an infliximab SEB based on Remicade as a reference product. It was approved by Health Canada in January 2014 for the following indications:

- Use in combination with methotrexate for a reduction in signs and symptoms, inhibition of the progression of structural damage, and an improvement in physical function in adult patients with moderately to severely active RA.
- Reduction of signs and symptoms and improvement in physical function in patients with active AS who have responded inadequately, or are intolerant to, conventional therapies.
- Reduction of signs and symptoms, induction of major clinical response, and inhibition of the progression of structural damage of active arthritis, and improvement in physical function in patients with psoriatic arthritis (PsA).
- Treatment of adult patients with chronic, moderate to severe plaque psoriasis (PsO) who are candidates for systemic therapy. For patients with chronic, moderate PsO, Inflectra should be used after phototherapy has been shown to be ineffective or inappropriate.

Inflectra was subsequently approved by Health Canada in June 2016 for the following indications, which are the indications under review for this recommendation:

- Reduction of signs and symptoms, induction and maintenance of clinical remission and mucosal healing, and reduction of corticosteroid use in adult patients with moderately to severely active CD who have had an inadequate response to a corticosteroid and/or an aminosalicylate. Inflectra can be used alone or in combination with conventional therapy.
- Treatment of FCD, in adult patients who have not responded despite a full and adequate course of therapy with conventional treatment.
- Reduction of signs and symptoms, induction and maintenance of clinical remission and mucosal healing, and reduction or elimination of corticosteroid use in adult patients with moderately to severely active UC who have had an inadequate response to conventional therapy (i.e., an aminosalicylate and/or a corticosteroid, and/or an immunosuppressant).

Inflectra is available as a 100 mg/vial powder for solution, administered as an intravenous infusion. For the inflammatory bowel disease (IBD) indications, Health Canada's–approved dose is 5 mg/kg to 10 mg/kg.

Submission History:
Inflectra was previously reviewed by CDEC for the treatment of RA, AS, PsA, and PsO and received a recommendation to "list" with conditions (see Notice of CDEC Final Recommendation, December 19, 2014).

The original CADTH Common Drug Review (CDR) of Inflectra included two pivotal clinical trials:

- PLANET-RA (N = 606) was a phase III, randomized, double-blind, parallel-group, clinical equivalence study to compare the efficacy and safety of Inflectra and Remicade in adult patients with active RA.
- PLANET-AS (N = 250) was a phase I, randomized, double-blind, parallel-group study to compare the pharmacokinetics, safety, and efficacy of Inflectra and Remicade in adult patients with active AS.

CDEC recommended that Inflectra be listed for RA and AS based on the demonstration of similar efficacy, safety, and pharmacokinetics in these clinical trials and its lower cost compared with Remicade. CDEC also recommended that Inflectra be listed for PsO and PsA based on extrapolation of data from PLANET-RA and PLANET-AS.

Summary of CDEC Considerations:
CDEC considered the following information prepared by CDR: a review of manufacturer-provided information on clinical efficacy, safety, biosimilarity, and extrapolation of data for Inflectra; a review and critique of the manufacturer's pharmacoeconomic evaluation; and patient group–submitted information about outcomes and issues important to patients.

Patient Input Information
The following is a summary of key information provided by two patient groups (The Gastrointestinal Society and Crohn's and Colitis Canada) that responded to the CDR call for patient input. CDEC heard the following:

- Patients report being constantly concerned about disease flare-ups, which occur unpredictably. Limitations in leisure activities, physical activities, use of public transportation, and work were reported. Sustained remission or treatment response, therefore, is desired.
- The course of IBD is often unpredictable and differs from patient to patient; thus, treatment must be individualized. The availability and choice of different treatments options are important.
- Patients hope that treatment will improve quality of life, relieve symptoms, alleviate anxiety and stress, and allow them to lead normal lives in respect to family, career/education, and without interruptions due to flare-ups. They want each drug to be proven safe and effective, specifically in IBD.
- Of those aware of SEBs, patients expect SEBs to be clinically tested in Canadians for all indications, and to be subjected to a rigorous review and approval process.
- Patients expressed concerns about the following:
    - the safety and efficacy of SEBs
    - the regulatory process for approving these drugs in Canada
    - switching between the reference product and the SEB, especially without their consent. It was important to patients that they get to choose with the physician (not chosen by a government or drug plan) the best drug for their condition.
- Patients do not want cost to be the only consideration when deciding which biologic to use.

Clinical Evidence
The manufacturer provided efficacy data from one key clinical study.

Note: CT-P13 refers to the infliximab SEB (marketed as Inflectra in Canada).

CT-P13 PMS (post-marketing surveillance) (N = 173) is an ongoing (four year) phase IV, open-label, single arm observational study of CT-P13 for all approved indications in South Korea. An interim analysis was conducted in adults with moderately to severely active CD (N = 83), FCD (N = 12), and moderately to severely active UC (N = 78) across 15 study centres in South Korea, with a follow-up of 30 weeks. Most patients (N = 113) were infliximab treatment-naive and 60 patients were switched from the reference product, Remicade. CT-P13 was administered every 8 weeks (± 5 days) after induction therapy of three 5 mg/kg doses at weeks

0, 2, and 6. Doses of 5 mg/kg to 10 mg/kg were administered to 41% of patients. The study is limited by an uncontrolled observational design, small sample size, absence of important efficacy outcomes (e.g., extra-intestinal manifestations, disease biomarkers, quality of life, and immunogenicity), and short duration of follow-up (30-week interim analysis). The generalizability of the observed outcomes in patients from South Korea to Canadian patients with IBD is uncertain.

Other lines of evidence for the use of Inflectra in CD and UC:

- CT-P13 4.1 is a small (N = 20) phase IV, ongoing (four year), open-label, single arm study conducted in treatment-naive, adult patients with CD or UC in South Korea. An interim analysis in 10 patients s.21 was available.
- Non-Celltrion sponsored studies — The manufacturer conducted a systematic search to identify non–Celltrion-sponsored studies that evaluated the use of CT-P13 in IBD. Six observational studies in adult patients were identified.
- Safety Evaluation Plan — The manufacturer conducted a systematic literature search of randomized controlled trials and observational studies of the reference product, Remicade, in patients with CD and UC. Rates of infusion-related reactions, infections, pneumonia, tuberculosis, malignancies, and need for surgery or hospitalization were compared with rates from observational studies of infliximab. The interpretation of this data is limited due to differences in study design, study populations, and outcome definitions.

Outcomes

CDEC discussed the following outcomes:

- Clinical response — defined as a reduction of at least 50% from baseline in the number of draining fistulas for patients with FCD; a ≥ 25% and ≥ 70 points decrease in Clinical Disease Activity Index (CDAI) score from baseline scores for patients with CD; and a decrease in partial Mayo scores from baseline of at least 2 points and at least 30%, with an accompanying decrease in the subscore for rectal bleeding of at least 1 point or an absolute subscore for rectal bleeding of 0 or 1 for patients with UC.
- Clinical remission — defined as the absence of draining fistulas for patients with FCD; CDAI score of < 150 for patients with CD; a total partial Mayo score of 2 points or lower, with no individual subscore exceeding 1 point for patients with UC.
- Disease control — defined as the exclusion of loss of response cases from disease control for patients with FCD; the exclusion of disease worsening cases from disease control for patients with CD and UC.
- Rescue medication — defined as any concomitant medication that was started after the first infusion date to treat new or unresolved symptoms of CD or UC.
- Mucosal healing — defined as Mayo endoscopic subscore of ≤ 1 point for patients with UC.
- Adverse events and serious adverse events.

The primary outcome in CT-P13 PMS was not stated.

Efficacy

CT-P13 PMS

Based on last observation carried forward imputation:

- Among CD infliximab-naive patients, 31/39 (79.5%) achieved clinical response and 23/39 (59.0%) achieved clinical remission at week 30.
- Among CD patients who were switched from Remicade to CT-P13, 25/31 (80.6%) achieved remission from visits two to six and 27/31 (87.1%) of patients did not experience disease worsening. Rescue medication was needed by 9/40 (22.5%).
- Among FCD infliximab-naive patients, 2/6 (33.3%) achieved clinical response and 1/6 (16.7%) achieved clinical remission.
- Among FCD patients switched from Remicade to CT-P13, clinical remission and disease control were achieved in one patient at visit six (data were available for only one patient).
- In UC infliximab-naive patients, 39/54 (72.2%) achieved clinical response and 20/54 (37.0%) achieved clinical remission at week 30.
- Among UC patients who were switched from Remicade to CT-P13, 5/11 (45.5%) achieved remission throughout visits two to five and no patients experienced disease worsening.

Based on a complete case analysis:

- Among UC infliximab-naive patients, 9/13 (69.2%) experienced mucosal healing at week 30 while 6/9 (66.7%) patients who were switched from Remicade to CT-P13 experienced mucosal healing throughout visits 2 to 5.

Harms (Safety and Tolerability)

CT-P13 PMS

- A total of 51 treatment-emergent adverse events (TEAEs) in 38 patients occurred.
  - In patients with CD, 19 events occurred in 15/83 patients (18.1%).
  - In patients with FCD, 2 events occurred in 2/12 patients (16.7%).
  - In patients with UC, 30 events occurred in 21/78 patients (26.9%).
- There were no notable differences in TEAEs between patients who were infliximab-naive (23.9%) and those switched from Remicade (18.3%).
- There were no notable dose-dependent differences in distribution of TEAEs between patients who received doses of 5 mg/kg or > 5 mg/kg.
- Infusion-related reactions (IRR), including hypersensitivity and anaphylaxis, were reported in 9 patients (5.2%).
- One patient (0.6%) had active tuberculosis after infliximab exposure.
- No malignancies, pneumonia, deaths, or any other events of special interest were observed during the 30-week interim period.

Other lines of evidence for the use of Inflectra in CD and UC

CT-P13 4.1

- s.21
-
-

Safety Evaluation Plan

- Safety data were generally similar between CT-P13 and Remicade in treatment-naive and switched patients combined for IRRs, pneumonia, tuberculosis, and malignancies. There were some differences in the rates of infection, surgery, and disease-related hospitalization.

Extrapolation

Inflectra was originally approved in Canada for PsO and PsA based on extrapolation of evidence from patients with RA and AS, given the similarities in pathology and mechanisms of action of tumour necrosis factor (TNF) alpha blockers in these indications. When originally approved, Health Canada did not support extrapolating from RA and AS to IBD due to differences in disease mechanisms (role of transmembrane TNF alpha and antibody-dependent cell-mediated cytotoxicity in IBD) and safety profiles of infliximab in IBD verses rheumatic diseases (higher risk of hepatosplenic T-cell lymphoma in IBD). In June 2016, Health Canada approved Inflectra for the adult IBD indications based on extrapolation of data in patients with RA and AS, comparable pharmacokinetics, and newly submitted physiochemical and biological data.

Cost and Cost-Effectiveness

The manufacturer submitted a cost comparison between Inflectra and Remicade for the indications reviewed. As validated by CDR, the manufacturer-submitted price of Inflectra ($525.00 per 100 mg vial) is 44% less than that of Remicade when using the price obtained for Remicade from the Ontario Drug Benefit Exceptional Access Program ($987.56 per 100 mg vial).

CDR identified the following issues for consideration:

- The clinical expert noted that physicians and patients may be reluctant to switch from Remicade to Inflectra when a patient is adequately managed on Remicade. As a result, it may be more likely that Inflectra is used in patients who are new to infliximab rather than those switching from Remicade.
- The manufacturer of Remicade sponsors infusion centres for the administration of Remicade, and covers costs of patient follow-up and monitoring. These costs are expected to be similarly covered by the manufacturer of Inflectra; therefore, this is not expected to result in additional costs to the publicly funded health care system.
- The reimbursement criteria for Remicade differ across publicly funded drug plans in Canada. The expected savings from Inflectra compared with Remicade are based on the assumption that the reimbursement criteria for Remicade would be applied to Inflectra.

Other Discussion Points:

- CDEC noted that there were no currently available reported studies directly comparing Inflectra with Remicade for patients with IBD. One study (CT-P13 3.4) is an ongoing phase III randomized, double-blind, parallel-group, efficacy, and safety study designed to demonstrate non-inferiority of CT-P13 to Remicade in adults during a 54-week period, and plans to enrol 214 patients. An interim analysis at week 14 focusing on the development of anti-drug antibodies suggests similarity between the two groups.

CDEC Members:
Dr. Lindsay Nicolle (Chair), Dr. James Silvius (Vice-Chair), Dr. Silvia Alessi-Severini, Dr. Ahmed Bayoumi, Dr. Bruce Carleton, Mr. Frank Gavin, Dr. Peter Jamieson, Dr. Anatoly Langer, Mr. Allen Lefebvre, Dr. Kerry Mansell, Dr. Irvin Mayers, Dr. Yvonne Shevchuk, Dr. Adil Virani, and Dr. Harindra Wijeysundera.

September 21, 2016 Meeting

Regrets:
Three CDEC members did not attend.

Conflicts of Interest:
None

About this Document:
CDEC provides formulary reimbursement recommendations or advice to CDR participating drug plans.

CDR clinical and pharmacoeconomic reviews are based on published and unpublished information available up to the time that CDEC deliberated on a review and made a recommendation or issued a record of advice. Patient information submitted by Canadian patient groups is included in the CDR reviews and used in the CDEC deliberations.

The manufacturer has reviewed this document and has/has not requested the removal of confidential information in conformity with the *CDR Confidentiality Guidelines*. CADTH has redacted the requested confidential information in accordance with the CDR Confidentiality Guidelines.

The CDEC recommendation or record of advice neither takes the place of a medical professional providing care to a particular patient nor is it intended to replace professional advice.

The Canadian Agency for Drugs and Technologies in Health (CADTH) is not legally responsible for any damages arising from the use or misuse of any information contained in or implied by the contents of this document.

The statements, conclusions, and views expressed herein do not necessarily represent the view of Health Canada or any provincial, territorial, or federal government or the manufacturer.

Appendix 2

Limited Coverage Drugs - Infliximab

Generic Name	infliximab
Strength	100 mg
Form	Vial for Infusion

Inflectra™ (new patients)

Remicade® (patients granted Special Authority prior to Feb. 19, 2016)

Special Authority Criteria	Approval Period
1. Treatment of **Rheumatoid Arthritis** according to established criteria* when prescribed by a rheumatologist.	First approval: 1 year Renewal: 1 year to indefinite
2. Treatment of **Psoriatic Arthritis** according to established criteria* when prescribed by a rheumatologist.	First approval: 1 year Renewal: 1 year to indefinite
3. Treatment of **Ankylosing Spondylitis** according to established criteria* when prescribed by a rheumatologist.	First approval: 1 year Renewal: 1 year to indefinite
4. Treatment of **moderate to severe Psoriasis**, according to established criteria*, when prescribed by a dermatologist.	First approval (induction period): 3 doses Renewal: 1 year

* Click on the appropriate Special Authority Form below for full criteria.

Inflectra™ (new patients)

Remicade® (patients granted Special Authority prior to Nov. 1, 2016)

5. Treatment of **moderate to severe active Crohn's disease or fistulising Crohn's disease** according to established criteria* when prescribed by a gastroenterologist.	First approval (induction period): 3 doses (Inflectra™ only) Renewal: 1 year (Inflectra™ and Remicade®)

* Click on the appropriate Special Authority Form below for full criteria.

Inflectra™ only

6. Treatment of **moderate to severe Ulcerative Colitis** according to established criteria* when prescribed by a gastroenterologist.	First approval (induction period): 3 doses Renewal: 1 year

* Click on the appropriate Special Authority Form below for full criteria.

Practitioner Exemptions

- None

Special Notes

- PharmaCare covers only the Inflectra brand for patients using infliximab for the first time for the indications above.
- For the rheumatoid and psoriasis indications above, PharmaCare covers Remicade and Inflectra for patients who were granted a Special Authority for Remicade before Feb. 19, 2016.
- For Crohn's disease, PharmaCare covers Remicade and Inflectra for patients who were granted a Special Authority for Remicade before Nov. 1, 2016.
- PharmaCare does not cover Remicade for the treatment of ulcerative colitis.

- PharmaCare covers a maximum of 56 days per fill for infliximab. One infusion (dose) usually provides treatment for 56 days or less.

Special Authority Request Form(s)

Rheumatoid Arthritis

- 5345 - Biologics for Rheumatoid Arthritis – Initial /Switch (PDF)
- 5354 - Biologics for Rheumatoid Arthritis - Renewal (PDF)
- 5383 - Health Assessment Questionnaire (HAQ) (PDF)

Psoriatic Arthritis

- 5360 - Biologics for Psoriatic Arthritis – Initial /Switch (PDF)
- 5361 - Biologics for Psoriatic Arthritis - Renewal (PDF)
- 5364 - Bath Ankylosing Spondylitis - Disease Activity Index (BASDAI) (PDF)
- 5383 - Health Assessment Questionnaire (HAQ) (PDF)

Ankylosing Spondylitis:

- 5365 - Biologics for Ankylosing Spondylitis – Initial /Switch (PDF)
- 5366 - Biologics for Ankylosing Spondylitis - Renewal (PDF)
- 5364 - Bath Ankylosing Spondylitis - Disease Activity Index (BASDI) (PDF)

Plaque Psoriasis:

- 5380 - Biologics for Moderate to Severe Psoriasis (PDF)
- 5379 - Psoriasis Area and Severity Index (PASI) Worksheet (PDF)

Crohn's Disease:

- 5368 – Biologics for Moderate to Severe Active Crohn's Disease (PDF)
- 5374 – Worksheet (based on Harvey-Bradshaw Index) (PDF)

Ulcerative Colitis (Inflectra brand only):

- 5388 – Infliximab for Ulcerative Colitis (PDF)

BRITISH COLUMBIA | Ministry of Health

Drug Coverage Decision for B.C. PharmaCare

About PharmaCare B.C. PharmaCare is a government-funded drug plan. It helps British Columbians with the cost of eligible prescription drugs and specific medical supplies.

Details of Drug Reviewed

Drug	**infliximab**
Brand Name	Inflectra®
Dosage Form(s)	100 mg vial
Manufacturer	Pfizer Canada Inc.
Submission Type	**New Indication**
Use Reviewed	Crohn's disease and ulcerative colitis
Common Drug Review (CDR)	Yes, CDR recommended: **to Reimburse with clinical criteria and/or conditions**. Visit the CDR website for more details: www.cadth.ca/node/88649.
Provincial Review	DBC now screens drug submissions under review by the CDR to determine whether or not a full DBC review is necessary, based on past DBC reviews, recommendations, and existing PharmaCare coverage. If a full DBC review is determined to not be required, the Ministry's drug coverage decision will be based on the Canadian Drug Expert Committee (CDEC) recommendation and an internal review only. Inflectra® was reviewed internally and was not reviewed by the Drug Benefit Council (DBC) for the treatment of Crohn's disease and ulcerative colitis in infliximab-naïve patients. The Ministry considered the final review completed by the CDR, which included clinical and pharmacoeconomic evidence review material and the recommendation from CDEC. The Ministry also considered Clinical Practice Reviews from three specialists and a patient input from one patient.
Drug Coverage Decision	**Limited Coverage Benefit.** Access the infliximab (Inflectra®) criteria from **www.gov.bc.ca/pharmacarespecialauthority**
Date	November 1, 2016
Reason(s)	Drug coverage decision is consistent with the CDEC recommendation. • Inflectra® is a biosimilar version of infliximab based upon the reference product Remicade®. It was approved by Health Canada and supported by the CDR for Crohn's disease and ulcerative colitis based upon data demonstrating similarity and no meaningful differences compared to Remicade®. • Based on the available evidence, Inflectra® is similar to Remicade® with respect to efficacy, safety and tolerability. • At the submitted price, the cost of Inflectra® is lower than the cost of Remicade®. • Pan-Canadian Pharmaceutical Alliance negotiated a lower transparent price that is available to all, public and private payers.
Other Information	None

The Drug Review Process in B.C.

A manufacturer submits a request to the Ministry of Health (Ministry).

An independent group called the Drug Benefit Council (DBC) gives advice to the Ministry. The DBC looks at:

- advice from a national group called the Common Drug Review
- whether the drug is safe and effective
- whether it is a good value for the people of B.C.
- the ethics of covering or not covering the drug
- input from physicians, patients, caregivers, patient groups and drug submission sponsors

The Ministry makes a decision based on many factors, including:

- advice from the DBC
- drugs used to treat similar medical conditions that B.C. PharmaCare already covers
- the overall cost of covering the drug

Visit the B.C. Drug Review Process and PharmaCare program for more information.

This document is intended for information only.
It does not take the place of advice from a physician or other qualified health care provider.

November 1, 2016 1067756

Dear Prescriber:

Re: PharmaCare coverage of infliximab (Inflectra®) for the treatment of Crohn's disease and ulcerative colitis.

Effective **November 1, 2016,** PharmaCare will cover infliximab (Inflectra®) as a Limited Coverage Drug through the Special Authority program for new patients requiring infliximab for the treatment of Crohn's disease or ulcerative colitis.

About Inflectra®

Inflectra® is "biosimilar" version of infliximab based on Remicade®. Health Canada approved Inflectra® on June 10, 2016, for the treatment moderate to severe Crohn's disease, fistulising Crohn's disease and ulcerative colitis. Subsequently, national Common Drug Review supported its use for these indications.

In fiscal year 2014/15, B.C. PharmaCare and other private payors in the province spent more than $100 million on Remicade®, making it B.C.'s top drug expenditure. Through national price negotiations, public drug plans negotiated a significantly lower list price of almost 50% less for Inflectra®. This price is available to all payers—public and private— garnering savings that can be invested in other health priorities.

PharmaCare coverage details

Effective November 1, 2016, all new Special Authority (SA) requests for infliximab for moderate to severe Crohn's disease, fistulising Crohn's disease will be approved for the Inflectra® brand only.

Effective November 1, 2016, PharmaCare will also start to cover Inflectra® for the treatment of ulcerative colitis as a first covered biologic for this indication.

PharmaCare will continue covering Remicade® only for patients granted Special Authority approval for that drug for the treatment of moderate to severe Crohn's disease and fistulising Crohn's disease before November 1, 2016; these patients will also be covered for the Inflectra® brand should they choose to switch (a new Special Authority form will not be required).

Coverage is, as usual, subject to the rules of a patient's PharmaCare plan, including any annual deductible requirements. Note also that PharmaCare cannot provide retroactive coverage. To secure coverage, active SA approval must be in place before the drug is dispensed.

Important: To ensure the patient`s pharmacy dispenses the Inflectra® brand when required, please specify "Inflectra" on the prescription.

For community pharmacies wishing to find out if they are eligible for ordering Inflectra®, please contact:

Email : specialtylogistics@innomar-strategies.com
Phone : 1-866-949-9927
Fax : 1-866-949-9917

For patients or health care professionals who want more information on the Inflectra® Patient Assistance Program, please contact:

Inflectra Program Call Centre
Phone: 1-844-466-6627
Fax: 1-844-295-0219

A list of BC Infusion Sites, as well as some additional information on Inflectra®, are provided in Appendix 1.

Sincerely,

Eric Lun, PharmD
Executive Director, Drug Intelligence & Optimization Branch
Medical Beneficiary and Pharmaceutical Services Division, Ministry of Health

Appendix 1

Below is the current list of clinics providing infusion support services for Inflectra®. For an updated list, or questions on how to access infusion services in a community not identified on this list, please contact:

Inflectra Program Call Centre
Phone: 1-844-466-6627
Fax: 1-844-295-0219

Clinic Name	Clinic Address	Clinic City
Burnaby Square Professional Building	7885 6th Street, unit 208	Burnaby
Innomar Kamloops	546 St. Paul St. Suite 160	Kamloops
Innomar Nanaimo	203-1450 Waddington Rd	Nanaimo
Innomar North Vancouver	#117 - 1433 Lonsdale Ave.	North Vancouver
Innomar Surrey	9648 128th Street, Unit 103	Surrey
Innomar Vancouver - Fairmont	750 West Broadway Ave, Suite 1406	Vancouver
Innomar Abbotsford	2168 McCallum Rd. Unit #2	Abbotsford
Innomar Victoria	1590 Cedar Hill Cross Rd. Suite 330	Victoria
Innomar Kelowna	3001 Tutt Street # 303	Kelowna
Innomar Cranbrook	44 12th Ave. S.	Cranbrook
Innomar Richmond	6091 Gilbert Rd. Suite #440	Richmond
Innomar Terrace	4724 Lazelle Ave	Terrace
Innomar Prince George	1811 Victoria Street, Suite 206	Prince George
Artus Health Centre	839 West Broadway	Vancouver
The Mary Pack Arthritus Centre	895 West 10th Ave.	Vancouver
G.I.R.I/Pacific Gastroentrology Assoc.	#770-1190 Hornby Street	Vancouver
Penticton Infusion Centre	725 Carmi Ave.	Penticton

Inflectra® Infusion Clinics (both physician in-office infusion clinics and INNOMAR infusion clinics) can be rapidly added as patient demand increases.

Patients living in extremely rural/remote areas can get Inflectra® infusions at local hospitals or health care sites.

Therapeutic Drug Monitoring is provided through the infusion clinic Patient Support Program.

Getting more information

For…	See…
Information on obtaining Inflectra®, infusion sites, and patient support programs	Innomar web information for health professionals www.innomar-strategies.com/about/integrated-model
PharmaCare's Drug Decision Summary	https://www.fmdb.hlth.gov.bc.ca ⇨ Select drug name from the alphabetical list
Health Canada's Summary Basis of Decision	at www.hc-sc.gc.ca/dhp-mps/prodpharma/rds-sdr/drug-med/rds-sdr-infectra-184564-eng.php
Common Drug Review—Review and Recommendation	https://www.cadth.ca/infliximab-19
Updated PharmaCare criteria and SA Request forms	www.gov.bc.ca/pharmacarespecialauthority ⇨ Select the drug name from the alphabetical list

BC PharmaCare Newsletter

November 10, 2016 Edition 16-009

Published by the Medical Beneficiary and Pharmaceutical Services Division to provide information for British Columbia's health care providers

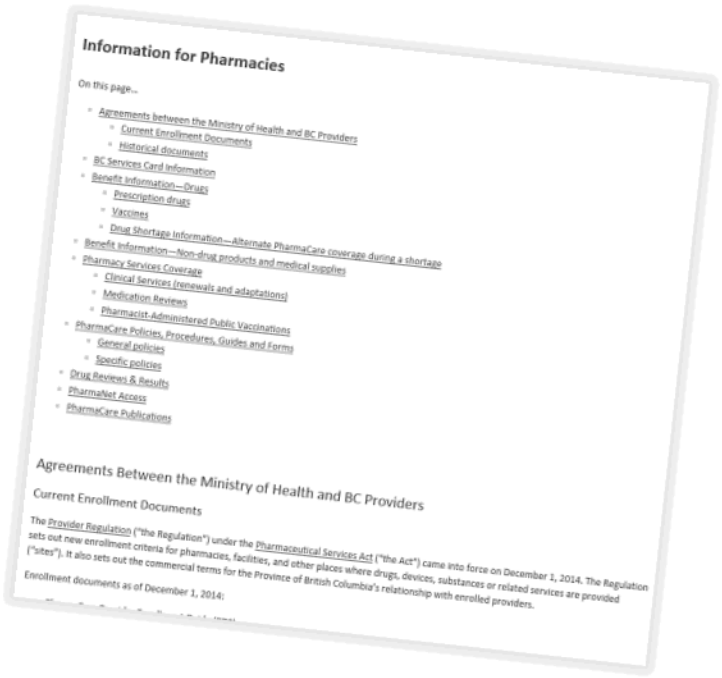
QuickLinks

PHARMACARE ONLINE RESOURCES FOR PHARMACISTS

Did you know our website provides a page dedicated to the information needs of pharmacists?

Visit www.gov.bc.ca/pharmacarepharmacists for information on:

- enrolling as a PharmaCare provider
- updating your enrollment information
- PharmaCare policies and procedures
- past newsletters
- claims information such as Product Identification Numbers and correct quantities for claims
- *and more…*



Information for Pharmacies

On this page...

- Agreements between the Ministry of Health and BC Providers
  - Current Enrollment Documents
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- BC Services Card Information
- Benefit Information—Drugs
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  - Drug Shortage Information—Alternate PharmaCare coverage during a shortage
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- Pharmacy Services Coverage
  - Clinical Services (renewals and adaptations)
  - Medication Reviews
  - Pharmacist-Administered Public Vaccinations
- PharmaCare Policies, Procedures, Guides and Forms
  - General policies
  - Specific policies
- Drug Reviews & Results
- PharmaNet Access
- PharmaCare Publications

Agreements Between the Ministry of Health and BC Providers

Current Enrollment Documents

The Provider Regulation ("the Regulation") under the Pharmaceutical Services Act ("the Act") came into force on December 1, 2014. The Regulation sets out new enrollment criteria for pharmacies, facilities, and other places where drugs, devices, substances or related services are provided ("sites"). It also sets out the commercial terms for the Province of British Columbia's relationship with enrolled providers.

Enrollment documents as of December 1, 2014:

BRITISH COLUMBIA | Ministry of Health

To subscribe or unsubscribe from our newsletter notification list, or to find out more about our programs, visit PharmaCare on the Web:
www.gov.bc.ca/pharmacare

BENEFITS

Limited Coverage Drug Program—Infliximab (Inflectra®)

Effective **Nov. 1, 2016**, PharmaCare covers infliximab (Inflectra®) as a Limited Coverage Drug through the Special Authority program for new patients requiring infliximab for the treatment of Crohn's disease or ulcerative colitis.

PharmaCare will continue covering Remicade® only for patients granted Special Authority approval for that drug for the treatment of moderate to severe Crohn's disease and fistulising Crohn's disease before Nov. 1, 2016; these patients will also be covered for the Inflectra brand should they choose to switch.

Inflectra is a "biosimilar" version of infliximab based on Remicade. Health Canada approved Inflectra on Jun. 10, 2016, for the treatment of moderate to severe Crohn's disease, fistulising Crohn's disease, and ulcerative colitis. Subsequently, the national Common Drug Review supported its use for these indications.

In fiscal year 2014/15, B.C. PharmaCare and other private payers in the province spent more than $100 million on Remicade, making it B.C.'s top drug expenditure. Through national price negotiations, the public drug plans negotiated a significantly lower list price of almost 50% less for Inflectra. This price is available to all payers – public and private – garnering savings that can be invested in other health priorities.

See the detailed Special Authority criteria.

Coverage is subject to the rules of a patient's PharmaCare plan, including any annual deductible requirement. Retroactive coverage cannot be provided for prescriptions filled before Special Authority approval is in place.

Getting more information

To find out if your pharmacy is eligible to order Inflectra, please email to specialtylogistics@innomar-strategies.com, phone 1-866-949-9927 or fax to 1-866-949-9917

To get more information on the Inflectra Patient Assistance Program, to obtain the most up-to-date list of clinics providing infusion support services for Inflectra, or for information on how to access infusion services patients and health care providers can phone the Inflectra Program Call Centre at 1-844-466-6627 or fax to 1-844-295-0219.

Clinic Name	Clinic Address	City
Burnaby Square Professional Building	7885 6th Street, unit 208	Burnaby
Innomar Kamloops	546 St. Paul Street, Suite 160	Kamloops
Innomar Nanaimo	203-1450 Waddington Road	Nanaimo
Innomar North Vancouver	#117 - 1433 Lonsdale Avenue	North Vancouver
Innomar Surrey	9648 128th Street, Unit 103	Surrey
Innomar Vancouver - Fairmont	750 West Broadway Avenue, Suite 1406	Vancouver
Innomar Abbotsford	2168 McCallum Road, Unit #2	Abbotsford
Innomar Victoria	1590 Cedar Hill Cross Road, Suite 330	Victoria
Innomar Kelowna	3001 Tutt Street # 303	Kelowna
Innomar Cranbrook	44 12th Avenue S.	Cranbrook
Innomar Richmond	6091 Gilbert Road Suite #440	Richmond
Innomar Terrace	4724 Lazelle Avenue	Terrace
Innomar Prince George	1811 Victoria Street, Suite 206	Prince George
Artus Health Centre	839 West Broadway	Vancouver
The Mary Pack Arthritis Centre	895 West 10th Avenue	Vancouver
G.I.R.I./Pacific Gastroenterology Association	#770-1190 Hornby Street	Vancouver
Penticton Infusion Centre	725 Carmi Avenue	Penticton

Changes to Palliative Care (Plan P) Formulary

Effective Dec. 1, 2016, PharmaCare will no longer cover the following medications under the BC Palliative Care Plan (Plan P):

- **Pantoprazole sodium**: Under the Modernized Reference Drug Program (RDP), pantoprazole sodium is only partially covered whereas pantoprazole magnesium and rabeprazole are fully covered. Pantoprazole magnesium and rabeprazole will, therefore, remain as regular benefits under Plan P. Pantoprazole sodium will be fully covered under Plan P only for patients who meet the current criteria for Special Authority approval.
- **Phenazopyridine**: This medication is no longer commercially available in Canada. PharmaCare does not cover compounded phenazopyridine in lieu of the discontinued commercial product.

Limited Coverage Drugs

COVERAGE EFFECTIVE	November 1, 2016		
DRUG NAME	Inflectra™ (infliximab)		
INDICATION	Crohn's disease and Ulcerative Colitis		
DIN	02419475	100 mg/vial Powder for solution	
PLAN G BENEFIT?	No		
PLAN P BENEFIT?	No		

COVERAGE EFFECTIVE	October 25, 2016		
DRUG NAME	Ferriprox™ (deferiprone)		
INDICATION	Transfusional iron overload		
DIN	02436523	100 mg/mL oral solution	
DIN	02436558	100 mg tablet	
PLAN G BENEFIT?	No		
PLAN P BENEFIT?	No		

Discontinued Benefits

As of **Dec. 10, 2016,** PharmaCare will no longer cover desiccated thyroid (Thyroid) tablets. The manufacturer increased the price of Thyroid significantly on Nov. 1, 2016. PharmaCare reviewed the price increase the manufacturer submitted and determined that other, less expensive therapeutic alternatives exist. Patients with current PharmaCare coverage for Thyroid will continue to receive coverage indefinitely.

PharmaCare will no longer cover the following products for patients being prescribed the product for the first time:

DIN	DRUG NAME
00023949	desiccated thyroid (Thyroid) 30 mg tablet
00023957	desiccated thyroid (Thyroid) 60 mg tablet
00023966	desiccated thyroid (Thyroid) 125 mg tablet