Drug Benefit Council (DBC)
Drug Review Summary
omalizumab (Xolair®)

Question for Consideration (DBC)

1. Based on the evidence provided, what is your recommendation to the British Columbia Ministry of Health (the Ministry) regarding the PharmaCare coverage status of omalizumab (Xolair®) for the treatment of asthma?

Issues for Consideration

- On November 18, 2004, omalizumab, manufactured by Novartis Pharmaceuticals Canada Inc., was granted a Notice of Compliance for the treatment of adults and adolescents (12 years of age and above) with moderate to severe persistent asthma who have a positive skin test or in-vitro reactivity to a perennial aeroallergen and whose symptoms are inadequately controlled with inhaled corticosteroids.
- On February 7, 2006, the Canadian Expert Drug Advisory Committee (CEDAC) released their Final Recommendation for omalizumab and recommended that omalizumab not be listed.
- On June 15, 2006, the Ministry decided not to list omalizumab.
- In 2015, the drug plans that participate in the Canadian Agency for Drugs and Technologies in Health (CADTH's) Common Drug Review (CDR) process requested that omalizumab be reviewed again for the treatment of asthma.
- On April 27, 2016, the Canadian Drug Expert Committee (CDEC) issued their Confidential, Embargoed Recommendation advising that omalizumab be reimbursed for adults and adolescents (12 years of age and above) with moderate to severe persistent asthma who have a positive skin test or in-vitro reactivity to a perennial aeroallergen if the following clinical criterion and conditions are met:

  Criterion:
  - Inability to use, intolerance to, or inadequate response to an inhaled corticosteroid (ICS)/long-acting beta-agonist (LABA) combination and at least one other reimbursed alternative asthma treatment.

  Conditions:
  - Patients should be managed by a physician with experience in treating asthma; and
  - At a reduced price.
- Currently, omalizumab is under review by the Ministry for the treatment of chronic idiopathic urticaria.
- Numerous therapeutic choices are currently available for the treatment of asthma as regular benefits or Limited Coverage drugs with criteria.

- The following drugs are regular benefits:
  - fluticasone propionate (Flovent HFA, Flovent Diskus);
  - ciclesonide (Alvesco);
  - mometasone furoate (Asmanex Twisthaler);
  - budesonide (Pulmicort Turbuhaler);
  - beclomethasone dipropionate (QVAR); and oral corticosteroids.
- The following drugs are Limited Coverage benefits with criteria. (See Appendix 1):
  - fluticasone propionate-salmeterol (Advair Diskus, Advair MDI);
  - budesonide-formoterol (Symbicort Turbuhaler); and
  - mometasone furoate-formoterol fumarate (Zenhale).
- The following drugs are not eligible PharmaCare benefits:
  - montelukast (Singulair, generics); and
  - zafirlukast (Accolate).
- The following drugs are currently under review for asthma:
  - fluticasone furoate (Arnuity Ellipta); and
  - fluticasone furoate-vilanterol trifenatate (Breo Ellipta).
- The DBC and CDR Patient Input reports are available on the DBC SharePoint site.

Generic name/Brand Name
omalizumab (Xolair)

Dosage Forms/Strengths
150 mg vial for subcutaneous injection

Manufacturer
Novartis Pharmaceuticals Canada Inc.

Health Canada Approved Indications
omalizumab (Xolair) is indicated for:

- adults and adolescents (12 years of age and above) with moderate to severe persistent asthma who have a positive skin test or in-vitro reactivity to a perennial acroallergen and whose symptoms are inadequately controlled with inhaled corticosteroids.
- the treatment of adults and adolescents (12 years of age and above) with chronic idiopathic urticaria (CIU) who remain symptomatic despite H1 antihistamine treatment.

Disease state overview
Asthma is a common chronic respiratory disorder characterized by reversible airway obstruction, pulmonary inflammation, airway hyper-responsiveness and airway remodeling. Described by a range of heterogeneous phenotypes, symptoms may differ by presentation, etiology, and pathophysiology. Patients with asthma typically present with paroxysmal or persistent symptoms of wheezing, dyspnea, chest tightness, sputum production and coughing that are associated with

airflow limitation and airway hyper-responsiveness to endogeneous and exogenous stimuli (e.g., exercise; viral respiratory infections; or exposure to certain allergens, irritants or gases). Although asthma can be diagnosed at any age, it often starts in childhood. In 2015, Statistics Canada estimated that 2.4 million Canadians aged 12 and older had a diagnosis of asthma, representing 12% of all Canadian children and 8% of all Canadian adults. Only a small subset of allergic asthma are moderate to severe asthma who are inadequately controlled with the current guideline recommended standard stepwise approach, such as combination therapy of an inhaled corticosteroid and a long-acting beta2-adrenergic agonist with or without additional asthma controllers such as leukotriene receptor antagonists. *(Please see Common Drug Review Clinical and Pharmacoeconomic Review Report on page 13 of 83)*

An estimated 300 million people are affected by asthma worldwide and the burden is likely to rise substantially in the next few decades. Estimates of the prevalence of asthma range from 7% in France and Germany to 11% in the USA and 15–18% in the United Kingdom. Approximately 20% of these patients have severe asthma, of which 20% is inadequately controlled.[1]

Comparative Cost of Therapy and Current Coverage Status of Comparators Drugs with 8 % mark-up Unless Otherwise Noted

Drug / Comparator	Strength	Dosage Forms	PharmaCare Status	Cost/Unit ($)	Recommended Daily Dose	Annual Cost of Therapy
omalizumab (Xolair)	150 mg	Vial	Under Review/ Non-Benefit	**642.60**	150 to 375 mg is administered SC every 2 or 4 weeks	**$8,354 - $50,123***
Inhaled Corticosteroid (ICS)						
fluticasone propionate (Flovent HFA)	50 mcg 125 mcg 250 mcg	MDI (120 doses)	Regular Benefit	0.22 0.37 0.74	100 mcg 250 mcg 500 mcg twice daily	$314 - $1,084
fluticasone propionate (Flovent Diskus)	100 mcg 250 mcg 500 mcg	Inhalant powder (60 doses)	Regular Benefit	0.43 0.74 1.16	100 mcg 250 mcg 500 mcg twice daily	$314 - $847
ciclesonide (Alco)	100 mcg 200 mcg	Actuation Inhalation (120 doses)	Regular Benefit	0.41 0.68	100/200 mcg twice daily	$299 - $495

[1] Sves.P. Peters, et. al. Uncontrolled asthma: A review of the prevalence, disease burden and options for treatment. Respiratory Medicine, Volume 100, Issue 7, Pages 1139–1151
http://www.sciencedirect.com/science/article/pii/S0954611106001788

Comparative Cost of Therapy and Current Coverage Status of Comparators Drugs with 8 % mark-up Unless Otherwise Noted						
Drug / Comparator	**Strength**	**Dosage Forms**	**PharmaCare Status**	**Cost/Unit ($)**	**Recommended Daily Dose**	**Annual Cost of Therapy**
mometasone furoate (Asmanex Twisthaler)	200 mcg 400 mcg	Inhalant powder (60 doses)	Regular Benefit	0.58 1.17	200/400 mcg once daily	$213 - $426
budesonide (Pulmicort Turbuhaler)	100 mcg 200 mcg 400 mcg	Inhalant powder (200 doses)	Regular Benefit	0.17 0.34 0.50	100/200/400 mcg twice daily	$123 - $366
beclomethasone dipropionate (QVAR)	50 mcg 100 mcg	Metered Dose Aero Inhalation (200 doses)	Regular Benefit	0.17 0.34	Total dose of 100 to 800 mcg, dosed twice daily	$123- $245
ICS/LABA Combinations						
fluticasone furoate-vilanterol trifenatate (Breo Ellipta)	100/25mcg 200/25mcg	Inhalant powder (30 doses)	Limited Coverage	4.32	100/25 mcg or 200/25 mcg once daily	$1,577
budesonide-formoterol (Symbicort Turbuhaler)	100/6 mcg 200/6 mcg	Inhalant powder (120 doses)	Limited Coverage	0.58 0.76	100/6 mcg or 200/6 mcg twice daily	$424 - $551
fluticasone propionate-salmeterol (Advair MDI)	125/25mcg 250/25mcg	MDI (120 doses)	Limited Coverage	0.88 1.24	125/25 mcg or 250/25 mcg twice daily	$1,280 - $1,817
fluticasone propionate-salmeterol (Advair Diskus)	100/50mcg 250/50mcg 500/50mcg	Inhalation powder (60 doses)	Limited Coverage	1.47 1.75 2.49	100/50 mcg or 250/50 mcg or 500/50 mcg twice daily	$1,069 - $1,818
mometasone furoate-formoterol fumarate (Zenhale)	50/5mcg 100/5mcg 200/5mcg	MDI (120 doses)	Limited Coverage	0.55 0.72 0.88	100/10 mcg 200/10 mcg 400/10 mcg twice daily	$807 - $1,291
Leukotriene Receptor Antagonists (LTRA)						
montelukast (Singulair, generics)	4 mg 5 mg 10 mg	Tablet	Non-Benefit	1.18 1.30 1.92	Age 6-14: 5mg daily Age ≥15: 10mg daily	$475 - $699
zafirlukast (Accolate)	20 mg	Tablet	Non-Benefit	0.84	20 mg twice daily	$613

* with 5 % markup

Key Outcome Measures

Primary Outcomes
- Hospitalizations, emergency room visits, medical doctor visits due to asthma exacerbation
- Acute asthma exacerbations
- Use of oral corticosteroids
- Quality of life
- Days of missed school or work

Secondary Outcomes
- Change in pulmonary function (forced expiratory volume in one second (FEV1))
- Symptom reduction (e.g.; Asthma control questionnaire (ACQ), asthma control test (ACT), Asthma Quality of Life Questionnaire (AQLQ))
- Change in number of asthma symptom-free days/nights
- Incidence of nocturnal awakenings
- Reduction of use of inhaled corticosteroid
- Reduction of use of rescue medications (short-acting beta-agonist or short-acting muscarinic antagonist)
- Mortality

Harms
- Adverse events
- Serious adverse events
- Withdrawals due to adverse events
- Notable adverse events/adverse events of special interest: anaphylaxis, Churg–Strauss syndrome, injection site reaction, and thromboembolic events.

Patent Expiry Date
July 23, 2016

Data Protection Date
None

Known Unapproved or Potential Indications for Use
According to UpToDate, omalizumab has been reported to be helpful in the management of food allergy, nasal polyposis, idiopathic anaphylaxis, allergic rhinitis, venom hypersensitivity and atopic dermatitis.[2]

[2] http://www.uptodate.com/contents/anti-ige-therapy?source=search_result&search=omalizumab&selectedTitle=5%7E66#H658225490

Adverse Drug Reaction Reporting from Health Canada as of May 4, 2016
3,360 adverse reactions, including 27 deaths were reported until December 31, 2015.

Health Canada Issues
On August 13, 2009, Health Canada issued the following Information Update:

> Archived: Health Canada is informing health care professionals and Canadians that it is conducting a safety review of the potential association between the asthma drug Xolair (the brand name for the drug omalizumab) and an increased risk of cardiovascular problems.
>
> The review comes in light of the interim findings of an ongoing study in the U.S. to assess the long-term safety profile of Xolair. The interim data suggests a disproportionate increase in cardiovascular problems among patients treated with Xolair relative to patients not treated with the drug. The problems reported include: heart attacks, abnormal heart rhythms, heart failure, fainting, mini-strokes, and blood clots.
>
> In Canada, Xolair is indicated for the treatment of asthma in people 12 years old and older who have moderate to severe persistent asthma, who react to airborne allergens and whose symptoms are not adequately controlled with inhaled corticosteroids.
>
> The study, entitled *Evaluating the Clinical Effectiveness and Long-Term Safety in Patients with Moderate to Severe Asthma* (EXCELS), is an observational study of approximately 5,000 patients who use Xolair and a control group of approximately 2,500 patients who do not. Study participants are 12 years of age and older with moderate to severe persistent asthma and who have an allergy to an airborne substance, such as pollen or spores. The final results of the five-year study are expected in 2012. *(Health Canada did not provide an update to this advisory).*
>
> At this time, Health Canada recommends that patients not stop taking Xolair without first speaking to their doctor. Patients should contact their health care professional if they have any concerns about the medicines they are taking.
>
> Health Canada has not concluded that there is a relationship between Xolair and cardiovascular problems. The Department is assessing the interim findings of this ongoing study as well as working with the market authorization holder, Novartis Pharmaceuticals Canada, to obtain further information. Should new safety information emerge from the review, Health Canada will inform Canadians and health care professionals and take appropriate action as necessary.

Miscellaneous Issues
None

Appendix 1

Limited Coverage Drugs - Special Authority Criteria

Generic Name / Strength / Form
salmeterol **OR** salmeterol in combination with fluticasone

Criteria	Approval Period
1. Diagnosis of asthma **PLUS** inadequate response on optimal dose of inhaled corticosteroid, **OR** 2. Diagnosis of COPD **PLUS** inadequate response on optimal short acting beta agonist therapy.	Indefinite

Practitioner Exemptions

Respirologists

Allergists

Special Notes

None

Online Form (PDF, 523KB)
Click on the link to complete a special authority request form.

Limited Coverage Drugs - Formoterol

Generic Name / Strength / Form
formoterol **OR** formoterol in combination with budesonide

Special Authority Criteria	Approval Period
Diagnosis of asthma **PLUS** inadequate response on optimal dose of inhaled corticosteroid.	Indefinite

Practitioner Exemptions

Allergists

Respirologists

Special Notes

None

Special Authority Request Form(s)

Online Forms (PDF, 523KB)
Click on the link to complete a special authority request form.

Limited Coverage Drugs – Vilanterol in combination with fluticasone furoate

Generic Name / Strength / Form
vilanterol in combination with fluticasone furoate / 25 mcg vilanterol - 100 mcg fluticasone furoate / dry powder inhaler

Special Authority Criteria	Approval Period
Diagnosis of chronic obstructive pulmonary disease (COPD) **PLUS** inadequate response on optimal short acting beta agonist therapy.	Indefinite

Practitioner Exemptions

Practitioners in the following specialties are not required to submit a Special Authority request form for coverage: respirologists.

Special Notes

None

Special Authority Request Form(s)

5328 - General Special Authority Request (PDF, 523KB)

Clinical Practice Review Report – CPR Specialist

Drug Product Generic name (Brand name)	**Omalizumab (Xolair)**
Manufacturer **(Distributor if applicable)**	**Novartis Pharmaceuticals Canada Inc**

Background on Clinical Practice Review (CPR) reports:
Prior to deciding whether or or not to list a particular drug, and how, the Ministry receives a recommendation from its independent advisory committee the Drug Benefit Council (DBC). The DBC is made up of nine professional members with expertise in critical appraisal, medicine, ethics, pharmacy and health economics, and three members of the public.

To inform DBC recommendations, the BC Ministry of Health (the Ministry), in partnership with the UBC Faculty of Medicine, Division of Continuing Professional Development, seeks clinical input, in the form of CPR reports, from clinicians to inform drug coverage decisions.

Broadly, your review includes:

- Reviewing documents, including budget analyses, available literature (mainly executive summaries) and interpretation of the evidence for the specified indication, and a national Common Drug Review (CDR) drug listing recommendation (if applicable).
- Preparing a concise, yet informative review that is likely to be 3 to 5 pages in length. Reviewers are NOT expected to re-write or to prepare clinical trials.
- Responding to the questions provided and explaining if the documents and analysis fits YOUR experience (including within your peer group).
- Providing examples of other factors to consider regarding the medication in question (e.g., its impact on your practice and patients, clinical trial data you are aware and that was not included in the analysis).
- Discussing whether the documents and analysis are what you see or expect to see in BC (e.g., disease prevalence, standards of therapy).
- Informing if you agree/disagree with the Common Drug Review listing recommendation (if applicable).
- Sending in more information that you think the DBC should take into account (this is an option and NOT a requirement or expectation).

A high quality report balances evidence-based information with clinical practice experience, and is an important factor in DBC drug coverage recommendations to the Ministry.

Question 1: Based on the Common Drug Review (CDR) Clinical Evidence Review Report, please provide your expert opinion and comments with respect to the following, including applicability to the British Columbia context (length up to 2 pages):

(a) Disease prevalence/incidence

In 2015 Statistics Canada estimated that 2.4 million Canadians 12 and older and a diagnosis of asthma. This represents 12% of all Canadian children and 8% of all Canadian adults. Of these, approximately half of asthma patients are atopic. The most recent asthma statistics suggests that the prevalence of asthma in BC has increased steadily since 2000/01 with an age standardized prevalence rate for 2012/2013 of 10.53% or an estimated 323,500 prevalent cases. Although deaths due to asthma have decreased over the past ten years over 50% of patients have asthma that is not well controlled, which leads to increased health care costs and loss of productivity and work losses.

(b) Standard of Therapy

Asthma is treated using multi-modality therapy including pharmaceutical therapy according to a stepwise approach as recommended by the BC Thoracic Society Guidelines. This stepwise approach emaphasizes the importance of regular inhaler therapy to prevent exacerbations and worsenings of asthma. Titration of inhaler therapy depends on level of asthma control, with recommended initial therapy being inhaled corticosteroids at low to moderate doses. If asthma control is still not achieved, add on therapy is recommended with the addition of a LABA (long acting beta agonist) or LTRA (leukotriene receptor antagonist). A small percentage of patients, despite being compliant with regular ICS/LABA and LTRA continue to suffer from asthma worsenings and exacerbations. For these patients, additional therapies such as omalizumab has been shown to improve quality of life, lessen exacerbations, hospitalisations and reduce the need for prednisone therapy.

(c) Identify appropriate patients to receive drug therapy

Appropriate patients to receive omalizumab are patients greater than age 12 with moderate to severe persistent asthma who have a positive skin test or in-vitro reactivity to a potential aeroallergen and whose symptoms are not controlled on ICS/LABA.

(d) Potential product utilization, including potential off-label use

Omalizumab is appropriate therapy, as mentioned above, for moderate to severe persistent asthma and a positive skin test to a potential aeroallergen and symptoms not controlled on ICS/LABA. In addition, potential off label use of omalizumab may incude other IgE mediated diseases such as chronic urticaria, severe allergic rhinosinusitis and allergic bronchopulmonary aspergillosis.

(e) Desired treatment outcome goals

There are a few desired treatment goals including improved asthma related quality of life (less nocturnal awakenings, less asthma symptom-free days/nights) and reduced asthma exacerbations resulting in reduction in the need for systemic corticosteroids. In addition one also expects less office visits, less ER visits, less hospitalisations and less days of missed school or work although the scientific evidence for this is not as impressive as the first 2 outcomes. Although there is an improvement in FEV1, the improvement is marginal.

(f) any other considerations missed

Despite the presence of effective therapies for the treatment of asthma, there continues to be a minority of patients who are not adequately controlled. These patients suffer with severe exacerbations requiring intermittent or occasionally, daily systemic corticosteroid therapy and multiple ER visits. Omalizumab provides the only therapy that is available for these patients to achieve better asthma control and lessen the need for systemic steroid therapy.

Question 2: The Manufacturer's Budget Impact Analysis is provided as a reference. Please comment and provide your expert opinion, with respect to the following (length up to 1 page):

Budget Impact Analysis for omalizumab was not available.

(a) Comparator drugs and appropriate doses:
Although there are a multitude of drugs that are available for the treatment of mild to moderate asthma as has been tabulated in the "Comparative Cost of Therapy" table, there are at this point, no drugs that are in the class of Omalizumab i.e. biological therapy.

(b) Switching rate

(c) Appropriateness of identified patient group

(d) any other considerations missed

Question 3: The Common Drug Expert Committee (CDEC) Confidential EMBARGOED Recommendation is provided for your review and consideration. Please provide your comments and opinions regarding the recommendation and reasons for recommendation as the following:

Agree as stated
Agree with modifications (length up to 1page)
Disagree with detailed reasons (length up to 2 pages)

My opinion is "Agree with Modifications"
I would prefer the criterion for approval be changed to "Inability to use, intolerance to, or inadequate response to an inhaled corticosteroid (ICS) long-acting beta-agonist comination, and ***have tried one other alternative asthma treatment.***
The criterion as mentioned in CADTH recommendation limits the alternative agent to only tiotropium as this is the only re-imbursed treatment in BC. Some patients will respond to ICS/LABA + Leukotriene receptor blocker, however, LTRA is not reimbursed in BC.

<u>Question 4</u>: Are there other clinical practice considerations deemed relevant to the drug review submission that are not discussed by the CDR Clinical Review Report or CDEC Recommendation or Reasons for Recommendation? (length up to 1 page)

Omalizumab has been available in BC for slightly over 10 years. Although the drug has not been covered by BC Pharmacare, patients have been using the drug reimbursed by private insurance companies and occasionally funded by pharmacare through special access. I personally have had approximately 15-20 patients on omalizumab over the last few years, and generally, have found the drug extremely successful in managing my patients with severe, often steroid dependent asthma. I can remember at least 2 cases where the drug allowed these patients to wean off very high doses of prednisone to the current state where there asthma is controlled on just inhaler therapy and omalizumab. For these patients, the drug has been a true life saver.

It is important to note that the vast majority of patients with asthma are controlled on standard therapies i.e. ICS/LABA, LTRA or LAMA, as long as compliance has been established. However, as respirologists we often see patients who exhibit poor control and have frequent exacerbations requiring systemic steroid therapy despite adequate inhaler therapies. For these patients, if atopic, omalizumab provides an option with very good success.

Patient Input for omalizumab (XOLAIR®) 3445 for the treatment of Severe, Persistent Asthma from Patients, Caregivers and Patient Groups

Prepared for:

Members of the Drug Benefit Council (DBC)

DBC Meeting:

Meeting held: June 6, 2016 8:30 am – 12:30 pm

Number of Eligible Questionnaires:

Patients (3), Caregivers (0), Patient Groups (1) (see Appendix A for details)

Participating Patient Group

The following patient group, who met the criteria for inclusion in this report, provided input to the Ministry of Health (Ministry) for its review of omalizumab (XOLAIR®) 3445:

- The Asthma Society of Canada
  - 401-124 Merton St, Toronto ON M4S 2Z2

Source:

Your Voice website - questionnaires posted from Wednesday March 23, 2016 to midnight on Wednesday April 20, 2016.

Conflict of Interest Declarations

Patient Responses:

The patients who completed questionnaires reported no potential conflicts of interest.

Patient Group Responses:

The patient group who completed a questionnaire reported the following potential conflicts of interest.

Patient Group	Potential Conflicts of Interest
The Asthma Society of Canada	The Asthma Society of Canada receives unrestricted grants to support educational programming and advocacy from the pharmaceutical industry. Total industry funding comprises less than 20% of our overall funding. in 2015 funds (greater than $5,000) were received from the following pharmaceutical companies: GlaxoSmithKline, Merck, Novartis, Roche, Teva, Sanofi, AstraZeneca, Boehringer-Ingelheim, Takeda, Innovative Medicines Canada and Johnson & Johnson.

The PharmaCare Drug Information Page

Patient Responses:

Two of the three patients who completed questionnaires reported they had read the PharmaCare Drug Information page.

Patient Group Responses:

The patient group representative who completed a questionnaire reported they had read the PharmaCare Drug Information page.

Responses to Drug-related Questions:

Question 9
Describe how the medical condition or disease which the drug under review would be used for affects the day-to-day lives of patients.

Patient Responses:
1.s.22

s.22

2

3

Patient Group Responses:

1. Canadian specific studies show that up to 53% of Canadian patients with asthma are poorly controlled. Severe Asthma is a chronic condition that limits social activities and leads to a decline in health. People with Severe Asthma remark about how the condition isolates them " it is hard to stay social with unpredictable flare-ups, and it becomes difficult to stay active when physical exertion exacerbates Severe Asthma. The physical toll the disease takes on the patient is often followed by a social toll, and it is not uncommon to hear Severe Asthma patients lament how diminished they feel about themselves and how Severe Asthma strains their family life. One man says that Severe Asthma keeps him from doing the things he loves, s.22
s.22 Severe Asthma has changed everything,' he says.Activities that other Canadians take for granted continue to be the dream of people with Severe Asthma. A significant number of patients indicated that the most important aspect of their asthma to control was the ability to sleep without night-time symptoms with 87% selecting this choice. Additionally, 75% indicated daytime exacerbations (attacks) were the most important aspect to control. A slightly smaller number identified medication cost and frequency of dosage as the most important aspect. Patients clearly identified that when it comes to controlling their asthma, the key factors are the ones that directly impact their overall health and well-being.Patients were asked how asthma directly affected their day to day life. More than 7 in 10 (71%) indicated that asthma limits the type and amount of physical activity making it more difficult and unlikely for them to get sufficient exercise. More than half (55%) mentioned that the lost productivity of their asthma, having to miss days of work or school had a significant impact. 40% indicated that their Severe Asthma affected their work or school 'a great deal'. Other options of note was the negative stigma of asthma (64.6%) and the impact of asthma on their family and/or caregiver (80%).Finally, patients were asked if there were activities which they were unable to do as a result of their asthma. Overwhelmingly, the participants indicated that physical activities, such as exercising and spending time outdoors was the area where they were the most limited, with 80% selecting that option. 87% noted that their asthma impacted their sleep, while 66% felt that their asthma impacted their ability to participate in social activities. Other feedback received included patients who indicated their asthma affected their job opportunities, their personal relationships and day-to-day housework and home upkeep.

Question 10
What drugs or other treatments has the patient used, either now or in the past, to treat the medical condition or disease which the drug under review would be used for?

Patient Responses:
1. s.22

2.

3.

Patient Group Responses:
1. Asthma, the third-most common chronic disease in Canada, affects nearly 3 million Canadians. Severe Asthma (SA), a more severe form of asthma and a greater threat to health, impacts the health and wealth of between 150,000 and 250,000 Canadians. Our patient survey participants were screened to ensure that all had Severe Asthma.For many, asthma is not controlled. Only 17% of the study's respondents believe their asthma is well controlled. Half believe their asthma is adequately controlled, 27% believe their asthma is not well controlled and 8% don't believe their asthma is controlled at all.Many patients report going through several years of trying different medications before finding the medication, or combination of medications, that will keep their asthma manageable. Some participants report having spent up to seven years experimenting with treatments before finding the right treatment. Financial challenges create significant barriers to better health outcomes. Many patients cannot afford their medication and many insurance carriers do not provide complete coverage to asthma patients. The expense of medications causes additional stress for many patients. A significant number of participants did not have complete coverage (if any) and reported skipping or delaying their prescription until they could afford it. One participant indicated that he simply cannot afford the treatment recommended by his doctor. 'Asthma is very expensive,' explains one participant. 'People don't realize how much the asthma drugs cost. When you are on a disability pension, even when insurance covers three-quarters, the other 25% kills you.' The majority of

respondents to the study reported that they use asthma medications on a daily basis. Most respondents (83.5%) use their controller medication daily, with 71.1% using it at least twice per day. Many respondents (42.2%) use their reliever medication daily, with 28.8% using it at least twice per day.A surprising number of patients are not receiving information about the newest kinds of therapies for their asthma. Only 27.4% of respondents felt that they had access to information and services for newer treatment options for Severe Asthma. Patients knew little about new biologics available for treatment of Severe Asthma and none had heard of bronchial thermoplasty despite its availability in several centres geographically near interview participants.

Question 11
If the patient has tried the drug under review, please tell us about the effects they experienced.

Patient Responses:
1. s.22

2.

3.

Patient Group Responses:
1. No response

Question 12
How can patients benefit from using the drug under review?
(For example: relief of existing symptoms; improvement in quality of life; or improvements to their condition and long-term health and well-being. Please provide details.)

Patient Responses:
1. s.22

s.22

2.

3.

Patient Group Responses:

1. It is not uncommon for asthma patients to journey through an experimentation with a multitude of pharmaceutical treatment options before finding the right combination to achieve optimal control of symptoms. Numerous patients interviewed indicated they had been prescribed upwards of 10 medications over their lifetime before finding the appropriate treatment. This often coincided with an eventual diagnosis of Severe Asthma. As the only available biologic treatment for Severe Asthma currently available in Canada, Xolair represents a new treatment option which could benefit asthma patients who have not previously been able to achieve proper control of their disease. Of the 196 patients who completed the quantitative online survey, 9 indicated that they were currently taking Xolair. Patients provided valuable responses to questions about their asthma treatment, control and barriers to optimal management. Patient's anecdotal comments were also included. When asked about how many times they needed to take medication for relief of coughing, wheezing, chest tightness or shortness of breath, one patient taking Xolair responded 'most of my symptoms have gone away since I have been on Xolair, which I started 1 year ago.' This is not dissimilar to comments we receive from other asthma patients from across the country in phone calls and emails to our office.Interesting comparisons emerged of those patients surveyed who indicated they were taking Xolair, versus the remaining patients who participated. For example, when asked how many times in the last 12 months they had been to an emergency department for asthma, 83% of Xolair patients had zero visits, while only 52% of the main surveyed population answered similarly. When asked how many times they'd been admitted to hospital with asthma, 100% of Xolair patients answered zero, while 81% of the main surveyed population replied similarly. Finally, when asked if they had missed work or school because of asthma in the past 12 months, 83% of Xolair patients replied no, compared to 51% of the general surveyed population.Patients were asked to describe their ideal treatment option. 50% felt that the frequency and convenience was very important. Meanwhile, 83% felt it was somewhat or very important that the drug be affordable to patients, and that it work quickly. Patients were evenly split on the favourability of receiving medication by injection once per month with 50% liking it a lot and 33% neither disliking it or liking it

and 17% somewhat disliking it. However when asked to choose between a pill once per day, an injection once per day, an inhaler once per month, a pill once per month and an injection once per month, 50% selected the once per month injection. Finally, patients were asked what else government and/or private payer plans could do to provide patients with adequate coverage for medications to treat their asthma. 83% indicated they'd want more of full coverage of medication costs, 67% of respondents selected lower the cost, assist or provide better coverage for low income families, cover more/better treatment options and invest in research for new treatments. These concerns about cost are emphasized by the fact that 50% of those surveyed had been denied coverage for Severe Asthma treatments by their insurance company or government insurance programs in the past.

Question 13
Are there any additional factors you would like PharmaCare to consider during its review of this drug?
(For example, does the drug meet any special patient needs that have not been met by other drugs or treatments, is the drug easier to use than other drugs, does the drug reduce visits to the hospital, does the drug reduce days off work or school, or are the drug's side effects acceptable or intolerable?)

Patient Responses:
1. s.22

2.

3.

Patient Group Responses:
1. No response

Appendix A – Number of Eligible Questionnaires for omalizumab (XOLAIR®) 3445 for the treatment of Severe, Persistent Asthma

Introduction:

In order for a response to be eligible for inclusion in this report, the respondent:

- must meet the eligibility criteria in question one of the questionnaire;
- must answer all mandatory questions in the personal information and conflict of interest sections of the questionnaire;
- must answer at least one drug-related question; and
- must, if responding on behalf of a patient group:
  - identify the patient group they are representing; and
  - ensure that the patient group has registered with the Ministry of Health (the Ministry) to provide input.

Patients:

Three patients provided input to the Ministry for its review of omalizumab (XOLAIR®) 3445.

These met the criteria listed above for inclusion in this report. We have included all information from these inputs in this report.

Caregivers:

No caregivers provided input to the Ministry's review of omalizumab (XOLAIR®) 3445.

Patient Groups:

One patient group provided input to the Ministry for its review of omalizumab (XOLAIR®) 3445.

This met the criteria listed above for inclusion in this report. We have included all information from this input in this report.

MINISTRY OF HEALTH
DECISION BRIEFING NOTE

Cliff # 1074210

PREPARED FOR: Tijana Fazlagic, Director - **FOR DECISION**

TITLE: Drug Review Listing Decision for omalizumab (Xolair®) for the Treatment of Chronic Idiopathic Urticaria

PURPOSE: To make a drug listing decision for omalizumab (Xolair®) for the treatment of chronic idiopathic urticarial.

BACKGROUND:

- On August 26, 2014, omalizumab (Xolair), manufactured by Novartis Pharmaceuticals Canada Inc., received Health Canada Notice of Compliance for the treatment of chronic idiopathic urticaria (CIU).
- Omalizumab for the treatment of CIU was reviewed by the Common Drug Review (CDR) and on May 7, 2015, the Canadian Drug Expert Committee (CDEC) recommended that omalizumab be reimbursed in accordance with the Health Canada-approved indication for the treatment of CIU if the clinical criterion and conditions are met (Appendix 1).
- On June 1, 2015, the Drug Benefit Council (DBC) recommended that omalizumab be listed for the treatment of CIU who remain symptomatic despite H1-antihistamine treatment, if the following clinical criterion and conditions are met (Appendix 2):
  Clinical Criterion:
  - To be prescribed by specialists only.
  - For patients with moderate to severe CIU who remain symptomatic (i.e. presence of hives and/or associated itching) despite optimum management with available oral therapies; 300 mg dosage only; coverage duration only for 24 weeks.

  Condition:
  - Significant reduction in price.
- Omalizumab for the treatment of asthma was re-submitted for a CDR by the participating drug plans due to the availability of new evidence since the CDR review in 2006. On May 18, 2016, the CDEC recommended that omalizumab be reimbursed for the treatment of asthma, with clinical criterion and conditions.
- Omalizumab for the treatment of asthma is under review by the Ministry, but the Special Authority reviews requests on exceptional case-by-case for this indication.
- Treatments indicated for the treatment of CIU include the H1 antihistamines. H1 antihistamines are available as non-prescription drugs and are not eligible PharmaCare benefits. PharmaCare generally does not provide coverage for non-prescription drugs.
- Other treatments options that are not indicated for CIU and are not PharmaCare benefits include montelukast (generics) and cyclosporine (generics). Cyclosporine is a Limited Coverage benefit for other conditions.

DISCUSSION:

- In their review, the Ministry considered the final review completed by the CDR, which included clinical and pharmacoeconomic evidence review material and the recommendation from CDEC and DBC, Clinical Practice Reviews from two specialists, a patient input from three patients, as well as a Budget Impact Assessment (BIA).
- Three randomized controlled trials (RCTs) demonstrated that omalizumab resulted in statistically superior improvements in the symptoms of CIU compared to placebo in

patients with CIU refractory to H1-antihistamines. There are no studies directly comparing omalizumab against less costly oral drugs for the treatment of CIU.

- Based on CDR analysis, omalizumab is not cost-effective when used as either second-line, or third- or fourth-line drug in patient refractory to H1-antihistamines.
- The Ministry participated in the pan-Canadian Pharmaceutical Alliance (pCPA) negotiations with the manufacturer. The participating jurisdictions were willing to accept the manufacturer's proposal for omalizumab as a second- or third-line treatment option whereas the Ministry was seeking criteria that would allow coverage for omalizumab as a fourth-line treatment. As such, the Ministry opted to withdraw from the pCPA negotiations for omalizumab.

FINANCIAL IMPLICATIONS:

- Annual cost of omalizumab for the treatment of CIU is $8,354 to $16,708.
- The BIA that was prepared for the DBC was based on omalizumab being listed as second-line treatment option, but the Ministry did not prepare a BIA for fourth-line coverage. However, the PharmaCare listing is expected to represent significant incremental budget impact.

OPTIONS:

Option 1: Effective November 29, 2016, do not list omalizumab (Xolair) for the treatment of CIU as an eligible PharmaCare benefit.

Pro: Consistent with the DBC and CDEC recommendation that optimum management with available oral therapies must be tried first and substantial reduction in price is needed. The Ministry would not incur a significant incremental budget impact.

Con: Treatment option is not covered for patients where other treatment options have not been successful.

s.13,s.17

RECOMMENDATION:

Option 1

T. Fazl

Approved
Tijana Fazlagic, Director
Formulary Management

November 29, 2016
Date Signed

Program ADM/Division:	Barbara Walman, ADM, Pharmaceutical Services
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Program Contact (for content):	Tijana Fazlagic, Director – Formulary Management
Drafter:	Edmond Margawang
Date:	November 16, 2016

File Name with Path: **P:\DIO-FM-Access Restricted\Drugs 70325-30\omalizumab\omalizumab (Xolair) 3366 CDR\Decision Briefing Note\omalizumab (Xolair) 3366 DBN.docx**

CDEC FINAL RECOMMENDATION

OMALIZUMAB
(Xolair — Novartis Pharmaceuticals Canada Inc.)
Indication: Chronic Idiopathic Urticaria

Recommendation:
The Canadian Drug Expert Committee (CDEC) recommends that omalizumab be listed for the treatment of adults and adolescents with chronic idiopathic urticaria (CIU) who remain symptomatic despite H_1 antihistamine treatment, if the following clinical criterion and conditions are met:

Clinical criterion:
- Moderate to severe CIU who remain symptomatic (presence of hives and/or associated itching) despite optimum management with available oral therapies

Conditions:
- Substantial reduction in price
- Six-month initial course of treatment.

Reasons for the Recommendation:
1. Three randomized controlled trials (RCTs) (ASTERIA I, ASTERIA II, and GLACIAL) demonstrated that 12 weeks of omalizumab 150 mg or 300 mg administered every four weeks resulted in statistically significant improvements in the symptoms of CIU (as measured with the Urticaria Activity Score over seven days [UAS7]).
2. Controlled efficacy data from the included trials were limited to 24 weeks of treatment; therefore, the available evidence does not support initial treatment beyond 24 weeks.
3. At the submitted price of $612.00 per vial, the CADTH Common Drug Review (CDR) estimated that the incremental cost per quality-adjusted life-year (QALY) for omalizumab 300 mg plus standard of care (SOC) versus SOC alone exceeds $120,000 per QALY; therefore, omalizumab is not considered to be cost-effective at the submitted price.

Of Note:
CDEC noted that some patients with CIU may benefit from re-treatment with omalizumab after 24 weeks; however, there were no data available to evaluate the efficacy and safety of omalizumab in patients requiring re-treatment.

Background:
Omalizumab is a humanized, recombinant, immunoglobulin G (IgG) monoclonal antibody that binds to immunoglobulin E (IgE) and prevents it from binding to its high-affinity receptor on mast cells and basophils, thereby reducing IgE-induced mast cell and basophil degranulation and the release of histamine. Omalizumab is indicated for the treatment of CIU in adults and adolescents who remain symptomatic despite H_1 antihistamine treatment, and for the treatment of moderate to severe persistent asthma in adults and adolescents whose symptoms are inadequately controlled with inhaled corticosteroids.

Omalizumab is supplied as a lyophilized, sterile powder in a single-use vial designed to deliver 150 mg of omalizumab for subcutaneous (SC) injection upon reconstitution. For the treatment of CIU, omalizumab is administered by a health care provider every four weeks at a dose of 150 mg or 300 mg.

Summary of CDEC Considerations:
CDEC considered the following information prepared by CDR: a systematic review of RCTs and pivotal studies, a critique of the manufacturer's pharmacoeconomic evaluation, and patient group–submitted information about outcomes and issues that are important to individuals with CIU.

Patient Input Information
The following is a summary of information provided by one patient group that responded to the CDR call for patient input:

- Patients reported that CIU attacks are unpredictable in both timing and severity, causing anxiety, affecting sleep, and impacting their diet and their ability to obtain employment. A majority of patients reported a decrease in self-confidence and feeling the need to hide the affected skin.
- Patients reported that CIU has a negative impact on family members and caregivers. Caregivers have to deal with the anxiety and depression of the patient and often need to help the patient with self-care, grooming, washing, and other self-care activities.
- Concerns with current treatment options include lack of effectiveness and intolerable side effects.

Clinical Trials
The CDR systematic review included three phase 3, double-blind, multi-centre, placebo-controlled RCTs: ASTERIA I (N = 319) was 24 weeks in duration; ASTERIA II (N = 323) was 12 weeks in duration, and GLACIAL (N = 336) was 24 weeks in duration. ASTERIA I and ASTERIA II randomized patients (1:1:1:1 ratio) to one of three doses of omalizumab (75 mg, 150 mg, or 300 mg) or placebo. These studies were conducted with adult and adolescent patients with refractory CIU receiving concomitant standard-dose H_1 antihistamine therapy. Patients were given the first dose of study medication at day one and were re-treated every four weeks. Only the 150 mg and the 300 mg doses of omalizumab are approved for treatment of CIU in Canada. Therefore, the data for the 75 mg omalizumab treatment group were not reported in the CDR review.

GLACIAL compared omalizumab 300 mg with placebo (3:1). The study was conducted with adult and adolescent patients with refractory CIU receiving concomitant therapy including H_1 antihistamines at up to four times the approved dose, and H_2 antagonists or leukotriene receptor

antagonists, or both. Patients were dosed and monitored in the same manner as in ASTERIA I and ASTERIA II. All three studies had a 16-week treatment-free follow-up period.

Outcomes

Outcomes were defined a priori in the CDR systematic review protocol.

- UAS7 — The Urticaria Activity Score (UAS) end points were collected via the electronic Urticaria Patient Daily Diary. The daily UAS is the sum of the daily Itch Severity Score and the daily Number of Hives Score. The UAS7 is the sum of the daily UAS scores over one week, with higher scores indicating more severe symptoms. The minimal clinically important difference (MCID) for UAS7 has been reported to be 9.5 to 10.5. UAS7 was assessed using the following end points:
  - Change from baseline to weeks 12 and 24
  - Proportion of patients with UAS7 ≤ 6 at weeks 12, 24, 28, and 40
  - Proportion of patients with complete response (UAS7 = 0) at weeks 12 and 24
  - Time to UAS7 MCID response
  - Proportion of responders who maintained their response (UAS7 ≤ 6) to week 28 or week 40
  - Time to relapse in week 12 or week 24 responders.
- Weekly Itch Severity Score (WISS) — the sum of the daily Itch Severity Score tabulated over seven consecutive days. The MCID for WISS has been reported to be 4.5 to 5.0.
- Weekly Number of Hives Score (WNHS) — the sum of the daily Number of Hives Score tabulated over seven consecutive days. The MCID for WNHS has been reported to be 5.0 to 5.5.
- Dermatology Life Quality Index (DLQI) — a 10-item questionnaire that assesses six different aspects that may affect quality of life: symptoms and feelings; daily activities; leisure activities; work or school; personal relationships; and treatment. Higher scores indicate a greater impairment in quality of life. The MCID for DLQI in CIU patients has been reported to be in the range of 2.24 to 3.10.
- Chronic Urticaria Quality of Life Questionnaire (CU-Q2oL) — a validated CIU-specific quality of life measure that includes a 23-item, self-administered questionnaire that assesses six quality of life dimensions: pruritus; swelling; impact on life activities; sleep problems; limits; and looks. Overall CU-Q2oL scores are converted to a 0 to 100 scale, with higher scores indicating greater quality of life impairment. The MCID for the CU-Q2oL is unknown.
- EuroQol 5-Dimensions Questionnaire (EQ-5D) — a generic quality of life instrument consisting of five dimensions of health (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) and a visual analogue scale for rating health today. Weighted scoring produces an EQ-5D index score, with a higher score indicating better general health.
- Total adverse events, serious adverse events, withdrawals due to adverse events, and notable harms.

The primary objective of ASTERIA I and ASTERIA II was to evaluate whether omalizumab was superior to placebo for improving WISS after 12 weeks. The primary objective of GLACIAL was to evaluate the safety of omalizumab compared with placebo.

Efficacy

- Both the 150 mg and 300 mg doses of omalizumab were statistically superior to placebo for improvement in UAS7, WISS, and WNHS in all three included studies. The least squares mean differences (LSMD) versus placebo were (150 mg and 300 mg, respectively):

  - Change from baseline in UAS7:
    - ASTERIA I: −6.54 (95% confidence interval [CI], −10.33 to −2.75) and −12.80 (95% CI, −16.44 to −9.16)
    - ASTERIA II: −7.69 (95% CI, −11.49 to −3.88) and −12.40 (95% CI, −16.13 to −8.66)
    - GLACIAL: −10.02 (95% CI, −13.17 to −6.86) with 300 mg.
  - Change from baseline in WISS:
    - ASTERIA I: −2.95 (95% CI, −4.72 to −1.18) and −5.80 (95% CI, −7.49 to −4.10)
    - ASTERIA II: −3.04 (95% CI, −4.85 to −1.24) and −4.81 (95% CI, −6.49 to −3.13)
    - GLACIAL: −4.52 (95% CI, −5.97 to −3.08) with 300 mg.
  - Change from baseline in WNHS:
    - ASTERIA I: s.21 (95% C s.21 to s.21) and s.21 (95% CI, −9.10 to s.21
    - ASTERIA II: −4.51 (95% CI, −6.65 to −2.36) and −7.09 (95% CI, −9.26 to −4.93)
    - GLACIAL: −5.90 (95% CI, −7.72 to −4.07) with 300 mg.
- A statistically significantly greater proportion of omalizumab-treated patients achieved the UAS7 MCID response compared with placebo. The hazard ratios for time to achieving a UAS7 MCID response for omalizumab versus placebo were (150 mg and 300 mg, respectively):
  - ASTERIA I: s.2 (95% CI s.2 to s.21 and s. (95% C s.21 to s.21
  - ASTERIA II: s.2 (95% CI, s. to s.2) and s. (95% CI, s.2 to s.21
  - GLACIAL s.2 (95% CI, s.2 to s.2) with 300 mg.
- With the exception of the omalizumab 150 mg group in the ASTERIA I trial, changes in DLQI and CU-Q2oL were statistically significant and favoured the omalizumab treatment groups over placebo. The LSMD versus placebo were (150 mg and 300 mg, respectively):
  - Change from baseline in DLQI:
    - ASTERIA I: −1.31 (95% CI, −3.46 to 0.84) and −4.08 (95% CI, −5.96 to −2.20)
    - ASTERIA II: −2.51 (95% CI, −4.64 to −0.38) and −3.79 (95% CI, −5.85 to −1.73)
    - GLACIAL: −4.67 (95% CI, −6.28 to −3.06) with 300 mg.
  - Change from baseline in CU-Q2oL:
    - ASTERIA I: −3.9 (95% CI, −11.2 to 3.4) and −10.6 (95% CI, −17.2 to −4.0)
    - ASTERIA II: −8.2 (95% CI, −14.3 to −2.1) and −14.0 (95% CI, −19.8 to −8.2)
    - GLACIAL: −13.4 (95% CI, −18.2 to −8.6) with 300 mg.
- With the exception of the omalizumab 300 mg group in the ASTERIA II trial ($P = 0.0062$), differences in change from baseline in EQ-5D index scores between the omalizumab groups and placebo were not statistically significant.
- The majority of efficacy outcomes assessed after the 16-week treatment-free follow-up period did not maintain statistical significance compared with placebo.

Harms (Safety and Tolerability)

- The proportions of patients who experienced at least one serious adverse event were:
  - ASTERIA I: 3.4% with omalizumab 150 mg, 0% with omalizumab 300 mg, and 5.0% with placebo
  - ASTERIA II: 0% with omalizumab 150 mg, 2.5% with omalizumab 300 mg, and 2.5% with placebo
  - GLACIAL: 2.8% with omalizumab 300 mg and 3.6% with placebo.
- The proportions of patients who experienced at least one adverse event were:
  - ASTERIA I: 69.0% with omalizumab 150 mg, 56.8% with omalizumab 300 mg, and 51.3% with placebo

  - ASTERIA II: 47.7% with omalizumab 150 mg, 44.3% with omalizumab 300 mg, and 40.5% with placebo
  - GLACIAL: 65.1% with omalizumab 300 mg and 63.9% with placebo.
- The most commonly reported adverse events were nasopharyngitis and headache. Across all three studies, the proportion of patients who reported headache was consistently greater in the omalizumab groups compared with the placebo groups.
- The proportions of patients who withdrew as a result of adverse events were:
  - ASTERIA I: 2.3% with omalizumab 150 mg, 1.2% with omalizumab 300 mg, and 2.5% with placebo
  - ASTERIA II: 1.1% with omalizumab 150 mg, 0% with omalizumab 300 mg, and 1.3% with placebo
  - GLACIAL: 1.2% with omalizumab 300 mg and 1.2% with placebo.

Cost and Cost-Effectiveness

The manufacturer submitted a cost-utility analysis comparing omalizumab plus SOC with SOC alone, over a 20-year time horizon, under the perspective of a publicly funded health care system, with adults and adolescents 12 years of age and over with moderate to severe symptomatic CIU (UAS7 ≥ 16) despite SOC. The manufacturer considered three different scenarios in its analysis, where the dosage of omalizumab varied (150 mg or 300 mg) and where different definitions of SOC were used:

- Scenario 1 compared omalizumab 300 mg as a third- or fourth-line drug added on to SOC, defined as up to four times the standard H_1 antihistamine dose, combined with H_2 antagonists, leukotriene receptor antagonists, or both, with SOC alone.
- Scenario 2 compared omalizumab 150 mg as a second-line drug added on to SOC, defined as standard H_1 antihistamine dose with SOC alone.
- Scenario 3 compared omalizumab 300 mg as a second-line drug added on to SOC, defined as standard H_1 antihistamine dose with SOC alone.

The model included five key health states based on the UAS7: severe urticaria (UAS7 score of 28 to 42), moderate urticaria (UAS7 score of 16 to 27), mild urticaria (UAS7 score of 7 to 15), well-controlled urticaria (UAS7 score of 1 to 6), and urticaria-free (UAS7 score of 0). Patients began in either the moderate or severe urticaria health states and cycled through the model every four weeks for 24 weeks. Patients who responded to treatment at 24 weeks (defined as UAS7 ≤ 6) were eligible for re-treatment upon relapse (defined as UAS7 ≥ 16). Progression through the model was also driven by whether patients experienced a spontaneous remission of symptoms or dropped out. Efficacy and safety data were sourced from ASTERIA I, ASTERIA II, and GLACIAL, while utility values were obtained from pooling the data from these trials. The manufacturer reported that omalizumab 300 mg plus SOC versus SOC alone is associated with an incremental cost-utility ratio (ICUR) of $52,213, $57,193, and $81,210 per QALY, for scenarios 1, 2, and 3, respectively.

CDR identified a number of limitations with the submitted economic evaluation:

- The manufacturer did not include a treatment waning effect.
- There is uncertainty in the natural remission rates (higher rates than those assumed by the manufacturer's base case are reported in literature).
- The manufacturer assumed that patients in the mild CIU health state following initial treatment would not be re-treated upon relapse, which is uncertain.

CDR reanalysis focused on the 300 mg dose of omalizumab, as the 150 mg dose did not provide a clinically significant response in terms of change in UAS7 score at weeks 12 and 24. At a dose of 300 mg SC every four weeks, when omalizumab is used as either a second-line, or third- or fourth-line drug added on to SOC in patients refractory to H_1 antihistamines, CDR found that the ICURs for omalizumab plus SOC compared with SOC alone were above $120,000 per QALY. At a price reduction of 60%, the ICUR for omalizumab 300 mg plus SOC compared with SOC alone would be $50,764 if omalizumab is used as a second-line drug, and $43,606 if it is used as a third- or fourth-line drug.

At the submitted price of $612 per 150 mg single-use vial and at the recommended dose of 150 mg or 300 mg every four weeks, the annual cost of omalizumab is $7,956 (150 mg dose) and $15,912 (300 mg dose).

Other Discussion Points:
CDEC noted the following:

- In accordance with clinical practice guidelines jointly issued by the European Academy of Allergy and Clinical Immunology, the Global Allergy and Asthma European Network, the European Dermatology Forum, and the World Allergy Organization, clinicians in Canada typically use maximally tolerated doses of second-generation H_1 antihistamines up to four times the indicated dose before adding additional medications for patients with inadequately controlled symptoms.
- Although statistically significant, the 150 mg dose of omalizumab in ASTERIA I and ASTERIA II failed to provide a clinically significant response on UAS7, WISS, or WNHS compared with placebo, based on published MCID values for these outcomes.
- The Canadian product monograph for omalizumab states that a five-year observational study demonstrated that there was a disproportionate increase of overall cardiovascular and cerebrovascular disorders observed in the omalizumab-treated cohort compared with the non-omalizumab cohort.

Research Gaps:
CDEC noted that there is insufficient evidence regarding the following:

- The included clinical trials were limited to 24 weeks of treatment; therefore, the longer-term efficacy of omalizumab in the treatment of CIU requires further evaluation.
- There are no data to evaluate how or when treatment should be stopped or reinitiated after discontinuation.
- There are no studies directly comparing omalizumab against less costly oral drugs (e.g., montelukast or cyclosporin A) for the treatment of CIU.

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

April 8, 2015 Meeting

Regrets:
None

Conflicts of Interest:
One CDEC member did not participate in the deliberation or vote due to a conflict of interest.

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 CDR reviews and used in 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.

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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

Drug Benefit Council (DBC) Recommendation and Reasons for Recommendation

FINAL

Omalizumab (Xolair®)
Novartis Pharmaceuticals Canada Inc.

Description:

Drug review of **omalizumab (Xolair®)** for the following Health Canada approved indication:

> For the treatment of adults and adolescents (12 years of age and above) with persistent moderate to severe chronic idiopathic urticaria (CIU).

In their review, the DBC considered the following: final review completed by the Common Drug Review (CDR) on May 7, 2015, 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 three patients, Clinical Practice Reviews from two specialists, as well as a Budget Impact Assessment.

Dosage Forms:

Xolair® is available as omalizumab 150 mg subcutaneous vial.

Recommendations:

1. The Drug Benefit Council (DBC) recommends that **omalizumab (Xolair®)** be listed for the treatment of adults and adolescents with chronic idiopathic urticaria (CIU) who remain symptomatic despite H1 antihistamine treatment, if the following clinical criterion and conditions are met:

   - To be prescribed by specialists only.
   - For patients with moderate to severe CIU who remain symptomatic (i.e. presence of hives and/or associated itching) despite optimum management with available oral therapies; 300 mg dosage only; coverage duration only for 24 weeks.
   - Condition: significant reduction in price.

Reasons for the Recommendation:

1. **Summary**

- Three double-blind randomized, placebo-controlled trials in patients with refractory CIU receiving concomitant standard-dose H1 antihistamine therapy found the 150 mg and 300 mg doses of omalizumab were statistically superior to placebo in the primary outcome measures and in two of three quality of life measures.
- Although statistically significant, the 150 mg dose of omalizumab did not provide a clinically significant response on the primary outcome and two important secondary outcomes compared with placebo.
- The three trials did not provide safety and efficacy data beyond 24 weeks.
- At the submitted price, the 300 mg dosage of omalizumab is not cost-effective when compared with the standard of care.

2. **Clinical Efficacy**

- The DBC considered the CDR systematic review, which included three phase 3, double-blind, multi-centre, randomized placebo-controlled trials: ASTERIA I (24 weeks in duration), ASTERIA II (12 weeks in duration), and GLACIAL (24 weeks in duration). These studies were conducted with adult and adolescent patients with refractory CIU receiving concomitant standard-dose H1 antihistamine therapy.
- ASTERIA I and ASTERIA II randomized patients to one of three doses of omalizumab (75 mg, 150 mg, or 300 mg) or placebo. Patients were given the first dose of study medication at day one and were re-treated every four weeks. The primary objective of ASTERIA I and II was to evaluate whether omalizumab was superior to placebo for improving Weekly Itch Severity Score (WISS) after 12 weeks.
- GLACIAL compared omalizumab 300 mg with placebo in adult and adolescent patients with refractory CIU receiving concomitant therapy including H1 antihistamines at up to four times the approved dose, and H2 antagonists or leukotriene receptor antagonists, or both. The primary objective of GLACIAL was to evaluate the safety of omalizumab compared with placebo.
- Only the 150 mg and the 300 mg doses of omalizumab are approved for treatment of CIU in Canada. As a result, the data for the 75 mg omalizumab treatment group were not reported in the CDR review.
- In all three included studies, both the 150 mg and 300 mg doses of omalizumab were statistically superior to placebo for improvement in the UAS7 (the total of the daily Urticaria Activity Score, tabulated over 7 consecutive days), WISS, and WNHS (Weekly Number of Hives Score, the sum of the daily Number of Hives Score tabulated over 7 consecutive days).
- Although statistically significant, the 150 mg dose of omalizumab in ASTERIA I and ASTERIA II failed to provide a clinically significant response on UAS7, WISS, or WNHS compared with placebo, based on published minimal clinically important difference (MCID) values for these outcomes.
- For quality of life measure, changes in the Dermatology Life Quality Index (DLQI) and Chronic Urticaria Quality of Life Questionnaire (CU-Q2oL) were statistically significant and, with the exception of the omalizumab 150 mg group in the ASTERIA I trial, favoured the omalizumab treatment groups over placebo.
- With the exception of the omalizumab 300 mg group in the ASTERIA II trial, differences in change from baseline in EuroQol 5-Dimensions Questionnaire (EQ-

5D) index scores between the omalizumab groups and placebo were not statistically significant.

3. **Safety**

- The proportions of patients who experienced at least one serious adverse event, who experienced at least one adverse event, and who withdrew as a result of adverse events were similar between omalizumab and placebo over all three trials.
- The most commonly reported adverse events were nasopharyngitis and headache. Across all three studies, the proportion of patients who reported headache was consistently greater in the omalizumab groups compared with the placebo groups.

4. **Economic Considerations**

- The CDR reanalysis of the manufacturer submission that at a dose of 300 mg every four weeks, when omalizumab is used as either a second-line, or third- or fourth-line drug added on to standard of care (SOC) in patients refractory to H1 antihistamines, the incremental cost-utility ratios (ICURs) for omalizumab plus SOC compared with SOC alone were above $120,000 per quality-adjusted life-year (QALY).
- At a price reduction of 60%, the ICUR for omalizumab 300 mg plus SOC compared with SOC alone would be $50,764 if omalizumab is used as a second-line drug, and $43,606 if it is used as a third- or fourth-line drug.

5. **Of Note**

- There was an absence of safety and efficacy data beyond 24 weeks in the three trials.
- The Canadian product monograph for omalizumab states that a five-year observational study demonstrated that there was a disproportionate increase of overall cardiovascular and cerebrovascular disorders observed in the omalizumab-treated cohort compared with the non-omalizumab cohort.
- Three patients responded to Patient Input Questionnaires. Patient described the serious emotional, physical and social impairments which result from having chronic hives, and the often serious side effects of medications commonly used to treat CIU such as prednisone and cyclosporine (including diabetes, weight gain, and kidney damage). One patient had tried omalizumab and reported a significant relief in CIU symptoms and was able to stop taking prednisone.

Omalizumab (Xolair) Budget Impact Analysis – May 12, 2016

Therapy: Omalizumab (Xolair) 150mg vial for subcutaneous injection

Objective

The objective of this report is to evaluate the budget impact associated with PharmaCare listing omalizumab (Xolair) as a limited coverage drug for the treatment of moderate to severe persistent asthma for adult and adolescent patients.

The CADTH Canadian Drug Expert Committee (CDEC) recommended that omalizumab be reimbursed for adults and adolescents (12 years of age and above) with moderate to severe persistent asthma who have a positive skin test or in vitro reactivity to a perennial aeroallergen if the following clinical criterion and conditions are met:

- Criterion:

  Inability to use, intolerance to, or inadequate response to an inhaled corticosteroid (ICS) long-acting beta-agonist (LABA) combination, and at least one other reimbursed alternative asthma treatment.

- Conditions:

  - Patients should be managed by a physician with experience in treating asthma.
  - At a reduced price

Utilization

Table 1 provides the utilization of omalizumab and comparator drugs among adult and adolescent asthma patients in BC.

Only adult and adolescent patients diagnosed with asthma are included in the analysis. These patients are 12 years of age or older, and have had at least one MSP claim with diagnosis code 493.* (ICD-9), or one DAD claim with diagnosis codes J45* (ICD-10).

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Table 1. Utilization of omalizumab and comparator drugs among adult and adolescent patients with asthma, FY2015/16

Drug Name	# of BC Patients	# of PharmaCare Patients	Total Billed Amount	Total PharmaCare Paid Amount	Annual Product Cost Per Patient
Omalizumab (Xolair)	315	82	$6,980,592	$2,028,347	$26,477
Inhaled Corticosteroid (ICS)					
Beclomethasone dipropionate (QVAR)	363	354	$37,067	$11,095	$75
Budesonide (Pulmicort)	18,375	13,183	$3,292,451	$954,420	$127
Ciclesonide (Alvesco)	10,426	10,264	$2,242,158	$619,930	$179
Fluticasone propionate (Flovent HFA/Diskus)	61,562	49,681	$11,160,755	$4,035,141	$172
Fluticasone furoate (Arnuity Ellipta)	16,246	0	$1,239,428	$0	$55
Mometasone furoate (Asmanex Twisthaler)	45,096	2,723	$3,343,880	$55,497	$57
Beta2-adrenergic Agonists, long-acting (LABA)					
Formoterol fumarate (Foradil,Oxeze)	961	572	$344,596	$114,109	$330
Salmeterol xinafoate (Serevent)	1,076	681	$463,059	$188,173	$411
ICS/LABA Combination					
Budesonide-formoterol (Symbicort turbuhaler)	39,445	16,811	$16,886,822	$4,254,801	$497
Fluticasone-salmeterol (Advair MDI,Diskus)	43,006	21,311	$28,557,443	$10,960,909	$472
Mometasone-formoterol (Zenhale)	4,125	1,677	$1,405,525	$322,345	$386
Fluticasone-vilanterol (Breo Ellipta)	2,190	1,222	$1,071,323	$368,077	$307
Beta2-adrenergic Agonists, short-acting (SABA)					
Salbutamol sulfate (Airomir, Ventolin, generics)	177,059	172,675	$10,478,500	$3,614,197	$25
Terbutaline (Bricanyl)	3,835	3,774	$240,559	$66,155	$32
Anticholinergic Agents					
Ipratropium (Atrovent HFA, generics)	21,653	20,602	$3,690,112	$2,183,840	$121
Tiotropium (Spiriva)	13,793	9,280	$8,355,597	$3,726,621	$448
Anticholinergic/SABA					
Ipratropium-fenoterol	2	0	$946	$0	$428

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(Duovent UDV)					
Ipratropium-salbutamol (Combivent UDV, generics)	2,518	2,125	$496,000	$285,285	$153
Oral corticosteroids					
Prednisone	55,234	53,320	$1,941,078	$681,129	$7
Leukotriene Receptor Antagonists (LTRA)					
Montelukast	11,082	302	$4,554,691	$182,621	$671
Zafirlukast	166	21	$74,963	$10,032	$551
Methylxanthines					
Oxtriphylline	13	13	$339	$160	$12
Theophylline	1,093	1,009	$155,173	$74,009	$73
TOTAL	**287,156**	**227,081**	**$107,013,059**	**$34,736,894**	

Note:

1. Drug costs in this table reflects confidential discounted prices for PharmaCare and includes mark-up (5% for omalizumab and 8% for comparators)
2. Annual cost of therapy is estimated using PharmaNet claims data. For drugs currently listed on PharmaCare formulary or with exceptional coverage, per-patient cost is calculated based on accepted ingredient cost (with discounts based on PLA) and number of patients with accepted claims; Cost for non-benefit drugs are estimated based on billed ingredient cost and number of patients with billed claims. The accuracy of the estimated cost is therefore dependent on the integrity of PharmaNet data elements involved.
3. PharmaCare is currently providing coverage of omalizumab for asthma patients on an exceptional case-by-case basis.

Budget Impact Analysis

This report considers two separate scenarios. In Scenario I, the limited coverage criteria for omalizumab is based on CDEC recommendation. In Scenario II, PharmaCare coverage requires that patients have tried all or almost all therapeutic options for asthma before going onto omalizumab. Detailed criteria for both scenarios are outlined in the "Key Assumptions" section.

Table 2a, 2b, 3a, 3b list the forecasted patient and budget impact to PharmaCare in the next three fiscal years for both scenarios.

Table 2a: Patient impact summary (Scenario I: CDEC criteria)

	FY2016/17	FY2017/18	FY2018/19
I. Eligible patients currently on omalizumab without PharmaCare coverage	10	13	17
II. Eligible patients on comparator drugs adding omalizumab to their therapy	5,018	5,075	5,134
TOTAL	**5,028**	**5,088**	**5,151**

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Table 2b: Budget impact summary (Scenario I: CDEC criteria)

	FY2016/17	FY2017/18	FY2018/19	Three-Year Total
I. Eligible patients currently on omalizumab without PharmaCare coverage	$230,000	$291,000	$371,000	$892,000
II. Eligible patients on comparator drugs adding omalizumab to their therapy	$90,491,000	$91,529,000	$92,579,000	$274,599,000
TOTAL	**$90,721,000**	**$91,820,000**	**$92,950,000**	**$275,491,000**

Note: Final numbers are rounded to the nearest $1000

Table 3a: Patient impact summary (Scenario II: All therapy criteria)

	FY2016/17	FY2017/18	FY2018/19
I. Eligible patients currently on omalizumab without PharmaCare coverage	9	12	15
II. Eligible patients on comparator drugs adding omalizumab to their therapy	49	50	50
TOTAL	**58**	**62**	**65**

Table 3b: Budget impact summary (Scenario II: All therapy criteria)

	FY2016/17	FY2017/18	FY2018/19	Three-Year Total
I. Eligible patients currently on omalizumab without PharmaCare coverage	$200,000	$267,000	$333,000	$800,000
II. Eligible patients on comparator drugs adding omalizumab to their therapy	$884,000	$902,000	$902,000	$2,688,000
TOTAL	**$1,084,000**	**$1,169,000**	**$1,235,000**	**$3,488,000**

Note: Final numbers are rounded to the nearest $1000

Key assumptions

This BIA assumes that PharmaCare lists omalizumab as a limited coverage drug for treating adult and adolescent patients with moderate to severe persistent asthma, at the beginning of FY2016/17.

The estimated budget impact is composed of:

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- Total costs of eligible patients on omalizumab currently taking the drug without coverage, and

- Total costs of eligible patients on comparator drugs adding omalizumab to their existing therapies

It is assumed that omalizumab will be used as an add-on therapy and patients will remain on their existing therapies.

In Scenario I, listing criteria are based on CDEC recommendation. Asthma patients (12 years of age and older), who have failed an inhaled corticosteroid (ICS) long-acting beta-agonist (LABA) combination, plus another reimbursed treatment, are eligible for PharmaCare coverage.

Based on literature, approximately 20% of asthma patients have severe symptoms and among them, 20% is inadequately controlled[1]. Thus, we assume that 4% of asthma patients have moderate to severe asthma and failed to respond to ICS/LABA therapy.

These patients are all assumed to have positive skin test or in vitro reactivity to a perennial aeroallergen, due to lack of data for these tests.

In Scenario II, Asthma patients (12 years of age and older) need to meet the following criteria to receive PharmaCare coverage for omalizumab:

- Currently on maximum dose of ICS, LABA (or ICS/LABA combination), SABA

  AND

- For adult patients, currently on oral prednisone for at least three courses per year (each course is defined as at least 5 days of therapy with 20mg or higher daily dose)

  AND

- At least one hospitalization for asthma in the past year

  AND

- Have tried or currently on anticholinergics

[1] S.P. Peters, et. al. Uncontrolled asthma: A review of the prevalence, disease burden and options for treatment. *Respiratory Medicine*, Volume 100, Issue 7, Pages 1139–1151

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AND

- Have tried or currently on montelukast

Average growth rates of asthma patient population are estimated from PharmaCare claims data between FY2013/14 and FY2015/16.

Confidential discounted prices are used for drugs where a Product Listing Agreement (PLA) exists.

Patient deductible levels (paid-to-accepted ratios), used to estimate the amount paid by PharmaCare for Fair PharmaCare patients, are assumed to be unchanged from their FY2015/16 values.

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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	**omalizumab**
Brand Name	Xolair®
Dosage Form(s)	150 mg vial
Manufacturer	Novartis Pharmaceuticals Canada Inc.
Submission Type	**New Indication**
Use Reviewed	Chronic idiopathic urticarial (CIU)
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/about-cadth/what-we-do/products-services/cdr/reports
Drug Benefit Council (DBC)	DBC met on June 1, 2015. DBC considered various inputs including: final review completed by the CDR, 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 Questionnaire responses from three patients.
Drug Coverage Decision	**Non-Benefit**
Date	November 29, 2016
Reason(s)	**Drug coverage decision is consistent with the DBC recommendation.** • Omalizumab was similar to or demonstrated some advantage over placebo with respect to efficacy, safety and/or quality of life. However, there are no studies directly comparing omalizumab against less costly oral drugs (e.g., montelukast or cyclosporine). • Based on economic considerations and the submitted product price, the drug was not cost-effective and/or did not offer optimal value for money. • The Ministry initially participated in negotiations with the manufacturer through the pan-Canadian Pharmaceutical Alliance (pCPA), but subsequently withdrew as the terms of the agreement did not meet the needs of the Ministry.
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:

- whether the drug is safe and effective
- advice from a national group called the Common Drug Review (CDR)
- what the drug costs and whether it is a good value for the people of B.C.
- ethical considerations involved with covering or not covering the drug
- input from physicians, patients, caregivers, patient groups and drug submission sponsors

The Ministry makes PharmaCare coverage decisions by taking into account:

- the existing PharmaCare policies, programs and resources
- the evidence-informed advice of the DBC
- the drugs already covered by PharmaCare that are used to treat similar medical conditions
- the overall cost of covering the drug

Visit the The Drug Review Process in B.C. - Overview and Ministry of Health - PharmaCare 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.

Omalizumab and Mepolizumab Budget Impact Summary

Table 1: Utilization of Mepolizumab and Omalizumab among adult patients with asthma, FY2015/16

Drug Name	# of BC Patients	# of PharmaCare Patients	Total BC Billed Amount	Total PharmaCare Paid Amount	Annual Product Cost Per Patient
Mepolizumab (Nucala)	0	0	$0	$0	s.13,s.17
Omalizumab (Xolair)	311	81	$6,892,313	$1,981,840	$17,890

Note: Cost of mepolizumab is calculated based on the confidential discounted (LOI) price.

Omalizumab Criteria:

- Asthma patients 12 years of age and older, **and**
- Currently on maximum dose of ICS, LABA (or ICS/LABA combination), SABA, **and**
- For adult patients, currently on oral prednisone for at least three courses per year (each course is defined as at least 5 days of therapy with 20mg or higher daily dose), **and**
- At least one hospitalization for asthma in the past year, **and**
- Have tried or currently on anticholinergics, **and**
- Have tried or currently on montelukast.

Patient Impact Summary

	FY2016/17	FY2017/18	FY2018/19
I. Eligible patients currently on omalizumab without PharmaCare coverage	9	12	15
II. Eligible patients on comparator drugs adding omalizumab to their therapy	49	50	50
TOTAL	**58**	**62**	**65**

Budget Impact Summary

	FY2016/17	FY2017/18	FY2018/19	Three-Year Total
I. Eligible patients currently on omalizumab without PharmaCare coverage	$200,000	$267,000	$333,000	$800,000
II. Eligible patients on comparator drugs adding omalizumab to their therapy	$884,000	$902,000	$902,000	$2,688,000
TOTAL	**$1,084,000**	**$1,169,000**	**$1,235,000**	**$3,488,000**

Mepolizumab Criteria:

- Asthma patients age 18 and older, **and**
- Omalizumab patients – currently on ICS and LABA or ICS/LABA combination; or
- Patients currently on ICS and LABA or ICS/LABA combination, and currently on oral prednisone for at least three courses per year (each course is defined as at least 5 days of therapy with 20mg or higher daily dose)

Patient Impact Summary

	FY2017/18	FY2018/19	FY2019/20
1. BC Asthma Omalizumab Patients (Age 18 and older) Without PharmaCare Coverage Switch to Mepolizumab	217	277	354
2. PharmaCare Covered Asthma Patients (Age 18 and older) on Comparator Drugs Add Mepolizumab to the Therapy	162	165	168
TOTAL	**379**	**442**	**522**

Budget Impact Summary

	FY2017/18	FY2018/19	FY2019/20	Three-Year Total
1. BC Asthma Omalizumab Patients (Age 18 and older) Without PharmaCare Coverage Switch to Mepolizumab	$1,295,000	$1,655,000	$2,117,000	$5,067,000
2. PharmaCare Covered Asthma Patients (Age 18 and older) on Comparator Drugs Add Mepolizumab to the Therapy	$871,000	$888,000	$905,000	$2,664,000
TOTAL	**$2,166,000**	**$2,543,000**	**$3,022,000**	**$7,731,000**

Updated Utilization

Brand Name	# of BC Patients	# of PC Covered Patients	Total Claimed Amount	Total PharmaCare Paid
FY2015/16				
Xolair	414	84	$7,731,214	$2,037,358
Nucala	0	0	$0	$0
2016/09-2017/08				
Xolair	613	115	$10,989,817	$2,697,955
Nucala	223	0	$460,536	$0