

the **DBL** *report*

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An Official Accompaniment to
the Alberta Health and Wellness
Drug Benefit List (AHWDBL)

The Expert Committee on Drug
Evaluation and Therapeutics (ECDET)
produced by Alberta Blue Cross

EXPERT COMMITTEE MEMBERS:

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Erwin G. Friesen, BSc (Pharm), PharmD,
FCSHP
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James L. Silvius, BA, MD, FRCP(C)

ALBERTA HEALTH AND WELLNESS LIAISON:

David Bougher, BSP, MHSA

ADMINISTRATIVE AND SCIENTIFIC SUPPORT:

Larry Shipka, BSc (Pharm)
Eugenia Palylyk-Colwell, BSc (Pharm), PhD
Carlyn Volume-Smith, BSc (Pharm), MSc, PhD

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UPDATE: Status of TNF-Antagonists

Highlights of New Products Added

■ **PROTOPIC** (tacrolimus) (TBB) – is a topical immunomodulator approved for the treatment of atopic dermatitis when conventional agents (e.g. steroids) cannot be used. This product was recommended for addition via special authorization following consultation with Alberta Dermatologists. As a result, the following criteria for coverage apply for **PROTOPIC 0.03%** ointment:

- For use in patients 2 to 15 years of age inclusive with atopic dermatitis who are unable to tolerate or have failed topical steroid therapy.
- For use in patients 2 to 15 years of age with atopic dermatitis who require ongoing use of potent (Class 3 or higher) topical steroids.
- For use in patients 16 years of age and older with atopic dermatitis affecting face and flexures who are unable to tolerate or have failed topical steroid therapy.
- For use in patients 16 years of age and older with atopic dermatitis who require ongoing use of potent (Class 3 or higher) topical steroids over greater than 30% of body surface area.

Please note that coverage for **PROTOPIC 0.1%** ointment will be made available only for adult patients meeting the last two criteria.

■ **SYMBICORT** (budesonide/formoterol fumarate dihydrate) (AZC) – 100 mcg/6 mcg and 200 mcg/6 mcg Turbuhalers are CFC-free, dry powder combination products for use as maintenance therapy in asthmatic patients 12 years of age and older, and for whom such combination therapy is warranted. The Expert Committee is of the view that in the case of all combination products, patients should first be stabilized on the individual components administered separately. However, the Committee acknowledged that it may be appropriate, once patients are thus stabilized, to be administered a combination product such as **SYMBICORT** and so recommended that it be listed as a **Restricted Benefit** on the AHWDBL according to the following criteria: “For patients 12 years of age and older for the maintenance treatment of asthma where use of a combination product is appropriate”.

Highlights of Deferred Products

■ **FOSAMAX** (alendronate sodium) (MFC) – 70mg tablet is administered once weekly for the treatment and prevention of osteoporosis in postmenopausal women. The Committee expressed concern that a weekly dosage form may create compliance issues. For example, an elderly population may neglect to take an entire week’s dose thereby resulting in a lack of efficacy. Alternatively, they may forget that they have taken a dose and cause an increase in toxicity. As a result, the Committee recommended that this product be deferred pending the receipt and review of information from the manufacturer that directly compares patient compliance with **FOSAMAX 70mg** once weekly and Fosamax 10mg daily.

UPDATE: Status of TNF-Antagonists

■ RHEUMATOID ARTHRITIS – DEFERRED

ENBREL (etanercept) (WAY) and **REMICADE** (infliximab) (SCH) continue to be under review for coverage in the treatment of Rheumatoid Arthritis (RA). Prior to making a recommendation for coverage for this indication, the Expert Committee identified the need for an accurate assessment of the cost-effectiveness of TNF-antagonists for the treatment of RA. Therefore, further discussion has been deferred pending the availability of the Canadian Coordinating Office of Health Technology Assessment (CCOHTA) evaluation of these agents in the treatment of RA.

■ CROHN'S DISEASE/ FISTULIZING CROHN'S DISEASE – NOT ADDED

The Expert Committee also deliberated on the use of **REMICADE** for the treatment of Crohn's Disease (CD) and Fistulizing CD. Information received from the manufacturer and following consultation with Alberta Gastroenterologists was reviewed as was the recently published CCOHTA evaluation of the use of **REMICADE** in CD and Fistulizing CD in detail. While the Expert Committee acknowledged that **REMICADE** may provide clinical benefit for treatment-resistant CD, the cost per quality-adjusted life year gained (QALY) is much higher than generally accepted therapies currently funded through the drug program. Hence, given the magnitude of the cost/QALY gained, continuing concerns relating to toxicity and lack of long-term outcome data, the Expert Committee has advised that the degree of clinical benefit expected from **REMICADE** for these indications does not justify the substantive expenditure of public funds required. As a result, it was recommended that **REMICADE** not be added to the AHWDBL for treatment of CD or Fistulizing CD.

Highlights of Products Not Added

■ **DITROPAN XL** (oxybutynin chloride) (JOI) – 5 mg and 10 mg tablets were not recommended for addition to the AHWDBL, as they did not offer a therapeutic or cost advantage. In the resubmission, the manufacturer's position is that due to the unique drug delivery system, patients using **DITROPAN XL** experience less adverse events (e.g., dry mouth and cognitive impairment) than do patients using immediate release oxybutynin. The Committee advised that the incidence of adverse events associated with immediate release oxybutynin is likely related to the use of excessively high doses of oxybutynin that are used in the elderly and may be effectively dealt with by more comprehensive individualization of dosage in some elderly patients.

■ **MERIDIA** (sibutramine hydrochloride monohydrate) (ABB) and **XENICAL** (orlistat) (HLR) were not recommended for addition to the AHWDBL. With regard to **MERIDIA**, the Committee referenced the March 2002 Health Canada Advisory that advised that a safety review of this product is currently being undertaken and that other countries have identified safety concerns which have led to suspension of sales of **MERIDIA** in one instance. The Committee advised that with evidence of benefit of only short-term weight loss, lack of cardiovascular outcome or morbidity/mortality data, and emerging safety concerns, the risk/benefit ratio of the drug should be re-examined.

Due to approval of a new indication for concomitant use with antidiabetic agents in overweight or obese Type 2 diabetics, **XENICAL** was resubmitted for the Expert Committee's consideration. While it was acknowledged that **XENICAL** appears to be efficacious in decreasing weight, which, in turn, may improve glycemic control, the Committee questioned the product's effectiveness and cost-effectiveness in comparison to alternative agents used in the management of Type 2 diabetes. When the magnitude of glycemic control induced with **XENICAL** was compared with that of other agents (i.e., thiazolidinediones) and the potential for use as add-on therapy considered, it was apparent that **XENICAL** could be cost additive without providing substantive clinical benefit over the long-term. Hence, **XENICAL** was not recommended for addition to the AHWDBL, as it does not offer a cost advantage and/or therapeutic advantage.

■ **NEXIUM** (esomeprazole magnesium trihydrate) (AZC) 20 mg and 40 mg tablets were resubmitted for consideration. The Committee noted that while it has been shown that **NEXIUM** shows statistically significant advantages vis-à-vis omeprazole in some clinical trial endpoints, much of the data reported no clinically significant differences. In addition, the committee cautioned that such results must be considered in the context of the relative dose equivalencies of the two compounds. It is noteworthy to consider that in studies where 40 mg of **NEXIUM** are compared with 20 mg of omeprazole, it is expected that the results would indicate that **NEXIUM** is clinically superior given that patients receiving **NEXIUM** 40mg are essentially being administered a 2-fold higher dose of drug. Hence, the Committee recommended that **NEXIUM** not be added to the AHWDBL, as it fails to offer a cost and/or therapeutic advantage.

■ **RENAGEL** (sevelamer hydrochloride) (GZM) – 400 mg and 800 mg tablets were not recommended for addition to the AHWDBL. The Committee's rationale for not recommending coverage was that there was no direct evidence provided substantiating a clear linkage between the progression of soft-tissue calcification and mortality and morbidity in patients with end-stage renal disease (ESRD). Despite the fact that patients with ESRD have a high propensity for cardiovascular disease, **RENAGEL** treatment has not been shown to have an effect on mortality and/or morbidity endpoints. If such data were available, then the high cost of the product, in comparison to treatment alternatives, could potentially be justified.