



Health Newsflash - a Quarterly Publication

New Drugs and Pipeline News Reviewed at the January to March 2009 DEC Meetings



The Drug Evaluation Committee (DEC) of ESI Canada conducts monthly reviews of all new drugs receiving their Notices of Compliance from Health Canada, to ascertain their place in therapy and their possible impacts on the private payer sector. Pricing information is included when the drug is available for sale. However, the availability of a drug does not immediately follow its approval by Health Canada. This publication, describing new drugs of significance, is provided to our insurance customers on a quarterly basis as a value-added service. We hope that you will find this Health Newsflash informative, timely, and useful.

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New Drugs

The following new drugs are expected to have minimal impact to private payer plans unless otherwise specified.

Alrex™ (0.2% loteprednol etabonate ophthalmic eye drops) is a new ophthalmic corticosteroid available from Bausch & Lomb. It is indicated for the temporary relief of the signs and symptoms of seasonal allergic conjunctivitis. The standard dosage is one drop instilled into the affected eye four times daily, for a maximum of 14 days. If the signs and symptoms do not improve in 2 days, the patient should be reevaluated.

The treatment of seasonal allergic conjunctivitis generally centers on antihistamines and mast cell stabilizers. Oral and ophthalmic antihistamines are useful for conjunctival symptoms. Ophthalmic antihistamines such as levocabastine (Livostin™), olopatadine (Patanol™), emedastine (Emadine™), and ketotifen (Zaditor™) provide relief in minutes with duration of effect of about 12 hours. Ophthalmic mast cell stabilizers such as cromoglycate (Opticrom™), nedocromil (Alocril™), and lodoxamide (Alomide™) require several days for onset and are initially administered four times daily. The place in therapy for an ocular corticosteroid is currently uncertain. Although the drug is effective at decreasing ocular discomfort, there are risks with use such as increased intraocular pressure (glaucoma risk) and eye infections. These risks are generally not attributed to the other options for the treatment of seasonal allergic conjunctivitis.

Currently, the price of Alrex™ is not yet available. However, it should be priced competitively to the other treatment options discussed.

Stelara™ (45 mg/0.5 mL, ustekinumab injection) is a new selective biologic immunomodulating agent indicated for the treatment of chronic moderate to severe plaque psoriasis in patients who are candidates for phototherapy or systemic therapy. The recommended starting dose of Stelara™ is 45 mg administered subcutaneously at weeks 0, 4 then every 12 weeks thereafter. For patients who inadequately respond to dosing every 12 weeks, consideration may be given to treating as often as every 8 weeks. Treatment should be discontinued if no response is seen after 12 weeks of therapy. This agent is marketed in Canada by Janssen-Ortho Inc.

Psoriasis occurs in 2% of the Canadians. It is characterized as a chronic condition with recurrent exacerbations and remissions. Plaque psoriasis is the most common form and accounts for 85% of psoriasis cases. First line treatment options are mainly topical medicines such as corticosteroids, keratolytic agents (salicylic acid), coal tars, anthracene derivatives (anthralin), retinoids (tazarotene), and vitamin D derivatives (calcipotriol). Among these, anthralin and tazarotene induce longer remissions than calcipotriol and corticosteroids.

Volume 11
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* All prices listed are Ontario prices, unless otherwise indicated.

** All ESI Canada Book of Business (BOB) data cited is for all of Canada, excluding Québec.



ESI CANADA®

www.esi-canada.com



Health Newsflash - a Quarterly Publication

New Drugs and Pipeline News Reviewed at the January to March 2009 DEC Meetings

Page 2



Optimizing the Value of Health Benefits

Unfortunately, topical treatment has its limits. Patients may have inadequate response to the most vigorous topical programs, or the affected skin area is so extensive that topical treatment is impractical. In such cases, phototherapy and systemic modalities are started. These are often rotated in patients every 1 to 2 years to avoid serious long-term side effects. Treatment options include acitretin (oral retinoid), methotrexate, cyclosporine, and the new biologic response modifiers. Biologics include alefacept (Amevive™), etanercept (Enbrel™), infliximab (Remicade™), adalimumab (Humira™), and now ustekinumab (Stelara™). Early clinical trials have shown Stelara™ to be significantly more effective in treating psoriasis than Enbrel™. However, more head-to-head trials against other agents are needed.

Stelara™ 45 mg/0.5 mL is priced at \$4,431.00 for a 0.5 mL vial. The cost for a year of treatment is approximately \$26,500.00. The cost per patient per year with Enbrel™ is approximately \$23,100.00, while Humira™ is approximately \$20,300.00. Stelara™ is priced at the higher end of the range of alternative treatments that can be self-administered by a patient. The drug may prove to have an intermediate impact on private payers.

Soliris™ (10 mg/mL (30 mL) eculizumab injection) is a new recombinant humanized monoclonal antibody and a complement inhibitor. Soliris™ is indicated for the treatment of paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis (red blood cell breakdown). The drug is given intravenously starting at 600 mg once weekly for 4 weeks, and following with 900 mg 1 week later; maintenance continues at 900 mg every 2 weeks thereafter. This biologic product is marketed by Alexion Pharmaceuticals Inc.

PNH is a descriptive term for red blood cell breakdown which releases hemoglobin into the urine. This causes dark-colored urine, most often in the morning. PNH results from an abnormality of bone marrow stem cells and is not inherited. There is little information on the incidence of PNH, but the rate is estimated to be 5- 10 times less than that of aplastic anemia which is 0.6-6.1 cases per million individuals.

The only cure for PNH is stem cell transplantation. Other options include the management of the signs and symptoms of the disease. Glucocorticoids can be used to treat acute episodes of hemolysis. Prolonged anticoagulation therapy may be of benefit when blood clots occur. Due to the PNH resultant anemia, iron therapy may be necessary as well. Erythropoietin is also an option to increase red blood cell production. Aside from stem cell transplantation, Soliris™ has been the most effective agent for the treatment of PNH. The drug is able to stabilize hemoglobin levels, reduce the number of transfusions and decrease the rate of red blood cell breakdown in treated adults with PNH.

Currently, the price for this agent is not yet available. This drug is likely to be administered in a hospital setting. Due to the very low incidence of the disease, the impact to private payers should be minimal.

Pristiq™ (50, 100 mg desvenlafaxine extended release tablet) is a new serotonin/norepinephrine reuptake inhibitor (SNRI) available on the Canadian market. It is indicated for the treatment of major depressive disorder in adults. The recommended dose for Pristiq™ is 50 mg once daily, with or without food. In clinical trials, higher doses demonstrated no additional benefit but did cause more adverse events and contributed to more discontinuations. The drug is marketed in Canada by Wyeth Pharmaceuticals.

Volume 11
Issue 2

May 7,
2009



ESI CANADA®

www.esi-canada.com



Health Newsflash - a Quarterly Publication

New Drugs and Pipeline News Reviewed at the January to March 2009 DEC Meetings

Page 3



Optimizing the Value of Health Benefits

Pristiq™ is the major active metabolite of venlafaxine (Effexor™ XR). One advantage of this drug is that it does not require dose titration, which allows therapy to be initiated at the recommended therapeutic dose. Furthermore, the metabolism of Pristiq™ does not involve the CYP2D6 pathway, which may prove to be beneficial when it is administered with other medications that do undergo metabolism via the CYP2D6 pathway. Another SNRI that is also available in Canada is duloxetine (Cymbalta™). Currently Pristiq™ has not been compared in head-to-head clinical trials to either Cymbalta™ or Effexor™ XR.

Both Pristiq™ 50 mg and 100 mg are priced at \$2.71 per tablet. The annual cost per patient is approximately \$989.00. The annual cost per patient with generic venlafaxine (key comparator) ranges from \$430.00 to \$883.00, depending on the dose. The annual cost per patient with Cymbalta™ is approximately \$1,372.00. Overall, both Pristiq™ and Cymbalta™ are more expensive than generic venlafaxine. However, because Pristiq™ is one of many antidepressants available on the Canadian market, the impact of this introduction to private payers should be minimal.

Nplate™ (250 mcg/0.5 mL, 500 mcg/1.0 mL romiplostim injection) is a new recombinant thrombopoiesis stimulating protein approved by Health Canada for the treatment of chronic immune (idiopathic) thrombocytopenic purpura (ITP) in adults. ITP is defined as a dangerous decrease in blood platelet count, but with normal bone marrow and the absence of other causes. Generally, in North America, the incidence of ITP in adults is approximately 66 cases per 1,000,000 per year. It is, therefore, a rare condition.

Nplate™ is used to increase platelet levels. The drug is administered by weekly subcutaneous injection. The recommended dose is 1 mcg/kg with subsequent doses adjusted according to the platelet count. The drug is marketed in Canada by Amgen Inc.

Nplate™ is intended for patients who are not splenectomized (spleen not removed) and who have had an inadequate response or are intolerant to corticosteroids and/or immunoglobulins. It is also indicated for splenectomized (spleen removed) patients who have had an inadequate response to splenectomy. The drug can be used alone or with other ITP therapies such as corticosteroids, azathioprine, danazol, and immunoglobulins.

Currently, the price for Nplate™ is not available. Due to the very low incidence of the disease, the impact to private payers should be minimal.

Vyvanse™ (30 mg, 50 mg, lisdexamfetamine dimesylate capsules) is a new drug recently approved for the treatment of Attention Deficit Hyperactivity Disorder (ADHD). This is a stimulant often used as an adjunct to psychological, educational, and social as well as other remedial measures in ADHD treatment. The initial dose is 30 mg once daily and may be increased in 20 mg increments at weekly intervals, to a maximum dose of 70 mg daily. The drug is marketed in Canada by Shire Pharmaceuticals Group plc.

ADHD affects all ages but it is more prominent among children and teenagers. It may be diagnosed as early as 6 years old. Other ADHD treatments available in Canada include mixed salt amphetamines (Adderall™ XR), methylphenidate (Concerta™, Ritalin™, Biphentin™), dextroamphetamine (Dexedrine™), and atomoxetine (Strattera™).

Volume 11
Issue 2

May 7,
2009



ESI CANADA®

www.esi-canada.com



Health Newsflash - a Quarterly Publication

New Drugs and Pipeline News Reviewed at the January to March 2009 DEC Meetings

Page 4



Vyvanse™ is a pro-drug of dextroamphetamine. After oral administration, Vyvanse™ is rapidly absorbed in the gastrointestinal tract and converted to dextroamphetamine which is responsible for the drug's activity. More comparative clinical trials are required to assess its place in therapy.

The price of Vyvanse™ is not yet available. However, it is expected to fall in-line with many other therapies available on the market and should therefore have minimal impact on private payers.

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New Formulation

Temodal™ (100 mg/vial, powder for reconstitution, temozolomide injection) is an antineoplastic agent used for the treatment of adult patients newly diagnosed with glioblastoma multiforme (primary brain tumor) concomitantly with radiotherapy and then as maintenance treatment. It is also used for the treatment of adult patients with *glioblastoma multiforme* or *anaplastic astrocytoma* (central nervous system cancer) with documented evidence of recurrence or progression after standard therapy. A new injectable intravenous formulation is now available. Oral capsules in strengths of 5, 20, 100, 140, 180, and 250 mg have already been on the market. Dosing is highly individualized. The drug is marketed in Canada by Schering-Plough Corp.

The current average annual incidence of primary malignant brain tumors in North America is 14.4 per 100,000 persons. Of that, *anaplastic astrocytomas* and *glioblastomas* constitute more than 50% of all malignant tumors of the brain. Therapies for these difficult cancers involve surgery, radiation, corticosteroids and chemotherapy. Temodal™ has been shown to provide significant improvement in survival during clinical trials. Median survival for patients with glioblastoma multiforme, without accounting for age, is approximately 1 year. Patients with anaplastic astrocytoma have a life expectancy of 3 to 5 years.

Currently the price for 100 mg vial of the injectable formulation is not available. An additional update will be provided once price becomes available.

New Indication

Avastin™ (25 mg/mL (4 mL), bevacizumab injection) is now indicated for use in combination with paclitaxel for the treatment of patients with metastatic HER2-negative breast cancer who are ECOG (Eastern Cooperative Oncology Group) Class 0-1. The drug received conditional Health Canada approval for this indication, pending the results of further studies to verify its clinical benefits. Avastin™ is also approved for the treatment of colorectal cancer and non-small cell lung cancer. The recommended dosage of Avastin™ for metastatic breast cancer is 10 mg/kg, given by intravenous infusion at weeks 1 and 3 of each four-week cycle. The medication is marketed in Canada by Hoffman-La Roche Ltd.

A preliminary clinical trial compared the efficacy of Avastin™-paclitaxel versus paclitaxel alone in patients with metastatic breast cancer who had received no prior chemotherapy for metastatic disease. The addition of Avastin™ prolonged progression-free survival from 5.8 months (paclitaxel alone) to 11.3 months (paclitaxel plus Avastin™). Overall median survival was increased from 24.8 months (paclitaxel) to 26.5 months (paclitaxel plus Avastin™).

Volume 11
Issue 1

May 7,
2009



ESI CANADA®

www.esi-canada.com



Health Newsflash - a Quarterly Publication

New Drugs and Pipeline News Reviewed at the January to March 2009 DEC Meetings

Page 5



Currently, HER2 is expressed in 18-20% of breast cancers. Therefore, Avastin™ may be a treatment option for the remaining ~80% of breast cancer patients encountered in clinical practice. Avastin™ (25 mg/mL) is priced at \$527.52 for a 4 mL vial. The cost for a cycle of treatment for a 70 kg patient would approximately be \$7400.00. Assuming a patient receives treatment for 11 cycles a year, the total annual cost of treatment would be approximately \$81,400.00. This new development may have an intermediate impact on private payers because the incidence of breast cancer is quite high in North America.

Author: Lucas Krajewski, R.Ph., B.Sc.Ph., Pharmacy Resident, ESI Canada

Editor: Priscilla Po, R.Ph., B.Sc.Ph., Clinical Specialist, ESI Canada

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Volume 11
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May 7,
2009



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