Health Newsflash — a Quarterly Publication

New Drugs and Pipeline News Reviewed at the July to September 2011 DEC Meetings

The Drug Evaluation Committee (DEC) of Express Scripts 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.

New Drugs

Banzel (rufinamide)

Dosage Form	DIN & Strength	Manufacturer	AHFS Class
Oral tablet	02369613 – 100mg 02369621 – 200mg 02369648 – 400mg	Eisai Limited	28:12.92 – Miscellaneous Anticonvulsants

Indication(s)

For adjunctive treatment of seizures associated with Lennox-Gastaut syndrome in children 4 years and older and adults.

Dose

Children and adults < 30kg:
100mg twice per day, titrated to a maximum of 1300mg/day.
Adults and children >30kg:
200mg twice per day, titrated to a maximum of 1800mg/day (for patients 30-50kg), 2400mg/day (for patients 50-70kg), 3200mg/day (for patients >70kg).

Therapeutic Alternatives

Adjunctive antiepileptic drugs: lamotrigine; topiramate (all available in generic form)

Clinical Notes

Lennox-Gastaut syndrome (LGS) is a severe form of epilepsy. Seizures usually begin before 4 years of age. Seizure types, which vary among patients, include tonic (stiffening of the body, upward deviation of the eyes, dilation of the pupils, and altered respiratory patterns), atonic (brief loss of muscle tone and consciousness, causing abrupt falls), atypical absence (staring spells), and myoclonic (sudden muscle jerks). There may be periods of frequent seizures mixed with brief, relatively seizure-free periods. Most children with Lennox-Gastaut syndrome experience some degree of impaired intellectual functioning or information processing, along with developmental delays, and behavioral disturbances. The long-term prognosis is poor; although the epilepsy often improves, complete seizure freedom is rare and conversely the mental and psychiatric disorders tend to worsen with time.

The goal of treating LGS is to reduce the frequency of seizures and to provide the best quality of life possible for the patient. Banzel (rufinamide) is a new antiepileptic drug (AED) that has been shown to be effective as adjunctive therapy (when added to other AEDs) for treating LGS and refractory partial seizures. It appears to show low levels of antiepileptic resistance which is common with other AEDs. It also has little negative effect on cognitive function which may be problematic with other AEDs.

All prices listed are Ontario prices, unless otherwise indicated.
All Express Scripts Canada Book of Business (BOB) data cited is for all of Canada, excluding Québec.

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Place in Therapy

LGS associated seizures are resistant to most drug therapies thus combination therapy using adjunctive AEDs is often required. Treatment is individualized and there is no data currently available which compares the various adjunctive AEDs for effectiveness in LGS; however, Banzel has evidence of effectiveness and has shown lasting efficacy after three years. There are fewer drug-drug interactions between Banzel and other commonly used AEDs, with low reports of serious adverse effects. Therefore, Banzel is a reasonable alternative agent which could be added to drug therapy choices currently available for a difficult to treat disease.

Comparative Pricing

	Banzel (rufinamide)	lamotrigine	topiramate
Estimated daily cost	$11 – $27	$0.50 – $4	$2 - $5

Impact

Banzel is significantly more expensive than other existing treatments, and is used for a disease with low prevalence; as such this drug may have an intermediate impact on certain private plans.

Plan Management Suggestions

This drug is substantially more expensive than other antiepileptic drugs. Use of Prior Authorization is recommended to ensure adherence to officially indicated use.

Jevtana (cabazitaxel)

Dosage Form	DIN & Strength	Manufacturer	AHFS Class
Intravenous Solution	02369524 – 40mg/ml	Sanofi Aventis Canada Inc.	10:00.00 – Antineoplastic agents

Indication(s)

Treatment of hormone-refractory metastatic prostate cancer (in patients previously treated with a docetaxel-containing regimen).

Dose

25mg/m^2/dose I.V. once every 3 weeks (in combination with prednisone).

Therapeutic Alternatives

Mitoxantrone HCl Injection 2mg/ml (no survival benefit); Docetaxel + oral prednisone regimen is covered by CCO (as rechallenge); Zytiga (abiraterone acetate) (see below)

Clinical Notes

Cabazitaxel (Jevtana) is a semisynthetic taxane similar to paclitaxel. Cabazitaxel is used with prednisone in the treatment of hormone-refractory metastatic prostate cancer, in patients previously treated with a docetaxel-containing chemotherapy regimen.

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Place in Therapy

Cabazitaxel in combination with prednisone provided superior overall survival (15.1 months) compared with mitoxantrone plus prednisone (12.7 months) in hormone-refractory metastatic prostate cancer previously treated with a docetaxel-containing regimen. Cabazitazel is the first drug to show a survival benefit in patients whose disease has progressed after standard chemotherapy and for whom there are currently no approved treatment options.

Comparative Pricing

	Jevtana	mitoxantrone	Taxotere (docetaxel)	Zytiga
Dose (assuming BSA = 1.9m²)	47.5mg every 3 weeks	25mg every 3 weeks	142.5mg every 3 weeks	1g (4 tablets) daily
Estimated cost per dose	Price not available	$455	$1,900	$3,400/3 weeks

Impact/Plan Management Suggestions

Impact not determined - Price not available.

Zytiga (abiraterone acetate)

Dosage Form	DIN & Strength	Manufacturer	AHFS Class
Tablet	02371065 – 250mg	Janssen Inc	10:00.00 – Antineoplastic agents

Indication(s)

Zytiga™ is indicated with prednisone for the treatment of metastatic prostate cancer (castration-resistant prostate cancer) in patients who have received prior chemotherapy containing docetaxel.

Dose

The recommended dosage of Zytiga™ is 1 g (four 250 mg tablets) as a single daily dose.

Therapeutic Alternatives

Jevtana (cabazitaxel)(see above); mitoxantrone (generic, no survival benefit); docetaxel rechallenge.

Clinical Notes

Abiraterone acetate (Zytiga) selectively inhibits the enzyme 17α-hydroxylase, which is required for androgen biosynthesis in testicular, adrenal and prostatic tumor tissues. Androgen deprivation therapy (ADT) is generally the initial treatment for men with metastatic prostate cancer. ADT decreases androgen production in the testes but does not affect androgen production by the adrenals or in the tumor. Despite high response rates to ADT, nearly all men eventually develop progressive castrate-resistant disease. Zytiga™ decreases serum testosterone and other androgens in patients to levels lower than those achieved with standard ADT.

Both cabazitaxel (Jevtana) and abiraterone acetate (Zytiga) have shown improved overall survival over either placebo or alternative therapy (e.g., mitoxantrone). Both cabazitaxel and abiraterone acetate have shown improved overall survival over either placebo or alternative therapy (e.g., mitoxantrone). For most patients with metastatic prostate cancer who have progressed on docetaxel, treatment with abiraterone may be preferred prior to using cabazitaxel, because of its more favorable side effect profile. However, for patients who have evidence of more aggressive disease, cabazitaxel should be preferred over abiraterone.

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Place in Therapy

Abiraterone acetate plus prednisone is indicated for the treatment of metastatic castration-resistant prostate cancer in patients who have received prior chemotherapy containing docetaxel.

Comparative Pricing

	Zytiga	Jevtana	mitoxantrone	Taxotere (docetaxel)
Dose (assuming BSA = 1.9m²)	1g (4 tablets) daily	47.5mg i.v. every 3 weeks	25mg i.v. every 3 weeks	142.5mg i.v. every 3 weeks
Estimated cost per dose	$3,400/3 weeks	Price not available	$455	$1,900

Impact/Plan Management Suggestions

Prior Authorization recommended to verify indication for use.

Benlysta (belimumab)

Dosage Form	DIN & Strength	Manufacturer	AHFS Class
Intravenous Injection	02370050 – 120mg Vial 02370069 – 400mg Vial	GlaxoSmithKline Inc	92:44.00 - Immunosuppressive Agents

Indication(s)

Benlysta™ is indicated in addition to standard therapy for reducing disease activity in adult patients with active, autoantibody-positive, systemic lupus erythematosus (SLE).

Dose

The recommended dosage regimen is 10mg/kg at 2-week intervals for the first three doses and at 4-week intervals thereafter. Benlysta™ should be infused over a 1-hour period.

Therapeutic Alternatives

NSAIDs (e.g., naproxen, celecoxib); hydroxychloroquine (Aralen); systemic corticosteroids (e.g., prednisone, methylprednisolone); immunosuppressive agents (e.g., azathioprine, cyclophosphamide, methotrexate, mycophenolate (off-label), Rituxan (rituximab)(off-label)).

Clinical Notes

SLE is a complex autoimmune disease that can affect multiple organ systems, including the kidneys, the skin, the lungs, the heart and the central nervous system. It is characterized by a recurring and variable pattern of disease flare and remission. Its symptoms can range from mild to potentially life-threatening kidney or cardiovascular involvement. SLE is traditionally treated with immunosuppressive drugs such as corticosteroids and cyclophosphamide, however a significant proportion of patients are unable to achieve full remission of symptoms and experience relapses despite long-term immunosuppressive therapy, which is associated with an increased risk of infection and cancer. Benlysta (belimumab) is an IgG1λ monoclonal antibody that prevents the survival of B lymphocytes which reduces the autoimmune response. Belimumab is the first new drug approved for SLE in over 50 years. In clinical trials the effects seen were relatively modest with an improvement over placebo 14% and 9.4% in the two trials.

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Place in Therapy

The place of this new drug in therapy is unclear. With modest results compared to placebo in the two key clinical trials, it is unclear whether this drug would be best utilized to treat active SLE or to maintain disease remission. There is also no data on its use in treatment of patients with end-organ involvement (e.g., kidney or heart)

Comparative Pricing

	Benlysta	hydroxychloroquine	cyclophosphamide	Rituxan (off-label)
Dose	700mg – assuming 70kg patient	200-400mg/day	500mg i.v. monthly	1gm i.v. every 2 weeks
Estimated cost per year	$23,000	$100-$200	$450	$10,000

Impact/Plan Management Suggestions

Prior Authorization recommended to verify indication for use.

Victrelis (boceprevir) and Victrelis Triple (boceprevir+peginterferon alfa-2B + ribavirin)

Dosage Form	DIN & Strength	Manufacturer	AHFS Class
Capsule	02370816 – 200mg	Merck Canada Inc.	08:18.92 – Miscellaneous Antivirals
Triple (Victrelis + Pegetron) Kit: (Capsules + subcutaneous injection)	02371448 – 200mg, 80µg/0.5ml, 200mg 02371456 – 200mg, 100µg/0.5ml, 200mg 02371464 – 200mg, 120µg/0.5ml, 200mg 02371472 – 200mg, 150µg/0.5ml, 200mg	Merck Canada Inc.	08:18.92 – Miscellaneous Antivirals

Indication(s)

Victrelis™ (boceprevir) is indicated for the treatment of chronic hepatitis C genotype 1 infection in combination with peginterferon alpha (PegIFNα)/ribavirin (RBV), in adult patients (18 years and older) with compensated liver disease, including cirrhosis, who were previously untreated or who have failed previous therapy.

Dose

Dosage of Victrelis™ (boceprevir) capsules is 800mg (4x200mg) three times daily, the dosage of Pegetron® is dependent on weight and patient response (hemoglobin levels, neutrophil counts). A four week lead-in of Pegetron®, using dosing in the table above, is recommended prior to initiating treatment with Victrelis™. The duration of therapy is dependent on viral RNA response to treatment.

Therapeutic Alternatives

Incivek (telaprevir)

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Clinical Notes

Victrelis™ (boceprevir) is a new protease inhibitor with direct activity against the hepatitis C virus (HCV). Boceprevir is an inhibitor of the HCV NS3/4A protease that inhibits viral replication in HCV-infected host cells. Chronic hepatitis C infection (CHC) is a significant medical and economic burden to Canadians. The estimated prevalence in Canada is approximately 0.8% to 1%. CHC can cause future problems such as decreased liver function, cirrhosis, and liver cancer. The current standard of treatment is combination therapy with peginterferon alpha (PegIFNα)/ribavirin (RBV). Victrelis™ Triple is the combination of Victrelis™ with Pegetron™ Redipen™ (PegIFNα-2b + ribavirin). The pivotal phase 3 trials for boceprevir have shown higher viral response rates in those adding boceprevir to standard treatment (PegIFNα-2b + RBV) vs. placebo. Also, using response-guided therapy, shorter treatment durations of poorly tolerated and expensive therapy could possibly be achieved. There are concerns with anemia, which frequently occurs with RBV, but was seen with increased frequency with boceprevir in clinical trials. This resulted in increased use of erythropoietin agents required to manage anemia. Also, a higher number of patients reported psychiatric symptoms with boceprevir during clinical trials, which also frequently occurs with standard therapy.

Place in Therapy

Victrelis™ is a new direct acting antiviral agent against HCV which offers possible improved therapy response for the most difficult to treat form of CHC, genotype 1. Another, similar drug, Incivek™ (telaprevir), has been released at almost the same time. Victrelis™ is also available in a single product combination with PegIFNα-2b + RBV, Victrelis™ Triple, which may provide added patient and prescriber convenience.

Comparative Pricing: See Table under **Incivek (telaprevir)**

Impact/Plan Management Suggestions

Intermediate impact – high cost drug therapy for a low prevalence disease state with no treatment alternatives. Single course of therapy required.

Incivek (telaprevir)

Dosage Form	DIN & Strength	Manufacturer	AHFS Class
Tablet	02371553 – 375mg	Vertex Pharmaceuticals (Canada) Incorporated	08:18.92 – Miscellaneous antivirals

Indication(s)

Incivek™ (telaprevir), in combination with peginterferon alfa (PegIFNα) and ribavirin (RBV), is indicated for the treatment of genotype 1 chronic hepatitis C in adult patients with compensated liver disease, including cirrhosis, who are treatment-naïve or who have previously been treated with interferon-based treatment, including prior null responders, partial responders, and relapsers.

Dose

The recommended dose of Incivek™ tablets is 750 mg (two 375-mg tablets) taken orally 3 times a day, the duration of treatment is dependent upon treatment response.

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Therapeutic Alternatives
Victrelis (boceprevir); Victrelis Triple (boceprevir/ribavirin/peginterferon alfa-2b)

Clinical Notes
Incivek™ (telaprevir) is a direct-acting antiviral agent against the hepatitis C virus. Telaprevir is an inhibitor of the HCV NS3/4A serine protease which is essential for viral replication. Chronic hepatitis C infection (CHC) is a significant medical and economic burden to Canadians. The estimated prevalence in Canada is approximately 0.8% to 1%. CHC can cause future problems such as decreased liver function, cirrhosis, and liver cancer. The current standard of treatment is combination therapy with PegIFNα and RBV. Three pivotal phase 3 clinical trials showed improved viral levels in patients who were both treatment naïve and with those who received prior treatment (null responders, partial responders, prior treatment relapsers) when compared to standard therapy with combination PegIFNα/RBV. The most common side effects included rash, pruritus, nausea, fatigue, headache, and anemia. Both serious rash and anemia were the most common causes for telaprevir treatment discontinuation, although most causes of anemia were sufficiently managed with RBV dose reduction.

Place in Therapy
Telaprevir offers an alternative to boceprevir, another orally administered NS3/4A protease inhibitor indicated for the treatment of chronic hepatitis C viral (HCV) infection genotype 1, in combination with peginterferon alfa and ribavirin in adults with compensated liver disease, including cirrhosis, who were previously untreated or previously failed interferon and ribavirin therapy. Boceprevir is added on after 4 weeks of peginterferon alfa and ribavirin therapy, while telaprevir does not require a lead-in period leading to a simpler treatment algorithm with telaprevir. No increases in psychiatric side effects were reported with telaprevir.

Comparative Pricing
See table below.

Impact/Plan Management Suggestions
Intermediate impact – high cost drug therapy for a low prevalence disease state with no treatment alternatives. Single course of therapy required

Comparative Pricing

	Victrelis 200mg	Incivek 375mg
Unit cost	$14/capsule	$74/tablet
Cost per week	$1,180	$3,100
Treatment cost (length of treatment)[3]	$28,320/24 weeks $37,800/32 weeks	$37,200/12 weeks

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	Victrelis Triple kit[1] (168 capsules Victrelis + Pegetron Redipen + ribavirin caps)	Pegetron Redipen kit[1] (Pegetron Redipen + ribavirin 200mg capsules)	Pegasys RBV kit[2] (PegIFNα-2a 180mcg pre-filled syringe + ribavirin 200mg tablets)	Incivek + Pegasys RBV
Unit cost	80mcg/56 caps - $2,800/kit 100mcg/56 caps - $2,800/kit 120mcg/70 caps - $2,900/kit 150mcg/84 caps - $2,900/kit 150mcg/98 caps - $2,900/kit	80mcg/56 caps - $800/kit 100mcg/56caps - $800/kit 120mcg/70caps - $880/kit 150mcg/84caps - $880/kit 150mcg/98caps - $880/kit	28 tabs - $420/kit 35 tabs - $420/kit 42 tabs - $420/kit	
Cost per week	$1,400 - $1,450	$400 - $440	$420	$3,520
Treatment cost (length of treatment)[3]	$34,400 - $35,680/28 weeks $38,400 - $40,080/48 weeks $45,600 - $47,280/36 weeks $48,000 - $49,920/ 48 weeks	$19,200 - $21,120/ 48 weeks	$10,080/24 weeks $20,160/48 weeks	$47,280/24 weeks $57,360/48 weeks

1. one kit provides sufficient drug for 2 weeks of treatment
2. one kit provides sufficient drug for 1 week of treatment
3. total length of treatment recommended in product monographs; note for Victrelis and Incivek does not include concurrent treatment with PegIFNα + RBV, based on response and baseline conditions

Trajenta (linagliptin)

Dosage Form	DIN & Strength	Manufacturer	AHFS Class
Tablet	02370921 – 5mg	Boehringer Ingelheim Canada Ltd	68:20.05 – Dipeptidyl Peptidase IV (DPP-4) Inhibitors

Indication(s)

Trajenta™ (linagliptin) is indicated in adult patients with type 2 diabetes mellitus (T2DM) to improve glycemic control, in conjunction with diet and exercise, as monotherapy in patients for whom metformin is inappropriate due to contraindications or intolerance, or in combination with metformin and/or a sulfonylurea.

Dose

The recommended dose is 5mg once daily.

Therapeutic Alternatives

Januvia (sitagliptin); Onglyza (saxagliptin)

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Clinical Notes

Linagliptin is a potent, reversible and selective inhibitor of the enzyme dipeptidyl peptidase 4 (DPP-4), which is involved in the rapid break down of the incretin hormones (glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP). Both incretin hormones are involved in the physiological regulation of glucose homeostasis. GLP-1 and GIP are secreted by the intestine at a low basal level throughout the day and concentrations are increased in response to a meal. GLP-1 and GIP increase insulin biosynthesis and secretion from pancreatic beta cells in the presence of normal and elevated blood glucose levels. Furthermore GLP-1 also reduces glucagon secretion from pancreatic alpha cells, resulting in a reduction in hepatic glucose production. Linagliptin binds to DPP-4 in a reversible manner and thus leads to an increase and a prolongation of active incretin levels. Linagliptin increases insulin secretion and lowers glucagon secretion in a glucose-dependent fashion thus resulting in an overall improvement in glucose homoeostasis.

Place in Therapy

The most recent guidelines from the Canadian Diabetes Association place incretin agents such as DPP-4 inhibitors as second line after metformin for the management of hyperglycemia in individuals with type 2 diabetes. While there may be some pharmacokinetic and pharmacodynamic differences between linagliptin and the other DPP-4 inhibitors currently on the market, there are few clinically relevant differences between them.

Comparative Pricing

	Trajenta	Januvia	Onzlyza
Unit Price	$2.70/tablet	$2.96/tablet	$2.91/tablet
Annual Cost	$986	$1080	$1062

Impact

Minimal impact – cost shift from similarly priced alternatives

Edurant (rilpivirine)

Dosage Form	DIN & Strength	Manufacturer	AHFS Class
Tablet	02370603 – 25mg	Janssen Inc	08:18.08 - Antiretrovirals

Indication(s)

Edurant™ (rilpivirine), in combination with other antiretroviral agents, is indicated for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in antiretroviral treatment-naïve adult patients.

Dose

The recommended dose of Edurant™ is one 25 mg tablet once daily. Edurant™ must always be given in combination with other antiretroviral medicinal products.

Therapeutic Alternatives

Sustiva (efavirenz); Intelence (etravirine)

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Clinical Notes

Edurant™ (rilpivirine) is a second-generation non-nucleoside reverse transcriptase inhibitor (NNRTI). US Department of Health and Human Services (HHS) recommends use of an NNRTI based triple therapy regimen (with 2 nucleoside reverse transcriptase inhibitors (NRTIs), usually emtricitabine and tenofovir because these can be administered once daily) as one possible preferred antiretroviral treatment alternative for treatment naïve adult and adolescent patients with HIV-1.

Place in Therapy

The most recent guidance from the HHS Guidelines (to which Canadian guidelines refer for specific recommendations) recommends efavirenz as the preferred NNRTI due to optimal and durable efficacy, favourable tolerability and toxicity profile and ease of use. Rilpivirine is now classified as an alternative NNRTI which is effective and tolerable but has potential disadvantages compared with EFV; however, it may be the preferred regimen for some patients.

Comparative Pricing

	Edurant	Sustiva
Unit cost	$14.50	$15.00
Monthly cost	$440	$455

Impact

Minimal impact – cost shift, comparably priced.

NEW FORMULATION

Ozurdex (dexamethasone intraocular implant)

Dosage Form	DIN & Strength	Manufacturer	AHFS Class
Intravitreal Implant	02363445 – 0.7mg	Allergan	52:08.08 – EENT – Corticosteroids

Indication(s)

Ozurdex™ (dexamethasone intravitreal implant 0.7mg) is indicated for the treatment of macular edema following central retinal vein occlusion (CRVO).

Dose

The recommended dose is one implant (entire contents of one single use Ozurdex™ 0.7mg device following central retinal vein occlusion. A second dose may be considered after six months in those who have experienced a response to initial treatment but who subsequently experienced a loss in visual acuity.

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Therapeutic Alternatives

- Triamcinolone acetonide intravitreal injection (Kenalog® and generics);
- Lucentis® (ranibizumab)
- Avastin® (bevacizumab) – officially indicated for colorectal, breast, lung, and brain cancers – off-label use associated with increased risk of intraocular infection.
- *Retisert™ (fluocinolone implant) – In US, this is indicated for the treatment of chronic non-infectious uveitis affecting the posterior segment of the eye.*

Clinical Notes

Retinal vein occlusion (RVO) is an important cause of visual loss among older adults throughout the world. RVO is the second most common cause of vision loss from retinal vascular disease, following diabetic retinopathy. CRVO is often associated with macular edema which then leads to loss of visual acuity. Medical treatments are usually used and consist of intravitreal glucocorticoid injections (triamcinolone acetonide), intravitreal anti-VEGF injections (ranizumab, bevacizumab), or glucocorticoid intravitreal implants (i.e., Ozurdex®).

Ozurdex® is a biodegradable dexamethasone implant delivered by injection into the vitreal space of the eye. The implant is a biodegradable polymer matrix that eventually dissolves over the course of several months into carbon dioxide and water. Dexamethasone is slowly released into the eye as the matrix dissolves, extending the action of the drug. Glucocorticoids are thought to be beneficial by inhibiting the activity of vascular endothelial growth factor (VEGF). No comparative trials are available comparing Ozurdex® with other CRVO therapies (e.g., anti-VEGF agents, intravitreal triamcinolone acetonide injections). Another intravitreal glucocorticoid implant, Retisert® (fluocinolone acetonide) has been used in a small trial for CRVO.

Place in Therapy

There are no widely accepted guidelines for the treatment of CRVO, however general practice is to offer anti-VEGF injections such as Lucentis® first (clinical trial data exists for this anti-VEGF agent, but bevacizumab is thought to have similar efficacy). For those who do not respond to this treatment, intravitreal triamcinolone acetonide (Kenalog®) injections are used next. Intravitreal glucocorticoid implants are relatively new and their precise place in therapy has not been established. Currently in US this is used infrequently. The disadvantage of glucocorticoid treatments are increases in intraocular pressure and increased cataract formation.

Impact

Minimal impact

Comparative Pricing

	Ozurdex Intravitreal Implant	Lucentis Intravitreal Injection*	Retisert Intravitreal Implant
Cost per dose	$1,400 (6 months)	$400 (0.5mg monthly)	$16,000 (30 months)
Estimated cost per Year	$2,800	$1,200 - $3,600 (3-9 injections/year)	$6,400

* Cost assumes no product waste

Impact

Minimal impact.

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Actonel DR (risedronate delayed-release)

Dosage Form	DIN & Strength	Manufacturer	AHFS Class
Delayed-release tablet	02370417 – 35mg	Warner Chilcott Canada Co.	92:24.00 – Bone Resorption Inhibitors

Indication(s)
For the treatment of osteoporosis in postmenopausal women

Dose
The recommended dose is one 35mg delayed release tablet taken orally once a week. The drug should be taken immediately after a meal.

Therapeutic Alternatives
Generic risedronate 35mg immediate release tablets

Clinical Notes
The use of bisphosphonates, such as risedronate, for the treatment of postmenopausal osteoporosis is advocated in the most recent Canadian Osteoporosis Clinical Practice Guidelines 2010 as first line pharmacotherapy in patients at high risk of fracture. They have been shown to decrease fracture rates as well as increase bone mineral density.

A major cause of decreased treatment adherence to bisphosphonate therapy is the need to take the drug in the fasting state, due to the inhibition of already low absorption of the drug in the presence of food. The formulation of a delayed release tablet addresses this unmet need for a product that can be taken after meals to more easily fit into patients' lifestyles and enhance adherence to the medication.

The delayed release tablet has been found to provide equivalent results on the bone mineral density of lumbar spine vertebrae over one year when compared to risedronate 5mg immediate release given once daily. The delayed release tablets were found to cause higher frequencies of gastrointestinal side effects than immediate release tablets when administered in the fasting state, therefore, the delayed release tablets should only be administered immediately after meals.

Place in Therapy
This new formulation offers an alternative for patients who are unable to adhere to therapy with immediate release tablets given in the fasting state.

Comparative Pricing

	Actonel DR 35mg	Apo-Risedronate 35mg
Unit cost	$12.50	$3.50
Estimated annual cost	$650	$200

Impact
Minimal impact.

Plan Management Suggestions
Tiered formulary.

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Sublinox (zolpidem)

Dosage Form	DIN & Strength	Manufacturer	AHFS Class
Sublingual orally disintegrating tablet	02370433 – 10mg	Meda AB (marketed by Valeant Pharmaceuticals International)	28:24.92 – Miscellaneous Anxiolytics, Sedatives & Hypnotics

Indication(s)
For the short-term treatment of insomnia characterized by difficulties with sleep initiation.

Dose
10mg once daily under the tongue immediately before bedtime

Therapeutic Alternatives
Ativan sublingual; temazepam; zopiclone

Clinical Notes
Sublinox (zolpidem) is a non-benzodiazepine hypnotic and is chemically unrelated to benzodiazepines, barbiturates, or other drugs with known hypnotic properties. It interacts with a GABA-BZ receptor complex and shares some of the pharmacological properties of the benzodiazepines. In contrast to the benzodiazepines, which nonselectively bind to and activate all BZ receptor subtypes, zolpidem binds the BZ1 receptor preferentially. This selective binding of zolpidem on the BZ1 receptor may explain the preservation of deep sleep (stages 3 and 4) in human studies of zolpidem tartrate at hypnotic doses.

Sublinox is bioequivalent to Ambien® tablets (which received NOC on November 20, 1996, but is currently not marketed in Canada).

Place in Therapy
Sublinox provides a non-benzodiazepine alternative for treatment of insomnia characterized by poor sleep initiation (as opposed to sleep latency), although superiority over short-acting, rapid onset benzodiazepines has not been demonstrated.

Comparative Pricing

	Sublinox	Apo-Zopiclone	Ativan Sublingual	Apo-Temazepam
Unit cost	Price not available	5mg - $0.25 7.5mg - $0.50	0.5mg - $0.15 1mg - $0.20 2mg - $0.25	15mg - $0.07 30mg - $0.08

Impact
Insufficient information – pricing not available

Plan Management Suggestions
To be determined based on pricing.

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FIRST TIME GENERICS

First-Time Generic Drugs (Notices of Compliance from June 3, 2010 – August 31, 2011)

Generic Name	Reference Drug (Brand)	Rank by ingredient cost in 2010	Manufacturer	Route of Administration	Approved Indications
Brinzolamide	Azopt	651	Sandoz Canada Incorporated	Ophthalmic	Glaucoma
Zolmitriptan	Zomig	63	Various	Oral	Migraine
Latanoprost	Xalatan	232	Various	Ophthalmic	Glaucoma

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