Health Newsflash

A Quarterly Publication

New Drugs and Pipeline News Reviewed at the July to September 2014 DEC Meetings

The Drug Evaluation Committee (DEC) of Express Scripts Canada conducts monthly reviews of all new drugs receiving their Notice of Compliance from Health Canada, to ascertain their place in therapy and their possible impact on the private payer sector. The prices quoted in this document are approximations for general information purposes only, and are not intended, nor should they be relied upon, for purposes of any actual claims adjudication or reimbursement. This publication, describing new drugs of significance, is provided to our 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

Firazyr® (icatibant acetate)			
Dosage Form	**DIN & Strength**	**Manufacturer**	**AHFS Class**
Subcutaneous injection	02425696 – 10mg/ml (30mg/3ml pre-filled syringe)	Shire Orphan Therapies Inc.	92:32.00 – Complement inhibitors

Indication(s)

For the treatment of acute attacks of hereditary angioedema (HAE) in adults with C1-esterase inhibitor deficiency.

Dose

30mg administered by slow subcutaneous injection in the abdominal area. Additional doses may be administered at 6 hour intervals to a maximum of 3 doses in 24 hours.

Therapeutic Alternatives

Berinert® (C1 esterase inhibitor [human])

Clinical Notes

Hereditary angioedema (HAE) is a rare disorder characterized by recurrent episodes of well-demarcated angioedema without urticaria, which most often affect the skin or mucosal tissues of the upper respiratory and gastrointestinal tracts. Prevalence is not known but has been estimated at between 1/10,000 to 1/150,000. Canadian prevalence has been estimated at approximately 700 persons. Although swelling resolves spontaneously in two to four days in the absence of treatment, laryngeal edema may cause fatal asphyxiation, and the pain of gastrointestinal attacks may be incapacitating. In HAE, angioedema results from excessive production of bradykinin, a potent vasodilatory mediator. During episodes of angioedema in patients with HAE, plasma bradykinin levels have been shown to be sevenfold higher than normal. Histamine and other mast cell mediators are not directly involved, which explains the lack of response to antihistamines and distinguishes this form of angioedema from that associated with urticaria.

Firazyr (icatibant) is a synthetic bradykinin B2 receptor antagonist. It is a synthetic polypeptide that is structurally analogous to bradykinin and acts by selectively and competitively antagonizing the bradykinin B2 receptor.

Place in Therapy

Firazyr is indicated for the treatment of acute attacks of HAE in adults. It is the only drug approved for self-administration by the patient, after receiving appropriate training from a healthcare professional.

Comparative Pricing

Drug	Estimated annual cost
Firazyr®	$273,500
Berinert®	price not available

Impact / Plan Management Suggestions

Intermediate Impact. Ensure appropriate reimbursement through Prior Authorization Program.

Saflutan (tafluprost)			
Dosage Form	**DIN & Strength**	**Manufacturer**	**AHFS Class**
Ophthalmic solution	02425149 – 0.0015%	Merck Canada Inc.	52:40.28 – EENT – Prostaglandin analogs

Indication(s)

Canadian Product Monograph not available; information from US FDA Prescribing Information for Zioptan
Indicated for reducing elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension.

Dose

One drop in affected eye(s) once daily.

Therapeutic Alternatives

Xalatan™ (latanoprost)*; Lumigan® RC (bimatoprost); Travatan® Z (travoprost)

*generics available

Clinical Notes

Saflutan (tafluprost) is a fluorinated analog of prostaglandin F2α. Tafluprost acid, a prostaglandin analog is a selective FP prostanoid receptor agonist which is believed to reduce intraocular pressure by increasing uveoscleral outflow. The exact mechanism of action is unknown at this time.

Prostaglandin analogs are slightly more efficacious than nonselective beta-blockers. Clinical experience with this class has not revealed any significant systemic adverse effects, but a few ocular effects have been noted, including darkening of some brown-coloured irides, lengthening of the eyelashes and mild conjunctival hyperemia. Any of these agents may be considered first-line therapy because of their potencies and excellent safety profiles.

If medical therapy has been chosen as initial treatment for open-angle glaucoma, prostaglandins are generally considered first-line therapy. Data appears to show similar intraocular pressure lowering effect between the different prostaglandin analogs.

Place in Therapy

Saflutan is the fourth prostaglandin analog to become available in Canada. Its place in therapy would be anticipated to be similar to other prostaglandin analogs as first line medical therapy for open-angle glaucoma.

Comparative Pricing

Drug	Estimated annual cost
Saflutan	price not available
Apo®-Latanoprost	$120
Lumigan® RC	$430
Travatan® Z	$365

Impact / Plan Management Suggestions

Insufficient information

Elelyso™ (taliglucerase alfa)			
Dosage Form	**DIN & Strength**	**Manufacturer**	**AHFS Class**
Intravenous injection	02425637 – 200 Units/vial	Pfizer Canada Inc.	44:00.00 – Enzymes

Indication(s)

Elelyso™ (taliglucerase alfa for injection) is indicated for long-term enzyme replacement therapy (ERT) for adults with a confirmed diagnosis of Type 1 Gaucher disease.

Elelyso™ may also be used in pediatric patients with a confirmed diagnosis of Type 1 Gaucher disease, and for the haematological manifestations in pediatric patients with a confirmed diagnosis of Type 3 Gaucher disease.

Dose

Dosage should be individualized to each patient. Administer Elelyso™ by intravenous infusion over 1-2 hours, every 2 weeks. Initial doses of taliglucerase alfa range from 30 units/kg to 60 units/kg of body weight, depending upon the clinical assessment of the treating physician.

Therapeutic Alternatives

Cerezyme® (imiglucerase); Vpriv™ (velaglucerase alfa)

Clinical Notes

Elelyso™ (taliglucerase alfa), a hydrolytic lysosomal glucocerebroside-specific enzyme for intravenous infusion, is a recombinant active form of the lysosomal enzyme, ß-glucocerebrosidase, which is expressed in genetically modified carrot plant root cells cultured in a disposable bioreactor system (ProCellEx®). ß-Glucocerebrosidase is a lysosomal glycoprotein enzyme that catalyzes the hydrolysis of the glycolipid glucocerebroside to glucose and ceramide.

Gaucher disease (GD) is a lysosomal storage disorder encompassing three main forms (types 1, 2 and 3), a fetal form and a variant with cardiac involvement (Gaucher disease – ophthalmoplegia – cardiovascular calcification or Gaucher-like disease). The prevalence is approximately 1/100,000. The annual incidence of GD in the general population is about 1/60,000, but it can reach up to 1/1,000 in Ashkenazi Jewish populations. The clinical manifestations of this disease are highly variable. GD type 1 (90% of cases) is the chronic and non-neurological form associated with organomegaly (spleen, liver), bone anomalies (pain, osteonecrosis, pathological fractures) and cytopenia. Type 2, the acute neurological form, is characterized by early onset, rapidly progressing brainstem dysfunction, associated with organomegaly and leading to death before the age of 2. Type 3, the subacute neurological form, affects children or adolescents and is characterized by progressive encephalopathy (oculomotor apraxia, epilepsy and ataxia) with the systemic manifestations seen in type 1.

The deficiency in glucocerebrosidase leads to the accumulation of glucosylceramidase (or beta-glucocerebrosidase) deposits in the cells of the reticuloendothelial system of the liver, the spleen and the bone marrow (Gaucher cells).

Place in Therapy

Elelyso™ provides an alternate form of enzyme replacement therapy for GD to those currently available: Cerezyme® (imiglucerase) and Vpriv™ (velaglucerase).

Pricing

Drug	Estimated annual cost*
Elelyso™	$187,000-$373,000
Cerezyme®	$672,000
Vpriv™	$560,000

*based on 70kg body weight

Impact / Plan Management Suggestions

Intermediate impact. Provides a potentially lower cost alternative to currently available therapies.

Ibavyr™ (ribavirin)			
Dosage Form	**DIN & Strength**	**Manufacturer**	**AHFS Class**
Tablet	02425890 – 400mg 02425904 – 600mg	Pendopharm Division of Pharmascience Inc.	08:18.32 – Nucleosides and Nucleotides

Indication(s)

Ibavyr (ribavirin tablets) is indicated in combination with other agents for the treatment of chronic hepatitis C (CHC) in adults.

Dose

Dosage is weight-based and dependent upon concurrent therapy. Range: 800mg – 1400mg daily. Duration of treatment dependent upon genotype and treatment response (range: 12-24 weeks).

Therapeutic Alternatives

None – ribavirin is currently available in Canada only in combination with interferons.

Clinical Notes

Ribavirin is a synthetic nucleoside analog. Ribavirin produces its antiviral effect primarily by altering the nucleotide pools and normal messenger RNA formation, which could account for its effectiveness against both DNA and RNA viruses. Ribavirin is virustatic whose mechanism is not completely understood, but does not alter viral attachment, penetration, or uncoating and does not induce cellular production of interferon.

Place in Therapy

Ribavirin is not effective as monotherapy and should never be used alone for the treatment of chronic hepatitis C virus infection. This single entity formulation has been developed to be used in conjunction with new direct-acting antivirals (e.g., sofosbuvir) in non-interferon based therapies.

Pricing

Drug	Estimated monthly cost
Ibavyr™	$1,300-$1,900

Impact / Plan Management Suggestions

Intermediate Impact. Ensure appropriate reimbursement through Prior Authorization Program.

Vimizim™ (elosulfase alfa)			
Dosage Form	**DIN & Strength**	**Manufacturer**	**AHFS Class**
Intravenous injection	02427184 – 1mg/ml	BioMarin International Ltd.	44:00.00 – Enzymes

Indication(s)

Vimizim™ (elosulfase alfa) is indicated for long-term enzyme replacement therapy in patients with a confirmed diagnosis of Mucopolysaccharidosis IVA (Morquio A syndrome, or MPS IVA).

Dose

The recommended dose is 2 mg per kg given intravenously over a minimum range of 3.5 to 4.5 hours, based on infusion volume, once every week.

Therapeutic Alternatives

None

Clinical Notes

Mucopolysaccharidosis type IVA (MPS IVA; Morquio A disease) is a rare autosomal recessive disorder caused by deficiency of N-acetylgalactosamine 6-sulfate sulfatase (GALNS), a lysosomal enzyme. Breakdown of the glycosaminoglycans (GAGs), keratin sulfate (KS), and chondroitin-6-sulfate (C6S) is partly dependent upon GALNS. Clinically, MPS IVA patients develop a characteristic spondyloepiphyseal skeletal dysplasia (including joint deformities/contractures, short stature, spinal cord compression) due to progressive storage of KS and C6S. Other clinical features include reduced pulmonary function, valvular heart disease, hearing loss, cataracts, and corneal clouding. Unlike other mucopolysaccharidoses, patients with MPS IVA have normal intelligence. Musculoskeletal and respiratory dysfunctions have the greatest impact on these patients' lives. Patients describe most bothersome symptoms as fatigue, decreased endurance, joint stiffness and pain. Up to one-third of MPS IVA patients who walk require a walking aid to ambulate. Patients with severe disease are usually wheelchair-bound by adolescence. Chest deformities, such as pectus carinatum, lead to restrictive lung disease, while laryngeal narrowing and tracheobronchial abnormalities may cause obstructive lung disease. Death is most commonly due to respiratory failure, cardiac disease, or central nervous system complications (i.e. atlantoaxial subluxation, spinal cord compression).

Elosulfase alfa is a recombinant form of human GALNS, and is identical to the naturally occurring human lysosomal enzyme in terms of the amino acid sequence and N-linked glycosylation. Elosulfase alfa provides exogenous GALNS that is taken up into the lysosomes and catabolyzes the GAGs keratan sulfate and chondroitin-6-sulfate. Elosulfase alfa uptake by cells into lysosomes is most likely mediated by the binding of mannose-6-phosphate-terminated oligosaccharide chains of elosulfase alfa to the cation-independent mannose-6-phosphate receptor (CI-M6PR).

Anaphylaxis and hypersensitivity reactions have been reported in patients treated with Vimizim™. In premarketing clinical trials, 18 of 235 (7.7%) patients treated with Vimizim™ experienced signs and symptoms consistent with anaphylaxis. These 18 patients experienced 26 anaphylactic reactions during infusion with signs and symptoms including cough, erythema, throat tightness, urticaria, flushing, cyanosis, hypotension, rash, dyspnea, chest discomfort, and gastrointestinal symptoms (e.g., nausea, abdominal pain, retching, and vomiting) in conjunction with urticaria. These cases of anaphylaxis occurred as early as 30 minutes from the start of infusion and up to three hours after infusion. Anaphylaxis occurred as late into treatment as the 47th infusion. Forty-four of 235 (18.7%) patients had hypersensitivity reactions, including serious (e.g., anaphylaxis) and non-serious reactions. Hypersensitivity reactions occurred as early as 30 minutes from the start of infusion but as late as six days after infusion. The most common hypersensitivity reactions (occurring in more than 2 patients) included anaphylactic reactions, urticaria, peripheral edema, cough, dyspnea, and flushing.

Vimizim™ treatment should be supervised by a physician or health professional experienced in the management of patients with mucopolysaccharidoses. Administration of Vimizim™ should be carried out by an appropriately trained health professional with the ability to manage medical emergencies. Home administration by a health professional trained in recognising and managing serious infusion reactions may be considered only for patients who are tolerating their infusions well under the direction of the prescribing physician.

Place in Therapy

Vimizim™ is the first pharmacotherapy available for MPS IV A. It is enzyme replacement therapy for patients with this rare disease.

Pricing

Drug	Estimated annual cost
Vimizim™	$1,200,000 (27kg child)

Impact / Plan Management Suggestions

High Impact. Ensure reimbursement provided after validating site of administration as patient monitoring is required due to significant risk of anaphylaxis and hypersensitivity reactions, which can occur at any time, even after many weeks of treatment.

Aptiom™ (eslicarbazepine acetate)			
Dosage Form	**DIN & Strength**	**Manufacturer**	**AHFS Class**
Tablet	02426862 – 200mg 02426870 – 400mg 02426889 – 600mg 02426897 – 800mg	Sunovion Pharmaceuticals Canada Inc.	28:12.92 – Miscellaneous Anticonvulsants

Indication(s)

Aptiom™ (eslicarbazepine acetate) is indicated as adjunctive therapy in the treatment of partial-onset seizures in patients with epilepsy who are not satisfactorily controlled with conventional therapy.

Dose

Start treatment at 400 mg once daily. After one week, increase dosage to 800 mg once daily, which is the recommended maintenance dosage. Some patients may benefit from the maximum recommended maintenance dosage of 1200 mg once daily, although this dosage is associated with an increase in adverse reactions. A maximum dose of 1200 mg daily should only be initiated after the patient has tolerated 800 mg daily for at least a week. For some patients, treatment may be initiated at 800 mg once daily if the need for additional seizure reduction outweighs an increased risk of adverse reactions during initiation.

Therapeutic Alternatives

Tegretol® (carbamazepine); Trileptal® (oxcarbazepine) [both available as generic]

Clinical Notes

Epilepsy is a chronic disease that requires long-term treatment. The World Health Organisation (WHO) estimates that around 50 million people in the world have epilepsy at any one time, which is roughly 1% of the world population. Recent studies have shown that up to 70% of newly diagnosed children and adults with epilepsy in both developed and developing countries can be successfully treated (i.e. their seizures can be completely controlled for several years) with AEDs. However, despite a broad range of AEDs available on the market, roughly 30-40% of patients with epilepsy are uncontrolled with available treatment and a further 25% suffer from significant adverse effects. This is due to poor response and to the associated toxicities of available AEDs.

Eslicarbazepine acetate (ESL) is a prodrug of eslicarbazepine, or S-licarbazepine, which is the drug entity responsible for the ESL pharmacological effect. Preclinical experiments suggest that both ESL and eslicarbazepine competitively interact with site 2 of the inactivated state of a voltage-gated sodium channel (VGSC), preventing its return to the active state and repetitive neuronal firing. The precise mechanism by which ESL exerts its antiepileptic effects remains to be fully elucidated. With oral administration ESL metabolizes to S- and R- licarbazepine and oxcarbazepine as does Trileptal (oxcarbazepine), just in a different ratio (different proportions). A difference with carbamazepine is that it does not auto-induce its own metabolism and is not metabolized to the epoxide form, which is a source of toxicity. A difference with oxcarbazepine is that it is not readily metabolized to a racemic mixture of S-licarbazepine and R-licarbazepine. Following oral administration, ESL is metabolized to yield mainly S-licarbazepine (eslicarbazepine) and to minor metabolites, R-licarbazepine and oxcarbazepine. The thinking is that this will minimize off-target effects and the frequency of adverse events.

Place in Therapy

Aptiom provides another alternative treatment for patient with partial onset seizures who are not controlled with single AED therapy. It is to be used in combination with other AEDs in patients who require a second agent for enhanced seizure control.

Comparative Pricing

Drug	Estimated annual cost
Aptiom™	$3,900-$7,700
Taro-Carbamazepine	$220-$330
Taro-Carbamazepine CR	$280-$420
Apo®-Oxcarbazepine	$1,350-$2,700

Impact / Plan Management Suggestions

Minimal impact. Potentially utilize Step Therapy to encourage the use of the more cost-effective iminostilbene derivatives prior to Aptiom™.

FIRST TIME GENERICS

First Time Generic Drugs (Notices of Compliance from May 21, 2014 to August 22, 2014)

Generic Name	Reference Drug (Brand)	Rank by ingredient cost in 2013	Manufacturer	Route of Administration	Approved Indications
rasagiline	Azilect	401	Teva Canada Ltd.	Oral	Parkinson's disease
nevirapine, extended-release	Viramune XR	661	Apotex Inc.	Oral	HIV-1 infection
escitalopram	Cipralex	8	multiple	Oral	Depression, Generalized Anxiety Disorder, Obsessive-Compulsive Disorder

Health Newsflash

A Quarterly Publication

New Drugs and Pipeline News Reviewed at the July to September 2014 DEC Meetings

PRODUCT LINE-EXTENSIONS

Product Line Extensions (Notices of Compliance (NOCs) from May 21, 2014 to August 22, 2014)

Band name	Chemical name	Manufacturer	Dosage form	Type of Line Extension	Specifics/Comments
Nexavar	sorafenib	Bayer Inc.	tablet	New indication	locally advanced or metastatic differentiated thyroid cardinoma (DTC)
Pradaxa	dabigatran etexilate	Boehringer Ingelheim (Canada) Ltd.	capsule	New indication	treatment and prevention of recurrent venous thromboembolic events (e.g., deep vein thrombosis [DTV], pulmonary embolism [PE])
Afinitor Disperz	everolimus	Novartis Pharmaceuticals Canada Inc.	tablet for oral suspension	New dosage form	non-solid dosage form alternative for patients (e.g., pediatric ≥ 1 year) who are unable to swallow solid tablets
Abraxane	nab-paclitaxel	Celgene Inc.	intravenous injection	New indication	metastatic adenocarcinoma of the pancreas
Helixate FS	recombinant antihemophilic factor	Bayer Healthcare LLC	intravenous injection	New indication	adult prophylaxis of hemophilia A
Actemra	tocilizumab	Hoffmann La Roche Ltd.	subcutaneous injection	New formulation	new subcutaneous injection
Kalydeco	ivacaftor	Vertex Pharmaceuticals (Canada) Inc.	tablet	New indication	treatment of cystic fibrosis (CF) in nine additional Cystic Fibrosis Transmembrane conductance Regulator (CFTR) gene mutations: G1244E, G1349D, G178R, G551S, S1251N, S1255P, SS49N, S549R, G970R [previously only approved for G551D mutation]
Kogenate FS	recombinant antihemophilic factor	Bayer Inc.	intravenous injection	New indication	adult prophylaxis of hemophilia A
Elocom Cream	mometasone furoate	Merck Canada Inc.	cream	New indication	expansion of indication to include maximum duration of treatment of 3 weeks on body and 5 days on face, scalp, axillae and scrotum
Inspra	eplerenone	Pfizer Canada Inc.	tablet	New indication	mild to moderate essential hypertension
Prezcobix	cobicistat/ darunavir	Janssen Inc.	tablet	New drug combination	HIV infection
Actikerall	fluorouracil/ salicylic acid	Almirall Hermal Gmbh	topical solution	New drug combination	actinic keratosis
Zeulide Depot	leuprolide acetate	Pendopharm Division of Pharmascience Inc.	intramuscular depot injection	New brand, Strength	product monograph not available

Authors: Aaron Aoki, RPh, BScPhm, MBA, CDE, CRE; Moe Abdallah, B.Sc., B.Sc.Phm; Priscilla Po, PharmD, RPh