Health Newsflash

A Quarterly Publication

New Drugs and Pipeline News Reviewed at the October to December 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

Duavive (bazedoxifene acetate/conjugated estrogens)			
Dosage Form	**DIN & Strength**	**Manufacturer**	**AHFS Class**
Tablet	02432854 – 20mg/0.4mg	Pfizer Canada Inc.	68:16.12 – Estrogen Agonists-Antagonists

Indication(s)

Canadian Product Monograph not available; information from US FDA Prescribing Information for Duavee

For treatment of the following conditions in women with a uterus:

- Treatment of moderate to severe vasomotor symptoms associated with menopause.
- Prevention of postmenopausal osteoporosis.

Dose

One tablet once daily.

Therapeutic Alternatives

Premarin + Evista (raloxifene)*

*generics available

Clinical Notes

Duavive is a fixed dose combination of conjugated estrogens and bazedoxifene. Conjugated estrogens are of equine origin and are a mixture of multiple estrogens including sodium estrone sulfate, sodium equilin sulfate, and sodium sulfate conjugates. Bazedoxifene is a selective estrogen modulator (SERM) with tissue selective estrogen receptor agonist and antagonist activity at various organs.

Unopposed estrogen increases the risk of endometrial cancer in women with a uterus. Currently only progestins are approved for use with estrogen to mitigate the risk of endometrial hyperplasia which may lead to endometrial cancer. Duavive is the first product that uses a non-progestin, bazedoxifene, to mitigate the proliferative effects of estrogen in the uterus. Bazedoxifene has anti-estrogenic effects in breast tissue which may potentially provide cancer protection to breast tissue as well.

Place in Therapy

Duavive is an alternative treatment for postmenopausal symptoms such as vasomotor symptoms and osteoporosis which may be lower risk for women at risk of breast or endometrial carcinoma.

Comparative Pricing

Drug	Estimated annual cost
Duavive	price not available
Premarin®	$120
PMS-Raloxifene	$170

Impact / Plan Management Suggestions

Insufficient information.

Dymista™ (azelastine hydrochloride/fluticasone propionate)			
Dosage Form	**DIN & Strength**	**Manufacturer**	**AHFS Class**
Metered-dose nasal spray	02432854 – 137µg/50µg	Meda Pharmaceuticals Ltd.	52:08.00 – Eye, Ear, Nose, Throat Anti-Inflammatory Agents

Indication(s)

For the symptomatic treatment of moderate to severe seasonal allergic rhinitis (SAR) and associated ocular symptoms in adults and adolescents aged 12 years and older for whom monotherapy with either antihistamines or intranasal corticosteroids is not considered sufficient.

Dose

One spray in each nostril twice daily.

Therapeutic Alternatives

Intranasal antihistamine: Livostin Nasal Spray (levocabastine)

Intranasal corticosteroids: beclomethasone; budesonide; Omnaris (ciclesonide); flunisolide; fluticasone propionate; Avamys (fluticasone furoate); mometasone; Nasacort AQ (triamcinolone)

Clinical Notes

Dymista Nasal Spray contains both azelastine hydrochloride (a histamine H1-receptor antagonist) and fluticasone propionate (a synthetic corticosteroid).

Azelastine hydrochloride exhibits histamine H1-receptor antagonist activity in isolated tissues, animal models, and humans.

Fluticasone propionate is a synthetic trifluorinated corticosteroid with anti-inflammatory activity. The precise mechanism through which fluticasone propionate affects allergic rhinitis symptoms is not known. Corticosteroids have been shown to have a wide range of effects on multiple cell types (e.g., mast cells, eosinophils, neutrophils, macrophages, and lymphocytes) and mediators (e.g., histamine, eicosanoids, leukotrienes, and cytokines) involved in inflammation.

Place in Therapy

Dymista is a fixed-dose combination H1 antihistamine and corticosteroid nasal spray which provides an alternative therapy when both types of therapy are required for the treatment of seasonal allergic rhinitis.

Comparative Pricing

Drug	Unit cost
Dymista™ Nasal Spray	price not available
Livostin® Nasal Spray	$28/15ml bottle
Apo-Fluticasone Nasal Spray	$22/120 DS bottle

Impact/Plan Management Suggestions

Insufficient information.

Gazyva™ (obinutuzumab)			
Dosage Form	**DIN & Strength**	**Manufacturer**	**AHFS Class**
Intravenous injection	02434806 – 25mg/ml	Hoffmann La Roche Ltd.	10:00.00 – Antineoplastics

Indication(s)

Treatment of patients with previously untreated chronic lymphocytic leukemia (CLL) in combination with chlorambucil.

Dose

Cycle 1: 100 mg on day 1, followed by 900 mg on day 2, followed by 1000 mg weekly for 2 doses (days 8 and 15)

Cycles 2 through 6: 1000 mg on day 1 every 28 days for 5 doses

Therapeutic Alternatives

fludarabine/cyclophosphamide/rituximab, fludarabine/rituximab, rituximab/chlorambucil

Clinical Notes

Chronic lymphocytic leukemia (CLL) is one of the chronic lymphoproliferative disorders (lymphoid neoplasms). It is characterized by a progressive accumulation of usually monoclonal, functionally incompetent lymphocytes. Obinutuzumab is a recombinant monoclonal humanised and glycoengineered Type II anti-CD20 antibody of the IgG1 isotype. It specifically targets the extracellular loop of the CD20 transmembrane antigen on the surface of non-malignant and malignant pre-B and mature B-lymphocytes, but not on haematopoietic stem cells, pro-B-cells, normal plasma cells or other normal tissue.

Place in Therapy

Gazyva is another option for patients with previously untreated CLL which has demonstrated an improvement in progression-free survival over existing therapies.

Pricing

Drug	Estimated treatment cost*
Gazyva™	$45,000
fludarabine/cyclophosphamide/rituximab	$26,000

*6 cycles

Impact / Plan Management Suggestions

Intermediate impact. Ensure appropriate utilization with Prior Authorization.

Harvoni™ (ledipasvir/sofosbuvir)			
Dosage Form	**DIN & Strength**	**Manufacturer**	**AHFS Class**
Tablet	02432226 – Lepidasvir 90mg/ Sofosbuvir 400mg	Gilead Sciences Canada	08:18.32 – Nucleosides and Nucleotides

Indication(s)

For the treatment of chronic hepatitis C virus (CHC) genotype 1 infection in adults.

Dose

One tablet once daily. Treatment duration is determined by treatment experience and the presence of cirrhosis and ranged from 12 to 24 weeks. An 8-week treatment course may be considered in treatment-naïve patients without cirrhosis who have pre-treatment HCV RNA less than 6 million IU/mL.

Therapeutic Alternatives

Sofosbuvir (Sovaldi) in combination with peginterferon + ribavirin (PegIFN/RBV); Simeprevir (Galexos) in combination with peginterferon + ribavirin.

Clinical Notes

Acute hepatitis C virus (HCV) infection refers to the presence of clinical signs or symptoms of hepatitis within six months of presumed HCV exposure. Continued presence of the virus is defined as CHC infection. Parenteral exposure to the hepatitis C virus is the most efficient means of transmission. The goal of treatment is to eradicate HCV RNA, which is predicted by the achievement of a sustained virologic response (SVR), defined by the absence of HCV RNA by polymerase chain reaction three to six months after stopping treatment. An SVR is associated with a 99 percent chance of being HCV RNA negative during long-term follow-up and can therefore be considered cure of the HCV infection.

Harvoni contains two inhibitors of HCV replication. Ledipasvir is a direct acting anti-viral agent that inhibits HCV RNA replication and virion production by targeting the HCV NS5A protein. The NS5A protein is thought to play multiple roles in mediating viral replication, host-cell interactions, and viral pathogenesis. Sofosbuvir is a pan-genotypic polymerase inhibitor of the HCV NS5B RNA-dependent RNA polymerase (RdRp). HCV NS5B is the essential initiating and catalytic subunit of the membrane-associated multiprotein complex that mediates HCV RNA replication and is critical for the viral replication cycle.

Sustained virologic response (SVR) was the primary endpoint to determine the HCV cure rate which was defined as HCV RNA less than Lower Limit of Quantitation (LLOQ) at 12 weeks after the cessation of treatment (SVR12). The reported SVR12 rates (i.e., proportion of subjects who achieved cure of HCV) ranged from 94-99%.

Place in Therapy

Ledipasvir/sofosbuvir is an option in patients with CHC genotype 1 particularly those for whom interferon/ribavirin-based therapies are not an option due to intolerance, or patients who have had prior treatment failures with peginterferon and ribavirin or protease inhibitors. The high cure rates also favour first-line use for treatment naïve individuals with CHC.

Pricing

Drug	Estimated treatment cost
Harvoni™	$48,000-$142,000
Sovaldi + PegIFN/RBV	$63,000
Galexos + PegIFN/RBV (12-24 wks)	$49,000-$59,000

Impact / Plan Management Suggestions

Intermediate Impact. Ensure appropriate reimbursement through Prior Authorization Program.

Imbruvica™ (ibrutinib)			
Dosage Form	**DIN & Strength**	**Manufacturer**	**AHFS Class**
Capsule	02434407 – 140mg	Janssen Inc.	10:00.00 – Antineoplastic agents

Indication(s)

For the treatment of patients with chronic lymphocytic leukemia (CLL), including those with 17p deletion, who have received at least one prior therapy, or for the frontline treatment of patients with CLL with 17p deletion.

Dose

The recommended dose of Imbruvica is 420 mg (three 140 mg capsules) once daily.

Therapeutic Alternatives

fludarabine/cyclophosphamide/rituximab, fludarabine/rituximab, rituximab/chlorambucil

Clinical Notes

Ibrutinib is a small-molecule, targeted inhibitor of Bruton's tyrosine kinase (BTK). Ibrutinib forms a covalent bond with a cysteine residue (Cys-481) in the BTK active site, leading to inhibition of BTK enzymatic activity. BTK, a member of the Tec kinase family, is a signaling molecule of the B-cell antigen receptor (BCR) pathway. The BCR pathway is implicated in the pathogenesis of several B-cell malignancies including CLL. The 17p deletion frequently results in abnormalities of a key tumour suppressor gene, TP53, which is associated with worse outcome, with short treatment free intervals, short median survival, and poor response to chemotherapy. Ibrutinib is a promising alternative for patients with the genetic marker.

Place in Therapy

Imbruvica may be considered for first-line therapy in patient with the more difficult to treat 17p deletion. It may also be considered for younger (< 70 yrs) patients without del (17p) who are refractory/relapsed after other therapy.

Comparative Pricing

Drug	Estimated monthly cost
Imbruvica™	$8,600
fludarabine/cyclophosphamide/rituximab	$4,600

Impact / Plan Management Suggestions

Intermediate impact. Ensure appropriate utilization with Prior Authorization.

Otezla® (apremilast)			
Dosage Form	**DIN & Strength**	**Manufacturer**	**AHFS Class**
Tablet	02434318 – Starter Pack (10, 20, 30mg tablets) 02434334 – 30mg	Celgene Inc.	92:36.00 – Disease-modifying antirheumatic drugs

Indication(s)

For the treatment of adult patients with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy.

Dose

The recommended dose of Otezla is 30 mg twice daily. An initial titration schedule is recommended and is accommodated by a starter pack.

Therapeutic Alternatives

Humira, Enbrel, Remicade, Stelara, methotrexate

Clinical Notes

Approximately 1 million people suffer from psoriasis in Canada, and 212,500 Canadians are estimated to suffer from moderate to severe plaque psoriasis.

The active substance of Otezla is apremilast, an oral small-molecule inhibitor of phosphodiesterase 4 (PDE4) with immunosuppressant properties. Apremilast works intracellularly to modulate a network of pro-inflammatory and anti-inflammatory mediators.

By controlling inflammation in this way, apremilast improves the redness and scaliness associated with plaque psoriasis. In clinical trials, about 31 percent of the individuals taking Otezla experienced a 75 percent improvement in the severity of their psoriasis after four months.

Place in Therapy

Otezla is an effective and relatively well-tolerated medication which provides an oral alternative for the treatment of moderate to severe psoriasis.

Comparative Pricing

Drug	Estimated annual cost
Otezla®	$15,000
Enbrel®	$22,000
Humira®	$21,000
Remicade®	$28,000
Stelara®	$22,000
methotrexate injection	$400
methotrexate tablets	$400

Impact / Plan Management Suggestions

Intermediate impact – potential cost shift.

Trintellix™ (vortioxetine)			
Dosage Form	**DIN & Strength**	**Manufacturer**	**AHFS Class**
Tablet	02432919 – 5mg 02432927 – 10mg 02432935 – 15mg 02432943 – 20mg	Lundbeck Canada Inc.	28:16.04 – Antidepressants

Indication(s)

For the treatment of major depressive episodes in adults.

Dose

The starting and recommended dose of Trintellix is 10 mg vortioxetine once daily in adults less than 65 years of age, titrated to a maximum dose of 20mg once daily or a minimum dose of 5mg once daily depending on patient response.

Therapeutic Alternatives

Venlafaxine, Duloxetine

Clinical Notes

Vortioxetine is a 5-HT_3, 5-HT_7, and 5-HT_{1D} receptor antagonist, 5-HT_{1B} receptor partial agonist, 5-HT_{1A} receptor agonist and inhibitor of the 5-HT transporter, leading to modulation of neurotransmission in several systems, including predominantly the serotonin but probably also the norepinephrine, dopamine, histamine, acetylcholine, GABA and glutamate systems, all of which may play a role in regulating mood.

Vortioxetine has been studied in 12 main short-term studies involving more than 6,700 patients with major depression (including one study in patients aged 65 and over), in which it was compared with placebo for 6 or 8 weeks. The main measure of effectiveness in each study was the change in a standard score for symptoms of depression; the studies showed that doses of vortioxetine ranging from 5 to 20 mg were generally more effective than placebo in improving depression and resulted in a clinically relevant decrease of the depression scores. Supportive data from 52-week extensions of several of these studies suggested that the improvements that were seen were maintained longer-term. The types of side effects seen were similar to those with other antidepressants that act through serotonin. One trial appears to show novel benefits of vortioxetine treatment for cognitive symptoms associated with depression which have not been demonstrated with other agents. These are purported to be due to activity at other serotonergic receptors.

Place in Therapy

Trintellix is another antidepressant option for patients with major depressive disorder. Clinical relevance of cognitive symptom effects remains to be demonstrated in real world experience.

Comparative Pricing

Drug	Estimated annual cost
Trintellix™	$1,000-$1,200
venlafaxine	$60-$250
Cymbalta®	$750-$3,000

Impact / Plan Management Suggestions

Minimal impact.

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FIRST TIME GENERICS

First Time Generic Drugs (Notices of Compliance from August 22, 2014 to November 26, 2014)

Generic Name	Reference Drug (Brand)	Rank by ingredient cost in 2013	Manufacturer	Route of Administration	Approved Indications/ Comments
clarithromycin	Biaxin XL	28	Apotex Incorporated	Oral	Antibiotic
calcitriol	Rocaltrol	361	Odan Laboratories	Oral	Activated form of vitamin D_3
celecoxib	Celebrex	20	various	Oral	COX-2 selective NSAID

PRODUCT LINE-EXTENSIONS

Product Line Extensions (Notices of Compliance (NOCs) from August 22, 2014 to November 26, 2014)

Band name	Chemical name	Manufacturer	Dosage form	Type of Line Extension	Specifics/Comments
Xolair	omalizumab	Novartis Pharmaceuticals Canada Inc.	subcutaneous injection	New indication	chronic idiopathic urticaria (CIU)
Yervoy	ipilimumab	Bristol-Myers Squibb	intravenous injection	New indication	first-line treatment of unresectable or metastatic melanoma
Arzerra	ofatumumab	GlaxoSmithKline Inc.	intravenous injection	New indication	first-line treatment of chronic lymphocytic leukemia (CLL) in patients for whom fludarabine-based therapy considered inappropriate
Trimeq	dolutegravir/ abacavir/ lamivudine	GlaxoSmithKline Inc.	tablet	New drug combination	HIV-1 infection
Lodalis	colesevelam	Valeant Canada	powder for oral suspension	New dosage form	new dosage form added to existing oral tablet formulation
Posanol	posaconazole	Merck Canada	intravenous injection	New dosage form	new dosage form added to existing oral delayed-release tablet and oral suspension formulations

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