Health Newsflash – A Quarterly Publication

New Drugs and Pipeline News Reviewed at the April to June 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

Bosulif® (bosutinib)			
Dosage Form	**DIN & Strength**	**Manufacturer**	**AHFS Class**
Tablet	02419149 - 100mg 02419157 - 500mg	Pfizer Canada, Inc.	10:00 Antineoplastic Agents

Indication(s)

For the treatment of adult patients with chronic, accelerated, or blast phase Philadelphia positive (Ph+) chronic myelogenous leukemia (CML) in adult patients with resistance or intolerance to prior tyrosine kinase inhibitors therapy and for whom subsequent treatment with imatinib, nilotinib, and dasatinib is not clinically appropriate. *(Notice of compliance with Conditions)*

Dose

500mg orally once daily. Dose escalation to 600mg is permitted if complete hematological response has not occurred by week 8 or complete cytogenetic response by week 12.

Therapeutic Alternatives

Tasigna® (nilotinib), Sprycel® (dasatinib)

Clinical Notes

Chronic myelogenous leukemia (CML) is a rare type of blood and bone marrow cancer that develops slowly, over months or years. CML develops when the bone marrow produces abnormal granulocytes (a type of white blood cell) called leukemia cells. CML accounts for 10-15% of all leukemias. Approximately 5500 Canadians are currently living with CML and more than 500 new cases are diagnosed each year.

The risk of developing CML increases with age, usually occurring in patients over 65 years, with a higher prevalence in men. The majority of patients (~95%) express a chromosome abnormality known as the Philadelphia (Ph) chromosome, resulting in the BCR-ABL fusion gene, which leads to development of CML. CML is characterized by 3 phases: chronic, accelerated, and blast phase. Approximately 85 to 90% of patients present in a chronic stable phase. Without treatment, this inevitably progresses to a more aggressive, accelerated phase and then culminates in a very difficult to treat blast crisis.

Bosulif® is a second generation oral tyrosine kinase inhibitor (TKI) that dually blocks action of Scr and Abl-enzymes (including BCR-ABL tyrosine kinases) which can be found in some receptors on the surface of leukemia cells where they are involved in stimulating the cells to divide uncontrollably. By blocking this action, Bosulif® inhibits cell division and controls the growth and spread of leukemia cells.

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Place in Therapy

Recommended first-line therapy in newly diagnosed patients with Philadelphia chromosome positive CML is imatinib, followed by either dasatinib or nilotinib in patients intolerant or resistant to imatinib therapy. Bosulif® would be considered a 3rd or 4th line TKI for patients who experience resistant disease or intolerant to prior TKI therapy, and for whom subsequent treatment with imatinib, nilotinib, dasatinib is not clinically appropriate.

Health Canada has given Bosulif® approval under the Notice of Compliance with Conditions (NOC/c) policy, meaning further follow-up is needed to verify clinical benefit.

Comparative Pricing

Drug	Unit cost	Estimated annual cost
Bosulif®	$40-$165	$14,600-$60,225
Tasigna®	$30-$40	$42,350-$60,350
Sprycel®	$40-$175	$57,500-$62,150

Impact/ Plan Management Suggestions

Intermediate Impact. Ensure appropriate reimbursement through Prior Authorization Program.

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Xeljanz™ (tofacitinib citrate)			
Dosage Form	**DIN & Strength**	**Manufacturer**	**AHFS Class**
Tablet	02423898 – 5mg	Pfizer Canada Inc.	92:36.00 – Disease-modifying Antirheumatic Drugs

Indication(s)

Xeljanz™ (tofacitinib) in combination with methotrexate (MTX), is indicated for reducing the signs and symptoms of rheumatoid arthritis (RA), in adult patients with moderately to severely active RA who have had an inadequate response to MTX. In cases of intolerance to MTX, physicians may consider the use of tofacitinib as monotherapy.

Dose

5mg twice daily

Therapeutic Alternatives

Biologic DMARDs: TNF-α Inhibitors: Enbrel® (etanercept); Humira® (adalimumab); Simponi® (golimumab) ; Cimzia® (certolizumab) ; Remicade® or Inflectra™ or Remsima™ (infliximab)

Biologics with alternate mechanisms of action: Kineret® (anakinra); Orencia® (abatacept); Rituxan® (rituximab); Actemra® (tocilizumab)

Clinical Notes

Tofacitinib inhibits JAKs which are intracellular enzymes, and modulates a signaling pathway that influences the cellular processes of hematopoiesis and immune cell function. Signals in this pathway arise from cytokine or growth factor-receptor interactions on the cellular membrane. Inhibition of JAK prevents the phosphorylation and activation of Signal Transducers and Activators of Transcription (STATs), which modulate gene expression and other intracellular activity.

Place in Therapy

While tofacitinib appears to have similar efficacy to currently available TNF-α inhibitors, long-term safety and efficacy data are needed to effectively place tofacitinib in the RA treatment pathway.

Comparative Pricing

Drug	Dosage	Unit cost	Estimated annual cost
Xeljanz™	1 tablet twice daily	$25/tablet	$17,800
Enbrel®	50mg once weekly	$400/syringe	$21,320
Humira®	40mg once every 2 weeks	$785/syringe	$20,310
Remicade®	3-5mg/kg once every 4-8 weeks	$1000/vial	$27,090-$54,180
Actemra®	4-8mg/kg once every 4 weeks	$475/vial	$18,435-$36,865

Impact/Plan Management Suggestions

Intermediate impact. Ensure appropriate reimbursement through Step Therapy or Prior Authorization Program.

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Incruse™ Ellipta® (umeclidinium bromide)			
Dosage Form	**DIN & Strength**	**Manufacturer**	**AHFS Class**
Dry Powder Inhaler	02423596 – 62.5µg/ dose	GlaxoSmithKline Inc.	12:08.08 - Antimuscarinics

Indication(s)

Canadian Product Monograph not available; information from US FDA Prescribing Information
For the long-term once-daily maintenance bronchodilator treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema.

Dose

One inhalation once daily

Therapeutic Alternatives

Spiriva® Handihaler® (tiotropium bromide); Tudorza™ Genuair™ (aclidinium bromide); Seebri® Breezhaler® (glycopyrronium bromide)

Clinical Notes

Chronic obstructive pulmonary disease (COPD) is a common disease that is both preventable and treatable. A key feature of COPD is airflow obstruction that progressively worsens with time, leading to breathlessness and other debilitating symptoms. These symptoms can lead to limitations in physical functioning and impairment of quality of life. COPD is a significant public health challenge and remains a leading cause of morbidity and mortality.

Bronchodilator medications are the mainstay of pharmacologic therapy for COPD to improve the airflow obstruction which characterizes the disease. These medications are commonly used on a regular basis to improve symptoms, exercise limitation, and health status.

Umeclidinium is a long-acting, antimuscarinic agent (LAMA), which is often referred to as a long-acting anticholinergic (LAAC). It has similar affinity to the subtypes of muscarinic receptors M1 to M5. In the airways, it exhibits pharmacological effects through the inhibition of M3 receptor at the smooth muscle leading to bronchodilation. The Ellipta® unit should be discarded within six weeks of removal from the foil blister packaging.

Place in Therapy

Pharmacologic therapy for COPD, such as LAMA bronchodilators, is used to reduce symptoms, reduce the frequency and severity of exacerbations, and improve health status and exercise tolerance. These do not modify the long-term decline in lung function. LAMAs are used for long-term maintenance treatment of airflow obstruction, not for acute symptoms.

Pricing

Drug	Unit cost	Estimated annual cost
Incruse™ Ellipta®	Not available	Not available

Impact/Plan Management Suggestions

Insufficient information to assess impact.

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Egrifta® (tesamorelin acetate)			
Dosage Form	**DIN & Strength**	**Manufacturer**	**AHFS Class**
Subcutaneous injection	02423677 – 2mg	Theratechnologies Inc.	68:30.04 – Somatropin and somatropin agonists

Indication(s)

Canadian Product Monograph not available; information from US FDA Prescribing Information
For the reduction of excess abdominal fat in HIV-infected patients with lipodystrophy.

Dose

2mg injected subcutaneously once daily

Therapeutic Alternatives

None currently available

Clinical Notes

HIV-lipodystrophy was first observed in the 1990s after the wide use of highly active antiretroviral therapies (HAART), particularly protease inhibitors. The syndrome is characterized by (i) loss of peripheral subcutaneous adipose tissue (SAT) especially in the face, limbs, and buttocks (ii) increased visceral fat accumulation or visceral adipose tissue (VAT), and (iii) lipomas particularly in the dorsocervical area (buffalo hump). Accompanying these are metabolic abnormalities such as low HDL-C, increased triglycerides, and insulin resistance changes which are thought to contribute to increase CV risk in the HIV-infected population. The physical stigma of the syndrome is psychologically distressing to patients and many have raised concerns that this would result in noncompliance to effective anti-retrovirals. There is also the potential of excess VAT increasing cardiovascular risk similar to that seen in patients with metabolic syndrome.

Egrifta® (tesamorelin acetate) is a synthetic growth hormone releasing factor (GRF) analog, also known as growth hormone-releasing hormone (GHRH). Tesamorelin binds and stimulates human GRF receptors, and acts on the pituitary somatotroph cells to stimulate the synthesis and release of endogenous growth hormone (GH) which is both anabolic and lipolytic. Some, but not all the effects, are primarily mediated by insulin-like growth factor (IGF-1) produced in the liver and in peripheral tissues. A number of treatment strategies (thiazolidinediones, metformin, testosterone, recombinant human growth hormone) have been evaluated, but unfortunately, most have limited success.

Place in Therapy

Egrifta® is the only drug indicated for the treatment of lipodystrophy associated with HIV.

Comparative Pricing

None currently available

Impact/Plan Management Suggestions

Insufficient information to assess the potential impact and which plan management tool is most appropriate to ensure proper utilization and reimbursement.

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Invokana® (canagliflozin)			
Dosage Form	**DIN & Strength**	**Manufacturer**	**AHFS Class**
Tablet	02425483 – 100mg 02425491 – 300mg	Janssen Inc.	68:20.18 – Sodium-glucose Cotransporter 2 (SGLT2) Inhibitors

Indication(s)

Invokana® (canagliflozin) is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (T2DM). It can be used:

- as monotherapy
- combination with metformin or sulfonylurea
- combination with metformin and either sulfonylurea or pioglitazone – triple therapy
- combination with insulin (with or without metformin)

Dose

100mg to 300mg once daily.

Therapeutic Alternatives

There are many therapeutic alternatives in several other classes of oral anti-diabetic agents (see comparative pricing table on next page).

Clinical Notes

Invokana® (canagliflozin) is a first-in-class sodium-glucose cotransporter 2 (SGLT2) inhibitor. The SGLT2 protein, expressed in the renal proximal tubules, is responsible for the majority of the reabsorption of glucose filtered through the glomerulus. By inhibiting SGLT2, canagliflozin lowers the renal threshold for glucose (RTG), resulting in increased excretion of glucose by the kidney. The increased urinary glucose excretion (UGE) directly lowers plasma glucose concentrations in patients with elevated glucose levels. In addition, the increased glucose excretion also results in a loss of calories, leading to weight loss. Although canagliflozin markedly lowers RTG, the new RTG setpoint is above the usual threshold for hypoglycemia (usually considered to be 70 mg/dL), so that the risk of hypoglycemia with this agent is low.

Inhibition of SGLT2 with increased UGE is a mechanism distinct from other current classes of anti-hyperglycemic agents (AHAs), not requiring the action of insulin for efficacy, with the potential for value in combination with a wide range of other agents in the treatment of patients with T2DM.

Place in Therapy

Invokana® is the first in a new class of oral anti-diabetic drugs, the SGLT2 inhibitors. Its unique non-insulin-dependent mechanism of action makes it an alternative to existing therapies as well as a complementary addition to any existing therapy.

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Comparative Pricing

Drug	Drug Class	Dosage	Unit cost	Estimated annual cost
Invokana®	SGLT2 inhibitor	300mg daily	$2.75	$1,010
Trajenta™	DPP-4 inhibitor	5mg daily	$2.70	$985
Apo-Pioglitazone	Thiazolidinedione	15-45mg daily	$1.6-$3.30	$575-$1,210
Diamicron MR®	Sulfonylurea	30-120mg daily	$0.15-$0.30	$55-$300
Teva-Metformin	Biguanide	500-2500mg/day	$0.06	$22-$110

Impact/Plan Management Suggestions

Minimal impact. Potentially utilize Step Therapy to encourage the use of the more cost-effective anti-diabetic agents prior to Invokana®.

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PRODUCT LINE-EXTENSIONS

Recent Notices of Compliance (NOCs)

Brand name	Chemical name	Manufacturer	Dosage form	Type of Line Extension	Specifics/Comments
Onreltea®	brimonidine	Galderma Canada Inc.	Topical Gel	New Formulation	New topical gel
Oraverse®	phentolamine	Septodont Inc.	Solution	New formulation	New submucosal solution
Latuda®	lurasidone	Sunovion Pharmaceuticals Canada Inc.	Tablet	1) New strength and indication 2) New indication	1) New 20mg strength for the treatment of depressive episodes in bipolar 1 disorder as monotherapy or adjunctive therapy with lithium or valproate. 2)For the management of the manifestations of schizophrenia
Adempas®	riociguat	Bayer Inc.	Tablet	New Indication	For the treatment of pulmonary arterial hypertension in adults
Inlyta®	axitinib	Pfizer Canada Inc.	Tablet	New strength	3mg and 7mg
Lotemax™	loteprednol	Bausch & Lomb Inc.	Ophthalmic Ointment	New formulation	New ophthalmic ointment
Atacand®	candesartan	Astrazeneca Canada Inc.	Tablet	New indication	For the treatment of hypertension in pediatric patients (6-17 years old)
Prolia®	denosumab	Amgen Canada Inc.	Subcutaneous injection	New indications (2)	1) Treatment to increase bone mass in men with nonmetastatic prostate cancer receiving androgen deprivation therapy (ADT) who are at high risk of fracture. 2) A treatment to increase bone mass in women with nonmetastatic breast cancer receiving adjuvant aromatase inhibitor therapy, who have low bone mass and are at high risk of fractures.
Revolade®	eltrombopag	GlaxoSmithKline Inc.	Tablet	New strength/New indication	New 75mg strength to increase platelet counts in thrombocytopenic patients with chronic hepatitis C virus infection to allow the initiation and maintenance of interferon-based therapy.
Bystolic®	nebivolol	Forest Laboratories Canada Inc.	Tablet	New indication	Can be used concomitantly with angiotensin converting enzyme (ACE) inhibitors.
Tretten®	catridecacog	Novo Nordisk Canada Inc.	Intravenous injection	New indication	For routine prophylaxis for bleeding in adult and pediatric patients with congenital Factor XIII A-subunit deficiency.
Posanol®	posaconazole	Merck Canada Inc.	Tablet, Delayed Release	New dosage form	New Delayed Release tablet dosage form

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