Health Newsflash

A Quarterly Publication

New Drugs and Pipeline News Reviewed at the April to June 2017 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

Portrazza™ (necitumumab)			
Dosage Form	**DIN & Strength**	**Manufacturer**	**AHFS Class**
Intravenous injection	02462478 – 16mg/ml	Eli Lilly Canada Inc.	10:00.00 – Antineoplastic Agents

Indication(s)

Portrazza (necitumumab) is indicated, in combination with gemcitabine and cisplatin, for the treatment of patients with locally advanced or metastatic squamous non-small cell lung cancer (NSCLC) who have not received prior chemotherapy for this condition. Patients with locally advanced disease should be considered surgically incurable or incurable by virtue of ineligibility to receive curative surgery.

Dose

Portrazza is administered in addition to gemcitabine and cisplatin-based chemotherapy for up to 6 cycles of treatment followed by Portrazza as a single agent in patients whose disease has not progressed, until disease progression or unacceptable toxicity.

The recommended dose of Portrazza is 800 mg (absolute dose) administered as an intravenous infusion over 60 minutes on Days 1 and 8 of each 3-week cycle. If a decreased infusion rate is indicated, the infusion duration should not exceed 2 hours.

Therapeutic Alternatives

Standard doublet chemotherapy – examples are: gemcitabine/cisplatin; carboplatin/docetaxel; carboplatin/paclitaxel; cisplatin/docetaxel; cisplatin/etoposide.

Clinical Notes

Necitumumab is a recombinant human IgG1 monoclonal antibody that binds to the human epidermal growth factor receptor (EGFR) and blocks the binding of EGFR to its ligands. Expression and activation of EGFR has been correlated with malignant progression, induction of angiogenesis, and inhibition of apoptosis in squamous NSCLC.

Lung cancer has one of the highest incidence rates and the highest mortality rate of any cancer. About 25 to 30% of all lung cancers are squamous cell carcinomas. Approximately 40% of patients with newly diagnosed NSCLC will have stage IV disease. The five-year survival rates for stage IV NSCLC is of 7.5%. Median age at diagnosis for lung cancer is of 70.

The SQUIRE (SQUamous NSCLC treatment with the Inhibitor of EGF REceptor) study (n = 1,093) was a Phase III, multicenter, open-label, ongoing pivotal study which assessed the efficacy of Portrazza plus gemcitabine and cisplatin as first-line treatment in patients with advanced squamous NSCLC. Patients were randomized (1:1) to receive Portrazza IV infusion on Days 1 and 8 of each 3-week cycle in combination with gemcitabine and cisplatin

every 3 weeks (one cycle) or gemcitabine and cisplatin alone, for a maximum of six cycles in the absence of disease progression or unacceptable toxicity. After the end of chemotherapy, patients who were free of disease progression continued to receive single-agent Portrazza on the same treatment schedule until radiographic disease progression, occurrence of toxic adverse events (AEs), or withdrawal of consent. The primary endpoint was overall survival (OS), defined as the time from randomization to death from any cause. The median overall survival (OS) was 11.5 months for Portrazza + gemcitabine + cisplatin compared with 9.9 months for gemcitabine + cisplatin (hazard ratio [HR] 0.84; [CI]: 0.74, 0.96; P = 0.01). The difference in median OS was 1.6 months, or 48 days. Median progression-free survival (PFS) (a secondary endpoint) was 5.7 months for the Portrazza arm vs. 5.5 months for gemcitabine + cisplatin (hazard ratio [HR] 0.85; [CI]: 0.74, 0.98; P = 0.02). The difference in median PFS was 0.2 months or 6 days. There was no statistically significant difference in overall response rate (ORR) between the study groups – ORR was 31% vs. 29%, for Portrazza + gemcitabine + cisplatin vs. gemcitabine + cisplatin, respectively. No apparent benefit toward improved OS or PFS was observed in the patients ≥70 years. The most common adverse events (AEs) in patients treated with Portrazza in clinical studies (incidence ≥ 15% and ≥ 2% higher than gemcitabine and cisplatin alone) were rash (44%), vomiting (29%), diarrhea (16%), and dermatitis acneiform (15%). The most common severe (Grade 3 or higher) AEs that occurred in Portrazza-treated patients were venous thromboembolism (VTE) [5%, including pulmonary embolism], rash (4%), and vomiting (3%). Approximately 12% of the patients treated in the Portrazza group discontinued treatment due to an adverse event. Portrazza has a Boxed Warning for cardiopulmonary arrest or sudden death, which occurred in 3% of patients (n = 15/538) treated in the Portrazza group vs. 0.6% of patients (n = 3/541) treated with gemcitabine and cisplatin alone. Hypomagnesemia, VTE events, dermatologic toxicities, infusion-related reactions, embryofetal toxicity and increased toxicity and mortality in non-squamous NSCLC are the other warnings/precautions associated with Portrazza treatment.

Place in Therapy

Unlike non-squamous NSCLC, the treatment options for squamous cell tumors are limited to only chemotherapy in the first-line setting. The National Comprehensive Cancer Network (NCCN) committee has voted unanimously to delete the necitumumab/cisplatin/gemcitabine regimen from its guidelines in 2017 (Portrazza was approved by the FDA in 2015), for patients with metastatic squamous cell NSCLC. Their decision reflects the fact that the addition of necitumumab to the regimen is not beneficial based on toxicity, cost and provides limited improvement in efficacy when compared with cisplatin/gemcitabine.

The addition of Portrazza to standard first-line doublet chemotherapy, cisplatin and gemcitabine, appears to provide minimal improvements in median OS and PFS compared with doublet chemotherapy alone. The difference between the treatment groups was statistically significant favoring Portrazza combination therapy for most of the endpoints; however, the actual difference between the treatment groups for median OS was only 1.6 months (approximately 6.4 weeks). Also, patients in the Portrazza arm experienced more dermatologic toxicities, VTE events, hypomagnesemia, and cardiopulmonary death.

Comparative Pricing

Drug	Estimated Annual Cost
Portrazza	Price not available
gemcitabine + cisplatin	$38,850
cisplatin + docetaxel	$43,150

Impact

Insufficient information.

Brinavess™ (vernakalant HCl)			
Dosage Form	**DIN & Strength**	**Manufacturer**	**AHFS Class**
Intravenous injection	02462400 – 20mg/ml	Cardiome UK Ltd. [distributed by: Innomar Strategies Inc.]	24:04.04 – Antiarrythmics

Indication(s)

Brinavess (vernakalant hydrochloride) is indicated for rapid conversion of recent onset fibrillation (AF) to sinus rhythm, for: non-surgery patients, with duration of AF ≤ 7 days, and post-cardiac surgery patients, with duration of AF ≤ 3 days.

Brinavess is NOT recommended for conversion of atrial flutter (AFL) to sinus rhythm.

Dose

Brinavess is dosed by patient body weight, with a maximum calculated dose of 565 mg (based upon a body weight of 113 kg). The recommended initial infusion is 3 mg/kg to be infused over a 10-minute period. For patients weighing ≥ 113 kg, the maximum initial dose of 339 mg (84.7 mL of 4 mg/mL solution) should not be exceeded. If conversion to sinus rhythm does not occur within 15 minutes after the end of the initial infusion, and the patient remains hemodynamically stable, a second 10-minute infusion of 2 mg/kg may be administered. For patients weighing ≥ 113 kg, the maximum second infusion of 226 mg (56.5 mL of 4 mg/mL solution) should not be exceeded. Cumulative doses of greater than 5 mg/kg should not be administered within 24 hours.

Therapeutic Alternatives

Flecainide, propafenone; Cordarone (amiodarone); Corvert (ibutilide)

Clinical Notes

Brinavess (vernakalant hydrochloride) is an anti-arrhythmic drug that acts preferentially in the atria by prolonging atrial refractoriness and slowing impulse conduction in a rate-dependent fashion. These actions on refractoriness and conduction are thought to suppress atrial re-entry, and are likely the predominant electrophysiological properties underlying the anti-arrhythmic effects of vernakalant. The relative atrial selective activity of vernakalant results in significantly prolonged atrial refractoriness without significant effects on ventricular refractoriness at clinically relevant plasma levels in clinical electrophysiologic studies.

Place in Therapy

The European Society of Cardiology (2016) places vernakalant as an alternative to flecainide and propafenone for pharmacological cardioversion.

Comparative Pricing

Drug	Estimated cost per treatment
Brinavess	Price not available
Corvert 0.1mg/ml	$300 - $600
Apo-Propafenone	$1
Apo-Flecainide	$2.50 - $3.20

Impact

The use of this drug would likely be limited to the hospital setting and would have no impact on private payers.

Tecentriq™ (atezolizumab)			
Dosage Form	**DIN & Strength**	**Manufacturer**	**AHFS Class**
Intravenous injection	02462990 – 60mg/ml	Hoffmann-La Roche Ltd.	10:00.00 – Antineoplastic Agents

Indication(s)

Tecentriq (atezolizumab) is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma who: have disease progression during or following platinum-containing chemotherapy; have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.

Marketing authorization with conditions was based on tumour response rate and durability of response. An improvement in survival or disease-related symptoms has not yet been established. [NOC/c]

Dose

The recommended dose is 1200 mg administered by IV infusion every three weeks.

It is recommended that patients are treated with Tecentriq until loss of clinical benefit or unmanageable toxicity.

Therapeutic Alternatives

gemcitabine; paclitaxel; docetaxel; pemetrexed (all off-label, 2nd line chemotherapy)

Clinical Notes

Tecentriq (atezolizumab) is an Fc-engineered humanized immunoglobulin G1 (IgG1) monoclonal antibody that directly binds to PD-L1 (programmed cell death protein 1 [PD-1] ligand) and blocks interactions with the PD-1 and B7.1 receptors, releasing PD-L1/PD-1 pathway-mediated inhibition of the immune response, including reactivating the anti-tumour immune response. Binding of PD-L1 to the PD-1 and B7.1 receptors found on T cells suppresses cytotoxic T-cell activity through the inhibition of T-cell proliferation and cytokine production. PD-L1 may be expressed on tumour cells and tumour-infiltrating immune cells, and can contribute to the inhibition of the anti-tumour immune response in the tumour microenvironment.

Platinum-based chemotherapy has been the standard of care in patients with metastatic disease with a median overall survival of 9 to 15 months. However, in patients with disease that relapses after this type of chemotherapy, the median survival is only 5 to 7 months. Recent data is encouraging regarding the effectiveness of checkpoint inhibitors for the treatment of urothelial carcinoma. Cancers with higher rates of somatic mutations have been shown to respond better to checkpoint inhibitors. Data from the Cancer Genome Atlas rank bladder cancer as the third highest mutated cancer, suggesting that checkpoint inhibitors may have a substantial impact as a treatment for this type of cancer. In the US, FDA has approved the two PD-1 inhibitors, nivolumab (Opdivo®) and pemprolizumab (Keytruda®) for metastatic urothelial cancer (mUC) in the post-platinum chemotherapy setting. Tecentriq is the first PD-L1 inhibitor to become available in Canada.

Approval of Tecentriq in mUC was based on the findings in the IMvigor210 Study. The IMvigor210 study was a two-cohort, phase 2 study of atezolizumab 1200 mg IV every three weeks. Cohort 1 consisted of 119 patients who were ineligible for cisplatin-based chemotherapy and had not been previously treated for metastatic disease. Cohort 2, upon which this approval was based, included 310 patients previously treated with platinum-containing chemotherapy. For both cohorts, the primary endpoint was ORR, and the subjects were stratified according to PD-L1 expression on immune cells (IC) ≥5%, ≥1% and <5%, or <1%. In Cohort 2, the ORR was 16% overall, including 6% complete response. The highest ORR was seen in the ≥5% PD-L1 expression group: 28%, with 14% complete responses. ORR was markedly lower in the <1% PD-L1 expression subgroup: 9% ORR with 2% complete response. Median OS in Cohort 2 was 7.9 months overall and 11.9 months among patients with ≥5% PD-L1 expression. Atezolizumab was well tolerated; the rate of Grade 3–4 AEs was 18% in Cohort 2.

Place in Therapy

Tecentriq provides a new non-chemotherapy option for patients who have failed or relapsed on first-line platinum-based chemotherapy.

Comparative Pricing

Drug	Estimated Annual Cost
Tecentriq	Price not available
Pemetrexed Disodium (Hospira)	$5,000

Impact

Insufficient information.

Cerdelga™ (eliglustat)			
Dosage Form	**DIN & Strength**	**Manufacturer**	**AHFS Class**
Oral capsule	02463261 – 84mg	Sanofi Genzyme, A Division of Sanofi-Aventis Canada Inc.	92:92.00 – Other miscellaneous therapeutic agents

Indication(s)

Cerdelga (eliglustat) is indicated for the long-term treatment of adult patients with Gaucher disease type 1 (GD1) who are CYP2D6 poor metabolizers (PMs), intermediate metabolizers (IMs) or extensive metabolizers (EMs), as determined by CYP2D6 genotype testing. Cerdelga should not be used in patients genotyped as: CYP2D6 ultra-rapid metabolizers (URMs) as these patients may not achieve adequate concentrations of Cerdelga to achieve a therapeutic effect, or CYP2D6 indeterminate metabolizers as a specific dosage cannot be recommended for these patients.

Dose

The recommended dose of Cerdelga depends on CYP2D6 metabolizer status, as follows CYP2D6 IMs and EMs: 84 mg Cerdelga twice daily, CYP2D6 PMs: 84 mg Cerdelga once daily. Co-administration of Cerdelga with other CYP2D6 and CYP3A inhibitors may require dosage adjustment depending on the patient's CYP2D6 metabolizer status to reduce the risk of potentially significant adverse reactions. Reduce the dosage of Cerdelga to 84 mg once daily for: CYP2D6 EMs and IMs taking moderate CYP2D6 inhibitors, CYP2D6 EMs and IMs taking moderate CYP3A inhibitors, CYP2D6 EMs taking strong CYP3A inhibitors.

Therapeutic Alternatives

Cerezyme (imiglucerase); Vpriv (elaglucerase alfa); Zavesca (miglustat) and generics.

Clinical Notes

Gaucher disease is a rare, progressive, genetic lysosomal storage disorder, which leads to debilitating visceral, hematologic, and skeletal manifestations. In the general population, its incidence is approximately 1/40,000 to 1/60,000 births, rising to 1/800 in Ashkenazi Jews. The majority of patients (90%) having Gaucher disease type 1 (GD1), which is characterized by effects on the viscera, while types 2 and 3 are also associated with neurological impairment. GD1 has a broad spectrum of severity, and the clinical presentation is different amongst patients. The goal of therapy is to treat patients before the onset of complications, which include splenomegaly, avascular necrosis (osteonecrosis), osteoarthritis, vertebral compression and other fractures, hepatic as well as lung fibrosis. GD1 patients should be considered for therapy when they present with symptomatic clinical or biological abnormalities.

Two options of treatment exist for GD1: enzyme replacement therapy (ERT) – as to supply the missing enzyme – or substrate reduction therapy (SRT), which reduces the production of the accumulating substrate. Cerdelga is a specific inhibitor of glucosylceramide synthase and acts as a SRT for GD1. Cerdelga is the second SRT-type drug to to become available, following Zavesca (miglustat), another orally-administered therapy. Cerdelga is more specific and more potent than Zavesca.

The efficacy of Cerdelga was established in three pivotal studies in patients with GD1. ENGAGE and ENCORE were Phase III randomized trials, and the third trial was a Phase II, 4-year extension study which established the long-term efficacy of Cerdelga. In ENGAGE [n = 40], at the end of the 9-month double-blind study, the percent change in spleen volume was statistically significant for patients treated with Cerdelga compared with placebo (-27.8% vs. 2.3%; $P < 0.0001$). There were also statistically significant improvements in hematologic parameters (hemoglobin and platelet counts) and a significant reduction in liver volume with Cerdelga compared with placebo.

In ENCORE [n = 159], Cerdelga was non-inferior to Cerezyme (imiglucerase for injection), an ERT administered intravenously, in maintaining the stability of hemoglobin and organ parameters. At 12 months, 84.8% of Cerdelga-treated patients compared with 93.6% of Cerezyme-treated patients met the primary composite endpoint (difference of 8.8%) of stability in spleen and liver volume, hemoglobin level and platelet count.

In the Phase II long-term study [n = 19], the mean hemoglobin level and platelet count increased by 2.3 ± 1.5 g/dL (baseline 11.3 ± 1.5 g/dL) and 95% (baseline 68,700 ± 21,200/mm3), respectively. The mean spleen and liver volumes decreased by 63% and 28%, respectively. Overall, improvements noted in all four parameters (hemoglobin level, platelet count, spleen and liver volumes) during the first two years were maintained for four years.

The most common adverse events in patients treated with Cerdelga in the pivotal studies (incidence ≥ 10%) were arthralgia (45%), fatigue (14%), headache (range, 13% to 40%), nausea (11%), diarrhea (12%), back pain (12%), pain in extremities (11%), and upper abdominal pain (10%).

Place in Therapy

Cerdelga is an orally-administered option as first-line treatment for GD1. It offers eligible patients an effective and well-tolerated alternative to biweekly infusions of ERT (Vpriv, Cerezyme). Zavesca, the other oral therapy for GD1, is indicated as second-line treatment when patients demonstrate failure or intolerance to ERT. Administration of Cerdelga requires patients to undergo metabolizer genotyping to assure optimal effect and avoid drug-drug interactions.

Comparative Pricing

Drug	Estimated Annual Cost
Cerdelga 84mg	$250,000 - $500,000
Zavesca 100mg cap	$119,000
Cerezyme 400U/vial	$704,000*
Vpriv 400U/vial	$560,000*

*based on 70kg patient

Impact

High impact – despite low disease incidence, very high cost.

Ocaliva™ (obeticholic acid)			
Dosage Form	**DIN & Strength**	**Manufacturer**	**AHFS Class**
Tablet	02463121 – 5mg 02463148 – 10mg	Intercept Pharmaceuticals Canada	56:92.00 – Miscellaneous GI Drugs

Indication(s)

Ocaliva (obeticholic acid) is indicated for the treatment of primary biliary cholangitis (PBC; previously known as primary biliary cirrhosis) in combination with ursodeoxycholic acid (UDCA, ursodiol) in adults with an inadequate response to UDCA, or as monotherapy in adults unable to tolerate UDCA. [NOC/c]

Dose

The recommended starting dosage of Ocaliva is 5 mg orally once daily in adults who have not achieved an adequate response to an appropriate dosage of UDCA for at least one year or are intolerant to UDCA.

If an adequate reduction in alkaline phosphatase (ALP) and/or total bilirubin has not been achieved after 6 months of Ocaliva 5 mg once daily, and the patient is tolerating Ocaliva, the dosage of Ocaliva may be increased to 10 mg once daily to improve response. The maximum recommended dosage of Ocaliva is 10 mg once daily.

Therapeutic Alternatives

Off-label use of: bezafibrate (Bezalip SR), fenofibrate (Lipidil Supra), budesonide

Liver transplant

Clinical Notes

Primary biliary cholangitis is characterized by a T-lymphocyte-mediated attack on small intralobular bile ducts. A continuous assault on the bile duct epithelial cells leads to their gradual destruction and eventual disappearance. The sustained loss of intralobular bile ducts causes the signs and symptoms of cholestasis and eventually may result in cirrhosis and liver failure.

PBC is rare, with a reported prevalence of 19 to 402 cases per million persons. The vast majority of patients (90 to 95 percent) are women, and most patients are diagnosed between the ages of 30 and 65 years (often in their 40s or 50s), though the disease has been reported in women as young as 15 years and as old as 93 years. A 2009 study from Canada estimated that the overall age and sex-adjusted annual incidence was 30.3 cases per million (48.4 per million women and 10.4 per million men). While the incidence had not changed between 1996 and 2002, the prevalence increased from 100 to 227 per million. One possible explanation for the increase in disease burden is better detection and increased awareness of PBC, rather than a true change in disease incidence. Familial clustering of PBC has also been noted, suggesting genetic susceptibility in some patients. The prevalence of PBC is 100 times higher in first-degree relatives of a patient with PBC compared with the general population.

Ocaliva is structurally similar to an endogenous bile acid, chenodeoxycholic acid, with the addition of an ethyl group in the 6-alpha position, which makes it a 100-fold more potent agonist at the Farnesoid X receptor (FXR), a nuclear receptor expressed in the liver and intestine. FXR is a key regulator of bile acid, inflammatory, fibrotic, and metabolic pathways. Activation of FXR reduces the intracellular concentrations of bile acids in hepatocytes by suppressing de novo synthesis from cholesterol and by increasing transport of bile acids out of the hepatocytes. In general, these mechanisms limit the amount of circulating bile acid, while promoting choleresis, and therefore reducing hepatic exposure to bile acids.

The approval of Ocaliva was based upon the results of one international, Phase III, randomized, double-blind, 12-month, placebo-controlled, pivotal study called POISE (PBC OCA International Study of Efficacy) which evaluated the efficacy of Ocaliva in patients with PBC who were either taking UDCA or were unable to tolerate UDCA (n = 216). Patients who had an inadequate response to ursodiol or who found the side effects of ursodiol unacceptable

were randomized to receive obeticholic acid at a dose of 10 mg (the 10-mg group), obeticholic acid at a dose of 5 mg with adjustment to 10 mg if applicable (the 5–10-mg group), or placebo. The primary end point was an alkaline phosphatase level of less than 1.67 times the upper limit of the normal range, with a reduction of at least 15% from baseline, and a normal total bilirubin level. The primary end point occurred in more patients in the 5–10 mg group (46%) and the 10 mg group (47%) than in the placebo group (10%; P<0.001 for both comparisons). Patients in the 5–10 mg group and those in the 10 mg group had greater decreases than those in the placebo group in the ALP level (least-squares mean, –113 and –130 U per liter, respectively, vs. –14 U per liter; P<0.001 for both comparisons) and total bilirubin level (–0.02 and –0.05 mg per deciliter [–0.3 and –0.9 µmol per liter], respectively, vs. 0.12 mg per deciliter [2.0 µmol per liter]; P<0.001 for both comparisons). Changes in noninvasive measures of liver fibrosis did not differ significantly between either treatment group and the placebo group at 12 months. Pruritus was more common with Ocaliva than with placebo (56% of patients in the 5–10 mg group and 68% of those in the 10 mg group vs. 38% in the placebo group). The rate of serious adverse events was 16% in the 5–10 mg group, 11% in the 10 mg group, and 4% in the placebo group.

Place in Therapy

The recent PBC clinical practice guideline made by EASL (March 2017) recommends consideration of the use of obeticholic acid in line with its indicated use as demonstrated in the POISE study: For use in combination with UDCA for those patients who have experienced an inadequate response to UDCA, or as monotherapy in those who are intolerant to UDCA with the same dosing regimen – initial dose of 5mg with dose titration to 10mg according to tolerability at six months. Evidence of efficacy of off-label alternatives is uncertain.

Comparative Pricing

Drug	Estimated Annual Cost
Ocaliva	$38,000
pms-Ursodiol C 500mg	$1,100
Apo-Feno-Super 160mg	$115
Jamp-Bezafibrate SR 400mg	$640

Impact

High impact – despite low utilization, cost is significantly higher than first-line therapy.

Acarizax™ (D. farina and D. pteronyssinus)			
Dosage Form	**DIN & Strength**	**Manufacturer**	**AHFS Class**
Sublingual tablet	02463644 – 12 SQ-HDM	ALK Abello A/S	80:02.00 – Allergenic Extracts

Indication(s)

Acarizax is indicated as allergy immunotherapy for the treatment of moderate to severe house dust mite-induced allergic rhinitis, with or without conjunctivitis, in adults 18 to 65 years of age confirmed by a positive skin prick test and/or in vitro testing for *Dermatophagoides farinae* or *Dermatophagoides pteronyssinus* IgE antibodies.

Dose

For house dust mite-induced allergic rhinitis (with or without conjunctivitis), the recommended dose of Acarizax is 1 sublingual tablet (12 SQ-HDM) daily. SQ-HDM is a method for standardization on biological potency, major allergen content and complexity of the allergen extract. Each tablet contains a 1:1:1:1 potency ratio of *D. farinae* group 1 allergen, *D. farinae* group 2 allergen, *D. pteronyssinus* group 1 allergen, and *D. pteronyssinus* group 2 allergen. The first dose of Acarizax should only be administered in a healthcare setting under the supervision of a physician with experience in the diagnosis and treatment of allergic diseases. After receiving the first dose, the patient should be kept under observation for 30 minutes to monitor for signs or symptoms of a severe systemic or a severe local allergic reaction. If the first dose is adequately tolerated, subsequent doses may be taken at home. Treatment with Acarizax can be initiated at any time during the year.

Therapeutic Alternatives

Allergenic Extract – Standard Mite Mixed Inj.

Clinical Notes

Dust mites (*D. pteronyssinus* and *D. farinae*) are arthropods of the class Arachnida that colonize bedding, sofas, carpets or any woven material. Dust mites are known to cause perennial allergic disease through production of fecal particles which contain a complex mixture of allergenic proteins, endotoxin, enzymes and dust-mite and bacterial DNA. It is estimated that 1 to 2% of the world population may be affected by HDM allergy. Effective avoidance measures include physical barriers and humidity control (humidity being a critical factor for mite prevalence, both inside and outside the house) as well as acaricide treatments.

Allergen extracts given sublingually are intended for absorption either in the mouth or within the small intestine. Systemic tolerance occurs as a result of a decline in T helper mechanisms or stimulation of T suppressor cells involved in the IgE production.

The efficacy of Acarizax for the treatment of house dust mite (HDM)-induced allergic rhinitis was investigated in two double-blind, placebo-controlled, randomized clinical field efficacy trials. Duration of trials was up to 12 months. Subjects presented with allergic rhinitis, and in some cases also presented with conjunctivitis, asthma or polysensitization to other allergens in addition to HDM. The first study evaluated 1482 subjects aged 12 to 85, with the primary outcome a measure of the total combined rhinitis score (TCRS), which is the sum of the daily auto-reported rhinitis symptom scores and daily medication scores, during approximately the last 2 months of treatment. Patients treated with Acarizax had significant relief of nasal symptoms and reduction in standard allergy medication use as measured by a decrease in TRCS, when compared to placebo-treated subjects (-17.2%, $p<0.001$ (95% CI -25.0%, -9.7%)). Treatment was well tolerated. The second study followed a similar model, evaluating Acarizax vs placebo in 646 patients aged 18 to 66, and showed a reduction in TCRS score of 16.1% ($p=0.004$, (95% CI -25.8%, -5.7%)). The most common side effects were oral pruritus, ear pruritus as well as throat irritation. Within pooled patients treated with Acarizax, 0.1% (1/1383) presented with treatment-related systemic allergic reactions.

A Cochrane review of sublingual immunotherapy indicated a significant reduction in symptoms and medication requirements in allergic rhinitis.

Place in Therapy

Until now, allergen immunotherapy for house dust mites required regular injections at the clinician's office. Acarizax is the first oral immunotherapy available. Sublingual immunotherapy can be self-administered by patients or caregivers and presents with a lower risk of anaphylaxis compared with injected immunotherapy. Optimal duration of a course of sublingual immunotherapy has not been defined.

Comparative Pricing

Drug	Estimated Annual Cost
Acarizax	Price not available
Allergenic Extract – Standard Mite Mixed INJ	$3,000 - 6,300

Impact

Insufficient information.

Adlyxine™ (lixisenatide)			
Dosage Form	**DIN & Strength**	**Manufacturer**	**AHFS Class**
Subcutaneous injection	02464349 Starter Kit (2x3ml pens – 100mcg/ml and 50mcg/ml) 02464276 50mcg/ml (3ml pen) 02464284 100mcg/ml (3ml pen)	Sanofi-Aventis Canada Inc.	68:20.06 – Incretin Mimetics

Indication(s)

Adlyxine is indicated for use as an adjunct to diet and exercise to improve glycemic control in adult patients with type 2 diabetes mellitus in combination with: metformin, a sulfonylurea (SU) (alone or with metformin), pioglitazone (alone or with metformin), a basal insulin (alone or with metformin), when the therapy listed does not provide adequate glycemic control.

Dose

Adlyxine is administered by subcutaneous injection once daily, within the hour prior to any meal of the day. It is preferable that the prandial injection of Adlyxine is performed before the same meal every day, when the most convenient meal has been chosen. The starting dose is 10mcg Adlyxine once daily for 14 days. Increase the Adlyxine dose to the maintenance dose of 20mcg once daily starting on day 15. If the 20mcg once daily maintenance dosage is not tolerated, the dosage can be temporarily reduced to 10mcg once daily. Consider increasing the dosage to 20mcg once daily within 4 weeks.

Adlyxine is to be injected subcutaneously in the thigh, abdomen or upper arm. Injection sites within an injection area must be alternated from one injection to the next. Adlyxine should not be administered intravenously or intramuscularly.

Therapeutic Alternatives

Bydureon (exenatide);
Byetta (exenatide);
Trulicity (dulaglutide);
Victoza (liraglutide).

Clinical Notes

Adlyxine (lixisenatide) is a once-daily glucagon-like peptide-1 (GLP-1) receptor agonist to be used as an adjunct to diet and exercise in the treatment of patients with type 2 diabetes mellitus. Adlyxine is used in combination with other antidiabetic drugs. Similar to other GLP-1 receptor agonists, lixisenatide improves pancreatic beta-cell glucose-dependent insulin release, decreases alpha-cell glucagon release, and slows gastric emptying.

The efficacy of Adlyxine was established in ten, Phase III, randomized, published pivotal trials as part of the GetGoal program. Adlyxine has been studied as monotherapy, in combination with oral antidiabetic drugs (OADs), and in combination with basal insulin (± OADs). In the pivotal trials, Adlyxine was compared with placebo, Byetta, and Apidra (insulin glulisine injection). In patients with type 2 diabetes, Adlyxine produced statistically significant reductions from baseline in glycosylated hemoglobin (HbA1C) compared with placebo. The efficacy of Adlyxine was compared with Victoza (liraglutide injection) in a non-pivotal trial.

As monotherapy, in a placebo-controlled trial (GetGoal-Mono, n = 361), Adlyxine reduced HbA1C by 0.7% to 0.85% (baseline 8.0%). When added to metformin, in a placebo-controlled trial (GetGoal-M, n = 680), Adlyxine reduced HbA1C by 0.8% to 0.9% (baseline 8.0%). Three placebo-controlled trials explored add-on therapy with Adlyxine. When added to metformin ± sulfonylurea (SU), (GetGoal-M-Asia, n = 391), Adlyxine reduced HbA1C by 0.83% (baseline 7.9%); when added to SU ± metformin (GetGoal-S, n = 859), Adlyxine reduced HbA1C by 0.85% (baseline 8.3%; and when added to pioglitazone ± metformin (GetGoal-P, n = 484) Adlyxine reduced HbA1C by 0.9% (baseline 8.1%). Three placebo-controlled and one active-controlled (vs. Apidra) pivotal trials assessed the glycemic efficacy of Adlyxine in addition to basal insulin. In GetGoal-L (n = 495) Adlyxine added to basal insulin ± metformin reduced HbA1C by 0.7% (baseline 8.4%). In GetGoal-Duo 1 (n = 446) Adlyxine, added to metformin ± SU, glinide and/or thiazolidinedione (TZD) + Lantus (insulin glargine U-100 injection), reduced HbA1C by 0.7% (baseline 7.6%). In GetGoal-Duo 2 (n = 894) Adlyxine, added to basal insulin ± one to three OADs was non-inferior to Apidra (QD or three-times daily [TID]), added to the same regimen; Adlyxine reduced HbA1C by 0.6% (vs. 0.6% for Apidra QD and 0.8% for Apidra TID) [baseline 7.8%].

In Get-Goal-L-Asia (n = 311) Adlyxine, added to basal insulin ± SU, reduced HbA1C by 0.77% (baseline 8.53%). Adlyxine demonstrated non-inferiority to Byetta for HbA1C reduction when both agents were added to metformin in GetGoal-X (n = 639). Over 24-weeks, HbA1C was reduced by 0.8% with Adlyxine and 1.0% with Byetta (baseline 7.94% and 7.14%, respectively). Other endpoints such as the proportion of patients with HbA1C < 7%, fasting plasma glucose (FPG) reductions, and weight reductions were similar between Adlyxine and Byetta. Victoza 1.8 mg demonstrated non-inferiority and superiority to Adlyxine for HbA1C reduction in a 26-week non-pivotal trial when both agents were added to metformin therapy (n = 404). HbA1C was reduced by 1.8% with Victoza and by 1.2% with Adlyxine (baseline 8.4% for both groups). The proportion of patients with HbA1C < 7% and FPG reductions were greater with Victoza than Adlyxine. Weight reduction was not statistically significantly different between the two groups.

The most common adverse events in patients treated with Adlyxine vs. placebo in the pivotal trials (incidence ≥ 5%) were nausea (25% vs. 6%), vomiting (10% vs. 2%), headache (9% vs. 6%), diarrhea (8% vs. 6%), and dizziness (7% vs. 4%). In the clinical trial comparing Adlyxine and Victoza, 72% and 64% of Victoza and Adlyxine patients, respectively, reported AEs. A similar number of patients discontinued therapy in each group (6.4% [n = 13] and 7.4% [n = 15] for Victoza and Adlyxine, respectively).

Cardiovascular outcomes were also evaluated in diabetic patients receiving Adlyxine following recent acute coronary event (in the previous 180 days) in the ELIXA trial. In the 6068 patients evaluated, Adlyxine demonstrated non-inferiority but did not show superiority for the primary composite end point of cardiovascular death, myocardial infarction, stroke or hospitalization for unstable angina when compared to placebo (p=0.81), as opposed to LEADER, the Victoza cardiovascular outcomes trial. While the patient population in ELIXA was different from that in LEADER, as there was a higher proportion of higher risk patients in ELIXA, it would be expected that ELIXA would be more likely to demonstrate cardiovascular benefits, if any existed.

Place in Therapy

In one study, Adlyxine was non-inferior to Byetta for the improvement of HbA1C when both agents were used in combination with metformin. Adlyxine is priced at 82% of cost of Byetta. Victoza demonstrated superiority to Adlyxine for reduction in HbA1C. A greater proportion of patients treated with Victoza also achieved HbA1C < 7.0% and had lower FPG compared with Adlyxine. Adlyxine is priced at 46 to 70% of Victoza price (depending on dose of Victoza). Additionally, Adlyxine failed to improve cardiovascular outcomes in a high-risk diabetic population when compared to placebo.

There are multiple oral and injectable agents indicated for the treatment of type 2 diabetes. This is the fifth GLP-1 agonist available in Canada. As a class, the GLP-1 agonists have robust glycemic efficacy (0.8% to 2.0% reduction in HbA1C) and are associated with a modest weight reduction (1 kg to 4 kg reduction in weight). All GLP-1 agonists are administered by SC injection. Administration schedule, dosing recommendations, and adverse event profiles differ between the GLP-1 agonists - Adlyxine is the second GLP-1 agonist to be dosed once daily, after Victoza. At this time, Adlyxine represents a therapeutic alternative to the other available GLP-1 agonists.

Comparative Pricing

Drug	Estimated Annual Cost
Adlyxine	$1,500
Victoza	$2,100 - $3,200
Trulicity	$2,700
Byetta	$1,800
Bydureon	$2,600

Impact

Minimal impact.

Ozanex™ (ozenoxacin)			
Dosage Form	**DIN & Strength**	**Manufacturer**	**AHFS Class**
Topical cream	02463504 – 1%	Ferrer Internacional S.A.	84:04.04 – Antibacterials

Indication(s)

Ozanex is indicated for the topical treatment of impetigo in patients aged 2 months and older.

Dose

Apply a thin layer of Ozanex to the affected area twice daily for 5 days. Patients not showing a clinical response within 3 days should be re-evaluated and alternative therapy should be considered.

Therapeutic Alternatives

Bactroban (mupirocin); Fucidin (fusidic acid).

Clinical Notes

Impetigo is one of the most common superficial skin infections seen in children, it is caused by *Staphylococcus aureus* and *Streptococcus pyogenes* and often associated with the production of pus and formation of a crust.

Based on data from studies published since 2000 the global population of children suffering from impetigo at any one time to be in excess of 162 million. It is an under-recognized disease and in conjunction with scabies, comprises a major childhood dermatological condition with potential lifelong consequences if untreated.

Ozanex is a new generation of non-fluorinated quinolones, that offers a short 5-day twice-a-day dosing regimen and has shown bacteriological eradication as early as day 3 of treatment. The antibacterial action of ozenoxacin is due to the inhibition of both bacterial enzymes, DNA gyrase A and topoisomerase IV which are essential enzymes in the replication, transcription and repair of bacterial DNA as well as partitioning of the chromosomal DNA during bacterial cell division. Ozenoxacin has a dual target of action, inhibiting both enzymes, thus demonstrating greater inhibitory activity against both of these enzymes compared to other quinolones.

The Health Canada approval was based on two multicenter, randomized, placebo controlled Phase III studies involving 875 adult and pediatric patients with impetigo. Clinical and microbiological evaluations were performed at day 3 - 4 on-therapy, at the end of therapy and 5 - 7 days after the last application. The primary efficacy endpoint in both studies was clinical response (success being defined as Skin Infection Rating Scale (SIRS) score of 0 for the signs or symptoms of: exudate/pus, crusting, itching/pain; and a score of no more than 1 for erythema/inflammation, tissue edema and itching, and no additional antimicrobial therapy necessary). In both studies, more patients in the Ozanex group achieved first positive clinical response and first bacteriological eradication at an earlier time point during treatment when compared to patients in the placebo group. The difference in success rates for the two studies was 15.5% and 16% higher than placebo.

Examination of age and gender subgroups did not identify differences in response to Ozanex among these groups.

Place in Therapy

The mechanism of action of ozenoxacin is different from that of aminoglycosides, macrolides, and β-lactam antibiotics and therefore ozenoxacin may be active against strains that are resistant to these antibiotics. Due to its double inhibitory target activity and its bactericidal property, ozenoxacin shows a very low frequency of spontaneous resistance compared to other quinolones.

Comparative Pricing

Drug	Estimated Annual Cost
Ozanex 1% Cr	Price not available
Fucidin 2% Cr	$23.24/30 g
Bactroban 2% Oint	$8.94/15 g

Impact

Insufficient information.

Vemlidy™ (tenofovir alafenamide)			
Dosage Form	**DIN & Strength**	**Manufacturer**	**AHFS Class**
Tablet	02464241 – 25mg	Gilead Sciences Canada Inc.	08:18.32 – Nucleosides and Nucleotides

Indication(s)

Vemlidy is indicated for the treatment of chronic hepatitis B in adults with compensated liver disease.

Dose

The recommended dose of Vemlidy is one tablet once daily, with or without food.

Therapeutic Alternatives

Heptovir (lamivudine), Viread (tenofovir disoproxil fumarate), Hepsera (adefovir dipivoxil), Baraclude (entecavir), Sebivo (telbivudine).

Clinical Notes

In Canada, an estimated 5% of the population have had an acute hepatitis B virus (HBV) infection at some point in their lives, and 0.7% to 0.9% are chronically infected with HBV.

As there is currently no cure for chronic hepatitis B, the ultimate goal of therapy is to improve quality of life and survival by preventing progression of the disease to cirrhosis, end-stage liver disease, and its complications such as hepatocellular carcinoma and death.

The Canadian Association for the Study of the Liver (CASL 2012) consensus guidelines recommend antiretroviral (ARV) treatment for CHB patients with the following clinical characteristics: hepatitis B e antigen (HBeAg)-positive patients with high levels of HBV DNA (> 20,000 IU/mL) with elevated alanine amino transferase (ALT) > upper limit of normal (ULN) for three to six months; HBeAg-negative patients with lower levels of HBV DNA (> 2000 IU/mL) and ALT > ULN for three to six months; and patients with either HBeAg-positive or HBeAg-negative status who have significant liver inflammation and fibrosis.

Viread or Baraclude are recommended as first-line therapy for treatment-naïve HBV patients because they are the most potent agents available with no tenofovir or very low entecavir rates of antiviral resistance. Viread is first-line therapy for lamivudine-resistant HBV. Entecavir should not be used in this setting due to the risk of development of entecavir resistance.

Vemlidy is a novel, targeted prodrug of tenofovir, an inhibitor of HBV replication. Vemlidy has demonstrated antiviral efficacy similar to and at a dose less than one-tenth that of Viread (tenofovir disoproxil fumarate 300mg). Data show that because Vemlidy has greater plasma stability and more efficiently delivers tenofovir to hepatocytes compared to Viread, it can be given at a lower dose, resulting in less tenofovir in the bloodstream. As a result, Vemlidy has improved renal and bone safety compared to Viread.

Place in Therapy

Vemlidy has been shown to have an improved renal and bone safety profile compared with Viread while achieving high rates of HBV DNA suppression across a wide range of CHB patients in clinical trials. Vemlidy provides an alternative to treatment with Viread.

Comparative Pricing

Drug	Estimated Annual Cost
Vemlidy	$7,100
Apo-Lamivudine	$1,290
Viread	$7,100
Apo-Adefovir	$7,500
Apo-Entecavir	$6,000
Sebivo	$7,200

Impact

Minimal impact – cost shift from similarly priced alternatives.

FIRST TIME GENERICS

First Time Generic Drugs (Notices of Compliance (NOCs) from February 25, 2017 to May 30, 2017)

Generic Name	Reference Drug (Brand)	Rank by ingredient cost in 2016	Manufacturer	Route of Administration	Approved Indications/ Comments
cyclosporine	Restasis	144	Teva Canada Inc.	Ophthalmic	Aqueous deficient dry eye disease
itraconazole	Sporanox	499	Mint Pharmaceuticals Inc.	Oral	Systemic fungal infections
ethacrynate sodium	Edecrin Sodium	1154	VPI Pharmaceuticals Inc.	Intravenous	Patients unresponsive to the commonly used diuretics
olmesartan medoxomil & olmesartan medoxomil/ hydrochlorothiazide	Olmetec & Olmetec Plus	98 &154	Apotex Inc.	Oral	Treatment of mild to moderate essential hypertension
caspofungin acetate	Cancidas	1110	Teva Canada Ltd.	Intravenous	Treatment of serious systemic fungal infections
moxifloxacin HCl	Avelox I.V.	360	Fresenius Kabi Canada Ltd.	Intravenous	Community acquired pneumonia, intra-abdominal infections due to polymicrobial and monomicrobial infections, complicated skin and skin structure infection
atazanavir	Reyataz	423	Teva Canada Inc.	Oral	Treatment of HIV-1 infection
emtricitabine/ tenofovir disoproxil fumarate	Truvada	69	Apotex Inc.	Oral	Treatment HIV-1 infection in adults
busulfan	Busulfex	1843	Sterimax Inc.	Intravenous	Conditioning regimen prior to hematopoietic progenitor cell transplantation
testosterone	Androgel	85	Taro Pharmaceuticals Inc.	Topical	Deficiency or absence of endogenous testosterone (hypogonadism)

NEW DRUGS AND PRODUCT LINE EXTENSIONS

New Drugs and Product Line Extensions (Notices of Compliance (NOCs) from February 25, 2017 to May 30, 2017)

Brand name	Chemical name	Manufacturer	Dosage form	Type of Line Extension	Specifics/Comments
Vimpat	lacosamide	UCB Canada Inc.	Tablet	New Indication	Monotherapy in the management of partial-onset seizures in adult patients with epilepsy.
Enbrel	etanercept	Amgen Canada Inc.	Subcutaneous injection	New indication	Treatment of pediatric patients ages 4 to 17 years with chronic severe plaque psoriasis who are candidates for systemic therapy or phototherapy.
Harvoni	ledipasvir/ sofosbuvir	Gilead Sciences Canada, Inc.	Tablet	New Indication	Chronic hepatitis c virus (HCV) genotypes (GT) 2, 3, 4, 5 or 6 infection, without cirrhosis or with compensated cirrhosis. Extension of use in GT 1 infection to pediatric patients 12-years of age and older.
Revolade	eltrombopag olamine	Novartis Pharmaceuticals Canada Inc.	Tablet	New strength and new indication	New strength 12.5mg; New indication: treatment of pediatric chronic immune thrombocytopenia purpura (ITP) to increase platelet counts in pediatric patients who have had an insufficient response to corticosteroids or immunoglobulins
Tivicay	dolutegravir	ViiV Healthcare ULC	Tablet	New strengths and new indication	New strengths 10 mg and 25 mg; Extension of indication: used in combination with other antiretroviral agents, is indicated for the treatment of human immunodeficiency virus (HIV-1) infection in adults and in INSTI-naïve children weighing at least 30 kg.
Sandoz-Levetiracetam	levetiracetam	Sandoz Canada Inc.	Tablet	New Strength	New Strength of 1000 mg.
Tepadina	thiotepa	Adienne S.A.	Intravenous injection	New brand	Used in combination with other chemotherapeutic products as part of a high-dose chemotherapy (HDCT) consolidation regimen followed by autologous stem cell transplantation (ASCT) for adult patients with central nervous system (CNS) lymphoma
Utrogestan	progesterone	Besins Healthcare S.A.	Vaginal capsule	New brand and dosage form	A new dosage form for vaginally-administered progesterone (vaginal capsules), for women undergoing *in vitro* fertilization (IVF) procedure

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NEW DRUGS AND PRODUCT LINE EXTENSIONS (continued)

New Drugs and Product Line Extensions (Notices of Compliance (NOCs) from February 25, 2017 to May 30, 2017)

Brand name	Chemical name	Manufacturer	Dosage form	Type of Line Extension	Specifics/Comments
Berinert	C1 esterase Inhibitor, human	CSL Behring Canada Inc.	Intravenous injection	New indication	Extension of indication for the treatment of acute abdominal facial or laryngeal attacks of hereditary angioedema (HAE) to pediatric patients.
Darzalex	daratumumab	Janssen Inc.	Intravenous injection	New indication	Treatment of patients with multiple myeloma who have received at least one prior therapy
Xolair	omalizumab	Novartis Pharmaceuticals Canada Inc.	Subcutaneous injection	New indication	Extension of indicated use in severe asthma to pediatric patients 6-years of age an older.
Tarceva	erlotinib	Hoffmann-La Roche Ltd.	Tablet	New indication	Modification of indication to include requirement of presence of EGFR-activating mutations in tumours.
Erelzi	etanercept	Sandoz Canada Inc.	Subcutaneous injection	Biosimilar	Alternative to Brenzys and Enbrel for treatment of moderately to severely active rheumatoid arthritis in adults, reducing signs and symptoms of moderately to severely active polyarticular juvenile idiopathic arthritis (JIA), active ankylosing spondylitis; Brenzys is not indicated for treatment of JIA.
Zeulide Depot	leuprolide acetate	Pendopharm, Division of Pharmascience Inc.	Intramuscular injection	New strength	New strength 22.5mg
Technivie	ombitasvir/ paritaprevir/ ritonavir	AbbVie Corp.	Tablet	New indication	Extension of indication to include those with compensated cirrhosis.
Opdivo	nivolumab	Bristol-Myers Squibb Canada	Intravenous injection	New indication	Treatment of recurrent or metastatic squamous cell carcinoma of the head and neck (SCCHN); previously indicated for melanoma, non-small cell lung cancer (NSCLC) and metastatic renal cell carcinoma (RCC).
Tafinlar	dabrafenib	Novartis Pharmaceuticals Canada Inc.	Capsule	New indication	Used in combination trametinib for treatment of patients with metastatic non-small cell lung cancer (NSCLC) with a BRAF V600 mutation whose disease has progressed following systemic therapy. Previously indicated for melanoma.

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NEW DRUGS AND PRODUCT LINE EXTENSIONS (continued)

New Drugs and Product Line Extensions (Notices of Compliance (NOCs) from February 25, 2017 to May 30, 2017)

Brand name	Chemical name	Manufacturer	Dosage form	Type of Line Extension	Specifics/Comments
Mekinist	trametinib	Novartis Pharmaceuticals Canada Inc.	Tablet	New indication	Used in combination dabrafenib for treatment of patients with metastatic non-small cell lung cancer (NSCLC) with a BRAF V600 mutation whose disease has progressed following systemic therapy. Previously indicated for melanoma.
Ibrance	palbociclib	Pfizer Canada Inc.	Capsule	New indication	In combination with fulvestrant for the treatment of women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative locally advanced or metastatic breast cancer whose disease progressed after prior endocrine therapy.
Blincyto	blinatumomab	Amgen Canada Inc.	Intravenous injection	New Indication	Pediatric patients with Philadelphia chromosome-negative relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL).
Kineret	anakinra	Swedish Orphan Biovitrum	Subcutaneous injection	New indication	Treatment of Neonatal-Onset Multisystem Inflammatory Disease (NOMID) in adults, adolescents, children and infants aged 8 months and older with a body weight of 10kg or above
Eylea	aflibercept	Bayer Inc.	Intravitreal injection	New Indication	Myopic choroidal neovascularization (CNV).

Authors: Aaron Aoki, RPh, BScPhm, MBA, CDE, CRE; Camille Gagnon, PharmD; Suzanne Easo, RPh, BScPhm; Ramanjeet Singh, BHS