Health Newsflash

A Quarterly Publication

New Drugs and Pipeline News Reviewed at the July to September 2016 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

Bepreve™ (bepotastine)			
Dosage Form	**DIN & Strength**	**Manufacturer**	**AHFS Class**
Ophthalmic solution	02456532 – 1.5%	Bausch & Lomb Inc.	52:02.00 – Antiallergic agents

Indication(s)

Bepreve 1.5% w/v is indicated for the treatment of itching associated with allergic conjunctivitis.

Dose

Instill one drop of Bepreve into the affected eye(s) twice a day.

Therapeutic Alternatives

Patanol, Pataday (olopatadine)*; Zaditor (ketotifen)*

*generic available

Clinical Notes

Bepotastine is a topically active anti-allergic medication. Primary mechanisms of action of bepotastine include selective antagonism of H1-histamine receptors, stabilization of mast cells, inhibitory action on eosinophilic migration to inflammatory sites, and suppression of vascular permeability. It inhibits production of interleukin-5 (IL-5), a key factor in eosinophil activation, as well as other mediators of inflammatory and allergic reactions, such as leukotriene B4 (LTB4), leukotriene D4 (LTD4), platelet activating factor (PAF) and substance P. Bepotastine demonstrates activity in both early and late phases of the allergic response.

The efficacy of bepotastine 1.5% ophthalmic solution was evaluated in two conjunctival allergen challenge (CAC) studies. Primary endpoints included ocular itching and conjunctival hyperemia (both measured on a 5-point scale). Bepotastine demonstrated clinical and statistical significance for the reduction of ocular itching (change of more than one unit on the grading scale) after 3 minutes and 8 hours, as compared to placebo. A significant reduction in conjunctival hyperemia was also achieved in the onset of action CAC studies. Bepreve is estimated to begin acting in approximately 3 minutes, and effect can last up to 16 hours. In clinical trials, Bepreve was generally well tolerated with its side effects being transient and mild.

Place in Therapy

Bepreve presents as another option of treatment for treating patients suffering from allergic conjunctivitis. Some formulations already available on the market have the advantage of being administered once daily, while Bepreve still requires twice daily instillation.

Comparative Pricing

Drug	Estimated Cost per Bottle
Bepreve™ 1.5%	Price not available
olopatadine 0.1%	$26
olopatadine 0.2%	$26
ketotifen 0.025%	$21

Impact/Plan Management Suggestions

Insufficient information.

Cinqair™ (reslizumab)			
Dosage Form	**DIN & Strength**	**Manufacturer**	**AHFS Class**
Intravenous Injection	02456419 – 100mg/10ml	Teva Pharmaceutical Products R&D, Inc.	48:10:20 - Respiratory Tract Agents

Indication(s)

Cinqair (reslizumab) is indicated as an add-on maintenance treatment of adult patients with severe eosinophilic asthma who:

- are inadequately controlled with medium-to-high-dose inhaled corticosteroids and an additional asthma controller(s) (eg, LABA) and
- have a blood eosinophil count of ≥400 cells/μL at initiation of the treatment.

Dose

The recommended dosage is 3 mg/kg once every 4 weeks by intravenous infusion.

Therapeutic Alternatives

Nucala (mepolizumab), Xolair (omalizumab)

Clinical Notes

Reslizumab is an IgG4κ interleukin-5 antagonist monoclonal antibody. IL-5 is the major cytokine responsible for the growth and differentiation, recruitment, activation, and survival of eosinophils. Reslizumab prevents the binding of IL-5 to the IL-5 receptor complex expressed on the eosinophil surface. Inflammation is an important component in the pathogenesis of asthma. Multiple cell types (e.g., mast cells, eosinophils, neutrophils, macrophages, lymphocytes) and mediators (e.g., histamine, eicosanoids, leukotrienes, cytokines) are involved in inflammation that causes and exacerbates asthma. Eosinophils have been highly implicated in asthma pathogenesis and there are a substantial number of asthma patients that remain uncontrolled despite existing therapies, a subset of these patients have evidence of eosinophil-driven pathology.

Reslizumab improves asthma control by inhibiting IL-5 signaling, to reduce the production and survival of eosinophils. Reslizumab is recommended in patients with Blood Eosinophil Counts >400 cells/μL.

Adults and adolescents (12 years of age and above) with asthma and elevated blood eosinophils who are inadequately controlled on inhaled corticosteroids, are believed to be 3-4% of asthma Patients. Despite a plethora of existing treatments there is still significant morbidity and mortality in North American patients with asthma. An estimated 80,000 to 160,000 individuals in Canada could be eligible for IL-5 inhibition treatment. Approximately 30% of these individuals may also be canditates for IgE inhibition therapy with Xolair®.

In clinical trials Reslizumab significantly reduced asthma exacerbations (50-59%) and increased forced expiratory volume in 1 second (FEV1) (93-137 ml over 16 weeks) and improved asthma control and asthma symptom scores.

Place in Therapy

Cinqair occupies a similar place in therapy as Nucala with a similar mechanism of action. It differs from Nucala in that it requires intravenous administration whilst Nucala is administered subcutaneously.

Comparative Pricing

Drug	Estimated monthly cost
Cinqair™	$2,025
Nucala™	$2,045
Xolair®	$1,300-2,650

Impact/Plan Management Suggestions

Intermediate impact – high cost but cost shift from other similar high cost alternatives.

Darzalex™ (daratumumab)			
Dosage Form	**DIN & Strength**	**Manufacturer**	**AHFS Class**
Intravenous injection	02455951 – 100mg/5ml 02455978 – 400mg/20ml	Janssen Inc.	10:00.00 – Antineoplastic Agents

Indication(s)

Darzalex (daratumumab) is indicated for the treatment of patients with multiple myeloma who have received at least three prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory agent (IMiD), or who are refractory to both a PI and an IMiD.

Marketing authorization with conditions was based on the primary efficacy endpoint of overall response rate demonstrated in a single-arm study. [NOC/c – conditional approval pending results from a confirmatory Phase 3 trial]

Dose

The recommended dose of Darzalex is 16 mg/kg body weight administered as an intravenous infusion according to the following dosing schedule (Table 1):

Table 1. Dosing schedule for Darzalex™

Schedule	Weeks
Weekly	Weeks 1 to 8
Every two weeks	Weeks 9 to 24
Every four weeks	Week 25 onwards until disease progression

Pre- and post-infusion medications are recommended to mitigate the risk of infusion-related reactions.

Therapeutic Alternatives

Pomalyst (pomalidomide) + dexamethasone – usually reserved for second or subsequent relapses.

Clinical Notes

Multiple myeloma, which is a malignant disorder of the plasma cells, is diagnosed in approximately 114,000 patients per year worldwide. The median age of patients at diagnosis is 65 years and the disease has a typical course characterized by a chronic phase and several relapses leading to an aggressive terminal phase. Progress, such that survival of patients with newly diagnosed multiple myeloma has increased from approximately 3 years with no improvement from the years 1985 to 1998 to 6 to 10 years today.

According to the 2011 Canadian Cancer Statistics report released by the Canadian Cancer Society, the total new cases of multiple myeloma diagnosed annually in Canada are estimated at 2,300, representing an incidence of 5 in 100,000 people. This corresponds to 1.4% of total new cases of cancer in men and 1.2% of total new cases of cancer in women. The total number of deaths from multiple myeloma was estimated at 1,350.

Despite these advances, multiple myeloma remains incurable. All patients eventually relapse. With each successive relapse, the chance of response and duration of response typically decreases. After relapse from PIs and IMiDs, patients are often retreated with drugs that have the same mechanism of action. Ultimately, the disease becomes refractory. Patients who are heavily pretreated and/or refractory to both a PI and IMiD have a dismal prognosis, are difficult to get back into a durable remission, and median survival is only between 8 to 9 months. The relapsed and refractory setting represents a serious and life threatening disease with an unmet medical need.

First line treatment options contain at least one of the novel therapies, i.e. proteasome inhibitors and/or immunostimulatory drugs, followed by autologous stem cell transplantation (ASCT), if indicated. Relapsed and/or refractory patients typically receive salvage therapy (if possible, this could include (2nd) autologous or allogeneic hematopoietic stem cell transplantation) until relapse or toxicity and then go onto the next salvage option. In this setting, for patients who have received at least 2 prior therapies, including bortezomib and an IMiD, and have shown relapsed or refractory disease, pomalidomide (Pomalyst®) (in combination with dexamethasone) is the only approved regimen in Canada. The proteasome inhibitor carfilzomib (Kyprolis™) and the monoclonal antibody elotuzumab (Empliciti™) both in combination with lenalidomide and dexamethasone were approved in Canada for the treatment of adult patients with multiple myeloma who have received at least one prior therapy.

In patients with relapsed and refractory multiple myeloma, whose prior therapy included a proteasome inhibitor and an immunomodulatory agent and who have demonstrated disease progression on the last therapy there are not any treatment options, other than the physician's best choice and palliative care.

Daratumumab is an IgG1κ human monoclonal antibody (mAb) that binds to the CD38 protein expressed at a high level on the surface of multiple myeloma tumour cells, as well as other cell types and tissues at various levels. CD38 protein has multiple functions such as receptor mediated adhesion, signalling and enzymatic activity.

The efficacy of daratumumab was based on the results of two clinical trials of treatment of patients with relapsed or refractory multiple myeloma: a Phase 1/2 dose escalation trial with dose expansion of five dose schedule regimens and a Phase 2 randomized dosing trial with dose expansion. The optimal dose (16 mg/kg) and regimen was studied in a two arm, open-label trial of single-agent daratumumab. The primary endpoint was objective response rate (ORR). Of the 124 patients enrolled, 106 received the proposed dose and were the focus of the efficacy analysis. Patients had received a median of 5 prior treatments. Patients had ECOG performance status ≤ 2. Results showed that ORR was achieved by 31 (29%) patients (95% CI: 21-39%) with a median duration of response (DOR) of 7.4 months. Stringent Complete Response was achieved by 3 (3%) patients (95% CI: 1-8%). Very Good Partial Response was achieved by 10 (9%) patients (95% CI: 5-17%). Data to support the effectiveness of daratumumab came from the 42 patients who received the proposed dose on the Phase 1/2 trial. ORR was achieved by 15 (36%) patients (95% CI: 22-52%) with a median duration of response (DOR) of 6.9 months.

The most common side effects with Darzalex (which may affect around 1 in 2 people) are infusion-related reactions such as breathing problems, cough, runny or blocked nose and chills. Due to the risk of these occurring patients should be monitored for some time after administration and preparations need to be made to treat serious emergent events. Other frequent side effects (affecting at least 1 in 5 patients) are tiredness, pyrexia (fever), nausea (feeling sick), back pain, upper respiratory tract infections (such as colds), anaemia (low red blood cell counts), neutropenia (low levels of neutrophils, a type of white blood cell) and thrombocytopenia (low blood platelet counts).

Place in Therapy

Darzalex provides a drug therapy option for heavily pre-treated patients with multiple myeloma who are refractory to or have relapsed after many prior therapies and for whom there are few to no other treatment options.

Comparative Pricing

Drug	Estimated Cost per Cycle	Estimated Annual Cost
Darzalex™	$7,200	$158,000 (first year)
Pomalyst®	$11,000	$144,000

Impact/Plan Management Suggestions

High impact. High cost with the need for treatment induction accelerating the cost at the front-end; however, this drug fills an unmet medical need for patients with no other potential therapy options.

Empliciti™ (elotuzumab)			
Dosage Form	**DIN & Strength**	**Manufacturer**	**AHFS Class**
Intravenous infusion	02455927 - 300mg/vial 02455919 - 400mg/vial	Bristol-Myers Squibb Canada	10:00.00 – Antineoplastic agents

Indication(s)

Empliciti (elotuzumab), in combination with lenalidomide and dexamethasone, is indicated for the treatment of patients with multiple myeloma who have received one to three prior therapies.

Dose

The recommended dosage of Empliciti is 10 mg/kg administered intravenously every week for the first two cycles and every 2 weeks thereafter when administered with lenalidomide and low dose dexamethasone. Treatment should continue until disease progression or unacceptable toxicity.

Therapeutic Alternatives

Kyprolis (carfilzomib), Velcade (bortezomib)

Clinical Notes

Elotuzumab is an immunostimulatory humanized, IgG1 monoclonal antibody that specifically targets the SLAMF7 (Signaling Lymphocytic Activation Molecule Family member 7) protein. SLAMF7 is expressed on myeloma cells and on Natural Killer (NK) cells, but not on normal tissues, which enables selective killing of myeloma cells. Elotuzumab directly activates NK cells through both the SLAMF7 pathway and Fc receptors. Elotuzumab also targets SLAMF7 on myeloma cells and facilitates the interaction with NK cells to mediate the killing of myeloma cells through antibody-dependent cellular cytotoxicity (ADCC). The combination of lenalidomide and elotuzumab results in enhanced NK activity as well as increased anti-tumor activity.

In an open-label phase 3 study (ELOQUENT-2) on relapsed or refractory multiple myeloma patients who had received one to three prior therapies, 321 patients were randomly assigned to receive elotuzumab plus lenalidomide and dexamethasone, while 325 patients were assigned to the control group (lenalidomide and dexamethasone). Treatment would continue until disease progression or unacceptable toxicity. Coprimary end points were progression-free survival (PFS) and overall response rate. Median follow-up was of 24.5 months. At 1 year, PFS was 68% for the elotuzumab group vs 57% for the control group, while it was 41% and 27% at 2 years, respectively. Median PFS in the elotuzumab group was 19.4 months vs 14.9 months for the control group (HR 0.70; 95% CI 0.57-0.85, $p<0.001$). The overall response rate (partial response or better) in the elotuzumab group was 79%, versus 66% in the control group ($p<0.001$). Patients in the elotuzumab group experienced serious side effects slightly more frequently with rates of grade 3 or 4 lymphocytopenia (77% vs 49%) and infections (81% vs 74%) slightly higher compared to placebo. The median duration of treatment was longer in the elotuzumab group (17 months vs 12 months).

Place in Therapy

Empliciti provides a new option of treatment for patients with multiple myeloma who have failed or not tolerated other lines of therapy.

Comparative Pricing

Drug	Estimated annual cost
Empliciti™	Price not available
Velcade®	$23,000-$100,000*
Kyprolis™	$84,000

*Treatment cost. Based on body surface area of 1.79m^2, cost range dependent upon transplant eligibility

Impact/Plan Management Suggestions

Insufficient information.

Epclusa™ (sofosbuvir/velpatasvir)			
Dosage Form	**DIN & Strength**	**Manufacturer**	**AHFS Class**
Tablet	02456370 – 400mg-100mg	Gilead Sciences Canada Inc.	08:18.40 – HCV Antivirals

Indication(s)

Epclusa (sofosbuvir/velpatasvir) is indicated:

- for the treatment of chronic hepatitis C virus (HCV) infection in adults without cirrhosis or with compensated cirrhosis
- in combination with ribavirin for the treatment of chronic hepatitis C virus (HCV) infection in adults with decompensated cirrhosis.

Dose

The recommended dose of Epclusa is one tablet of 400 mg/100 mg sofosbuvir/velpatasvir, taken orally, once daily with or without food (see Table 2).

Table 2. Recommended Treatment Regimen (All HCV Genotypes)

Patient Population	Recommended Dose and Duration of Treatment
Patients without cirrhosis, Patients with compensated cirrhosis	Epclusa one tablet daily for 12 weeks
Patients with decompensated cirrhosis	Epclusa one tablet daily + ribavirin* for 12 weeks

*When administered with Epclusa, the recommended dose of ribavirin is based on weight: 1000 mg per day for patients less than 75 kg and 1200 mg for those weighing at least 75 kg, divided and administered twice daily with food.

Therapeutic Alternatives

These vary by genotype (including subtype), treatment experience and level of liver fibrosis – consult relevant guidelines (e.g., CASL, AASLD/IDSA) for potential alternatives.

Clinical Notes

Epclusa is a fixed-dose combination tablet containing sofosbuvir and velpatasvir for oral administration. Sofosbuvir is a nucleotide analog HCV NS5B polymerase RNA-dependent RNA inhibitor. It is pan-genotypic with high potency and a high barrier to resistance. Velpatasvir is an NS5A protein inhibitor. It is pan-genotypic with a very high level of potency but a low barrier to resistance. Each tablet contains 400 mg sofosbuvir and 100 mg velpatasvir.

Thus, Epclusa is a pan-genotypic direct-acting antiviral (DAA) for the treatment of chronic HCV infection that can be used in all genotypes from 1 through 6, with a simple 12-week treatment duration, requiring the addition of ribavirin only for individuals with decompensated cirrhosis.

Place in Therapy

Epclusa is the first available truly pan-genotypic direct-acting antiviral drug combination for the treatment of chronic hepatitis C virus infection of all six genotypes. It has a relatively simple dosing regimen which is the same regardless of cirrhosis (compensated) status or treatment experience. It can also be used, along with weight-based dosing of ribavirin, for individuals with decompensated cirrhosis, particularly those with genotype 5 or 6 disease. Epclusa is also a theoretically preferred therapy for those rare individuals with mixed genotype infections.

Comparative Pricing

Drug	Patient Population	Estimated Treatment Cost
Epclusa™	Non-Cirrhotic or Compensated Cirrhosis	$63,300
	Decompensated Cirrhosis	$66,500-$67,100*

* includes weight-based ribavirin

Impact/Plan Management Suggestions

Intermediate impact – Epclusa fills potential gaps in therapy where few other options existed.

Ninlaro™ (ixazomib citrate)			
Dosage Form	**DIN & Strength**	**Manufacturer**	**AHFS Class**
Capsule	02456796 – 2.3mg 02456818 – 3mg 02456826 – 4mg	Takeda Canada Inc.	10:00.00 - Antineoplastics agents

Indication(s)

Ninlaro [ixazomib (as ixazomib citrate)] in combination with lenalidomide and dexamethasone is indicated for the treatment of adult patients with multiple myeloma who have received at least one prior therapy.

Dose

Recommended starting dose is 4 mg taken orally on Days 1, 8, and 15 of a 28-day cycle.

The recommended starting dose of lenalidomide is 25 mg administered daily on Days 1 through 21 of a 28-day treatment cycle.

The recommended starting dose of dexamethasone is 40 mg administered on Days 1, 8, 15, and 22 of a 28-day treatment cycle.

Dose reductions to 3mg and 2.3mg may be made due to adverse effects and/or renal/hepatic impairment.

Therapeutic Alternatives

Velcade (bortezomib), Kyprolis (carfilzomib)

Clinical Notes

Ixazomib is a reversible proteasome inhibitor. Ixazomib preferentially binds and inhibits the chymotrypsin-like activity of the beta 5 subunit of the 20S proteasome, leading to activation of signaling cascades, cell-cycle arrest, and apoptosis (cell death).

The benefit of ixazomib was demonstrated in a randomized, double-blind placebo controlled trial in patients with relapsed multiple myeloma who received 1 to 3 prior lines of therapy. A total of 722 patients were randomized to receive the combination of ixazomib, lenalidomide and dexamethasone or the combination of placebo, lenalidomide and dexamethasone. Progression free survival was 14.7 months (95% CI 12.9, 17.6) in the placebo arm to 20.6 months (95% CI; 17.0, NE) in the ixazomib arm. The stratified hazard ratio was 0.74 (95% CI 0.59, 0.94) with statistically significant p-value of 0.013. The primary efficacy benefit demonstrated was an improvement in progression free survival on average of 4 to 6 months when ixazomib is added to lenalidomide and dexamethasone.

Place in Therapy

Ninlaro is an oral alternative to Velcade and Kyprolis for the treatment of multiple myeloma in patients who have received at least one prior therapy.

Comparative Pricing

Drug	Estimated Annual Cost
Ninlaro™	Price not available
Velcade®	$23,000 - $100,000*
Kyprolis™	$84,000

*Treatment cost. Based on body surface area of 1.79m^2, cost range dependent upon transplant eligibility

Impact/Plan Management Suggestions

High impact.

Rupatadine (rupatadine)			
Dosage Form	**DIN & Strength**	**Manufacturer**	**AHFS Class**
Tablet Oral solution	02456451 – 10mg 02456478 – 1mg/ml	Pediapharm Inc.	04:00:00 – Anti-Histamines

Indication(s)

Rupatadine is indicated:

- for the symptomatic relief of nasal and non-nasal symptoms of seasonal allergic rhinitis (SAR) and perennial allergic rhinitis (PAR) in patients 2 years of age and older.
- for the relief of the symptoms associated with chronic spontaneous urticaria (CSU), e.g. pruritus and hives, in patients 2 years of age and older.

Dose

Tablet: The maximum recommended 10 mg daily.

Oral Solution (Children 2-11 years of age) based on Body Weight:

10 to 25 kg - 2.5 mL (2.5 mg) once daily with or without food.

>25 kg - 5 mL (5 mg) once daily with or without food.

Therapeutic Alternatives

Reactine (cetirizine), Aerius (desloratadine), Claritin (loratadine); Blexten (bilastine)

Clinical Notes

Rupatadine is a second-generation antihistamine, non-sedating long-acting histamine antagonist with selective peripheral H1-receptor and platelet activating factor (PAF) antagonistic activities. Some of the metabolites (desloratadine and its hydroxylated metabolites) retain an antihistaminic activity and may partially contribute to the overall efficacy of the drug, maintaining activity for up to 24 hours.

Place in Therapy

Rupatadine is an alternative for patients who require a non-sedating antihistamine to treat seasonal allergic rhinitis and/or chronic spontaneous urticarial and are no longer responding to other therapies such as cetirizine, desloratadine or loratadine.

Comparative Pricing

Drug	Estimated Daily Cost
Rupatadine	Price not available
desloratadine 5mg	$0.55
loratadine 10mg	$0.40
cetirizine 20mg	$0.75

Impact/Plan Management Suggestions

Insufficient information.

Tagrisso™ (osimertinib mesylate)			
Dosage Form	**DIN & Strength**	**Manufacturer**	**AHFS Class**
Tablet	02456214 – 40mg 02456222 – 80mg	AstraZeneca Canada Inc.	10:00.00 – Antineoplastic Agents

Indication(s)

Tagrisso (osimertinib) is indicated for the treatment of patients with locally advanced or metastatic epidermal growth factor receptor (EGFR) T790M mutation-positive non-small cell lung cancer (NSCLC) who have progressed on or after EGFR tyrosine kinase inhibitor (TKI) therapy. [NOC/c - Marketing authorization with conditions]

A validated test is required to identify EGFR T790M mutation-positive status prior to treatment.

Dose

The recommended dose of Tagrisso (osimertinib) is 80 mg tablet taken orally once a day until disease progression or unacceptable toxicity.

Therapeutic Alternatives

Tarceva (erlotinib); Giotrif (afatinib); Iressa (gefitinib) – although Tagrisso would be used after failure of these TKIs.

Clinical Notes

Lung cancer is an aggressive, heterogeneous, and life-threatening disease. It has been one of the most common cancers in the world for several decades (1.8 million new cases in 2012, 12.9% of all new cancers worldwide. In 2015, an estimated 26,600 Canadians would be diagnosed with lung cancer and 20,900 would die of it. Lung cancer remains the most frequent cancer in Canada and the leading cause of cancer death for both men and women. It is also the most common cause of death from cancer worldwide, estimated to be responsible for nearly 1 in 5 cancer deaths (1.59 million deaths; 19.4% of all deaths from cancer) in 2012. NSCLC represents approximately 80 to 90% of all lung cancers. For the minority of patients with NSCLC who have resectable disease, surgery offers the best chance of cure. Despite progress in early detection and treatment, NSCLC is most often diagnosed at an advanced stage and has a poor prognosis. Once NSCLC has progressed to a locally advanced or metastatic stage there is no cure and treatment is therefore focused on extending life, delaying disease progression, and improving symptoms and quality of life.

Progress in molecular biology has changed the therapeutic approach to NSCLC, and the treatment of advanced NSCLC can now be guided by the presence of certain mutations, e.g., epidermal growth factor receptor (EGFR), or anaplastic lymphoma kinase (ALK).

Since the discovery of the common somatic mutations in the kinase domain of EGFR in 2004, NSCLC patients with activating EGFR mutations in exons 18-21 of EGFR (including L858R and exon 19 deletions [Ex19del], collectively described as EGFRm) are considered a subset of NSCLC in terms of pathogenesis, prognosis and treatment.

First- or second-generation EGFR TKIs (gefitinib, erlotinib, afatinib) would generally be considered first choice treatment for patients with activating mutations in EGFR. Despite achieving very good initial response rates (ORRs of approximately 60-70%) and durable benefit, these patients will eventually develop treatment resistant disease after 9-14 months.

The most common cause of acquired resistance (50-60%) is the EGFR T790M point mutation. Osimertinib is a TKI and an irreversible inhibitor of EGFRs harbouring sensitising-mutations (EGFRm) and TKI-resistance mutation T790M.

The efficacy of osimertinib was demonstrated in two single arm trials: AURA extension [n=201] and AURA2 [n=210]. These trials demonstrated an ORR of 57.2% (95% CI: 50.1%, 64.2%) and 61.0% (95% CI: 54.0%, 67.6%), respectively, in patients with metastatic EGFR/T790M positive NSCLC. The majority of patients had ongoing responses at the time of primary analysis of AURA extension and AURA2 and the median DOR had not been reached. Supportive evidence from the phase 1 portion of AURA (AURA phase 1) demonstrated ORR of 50.8% (95% CI: 37.9%, 63.6%) and DOR of 12.4 months (8.3, NC) in 63 patients with metastatic EGFR T790M positive NSCLC. All patients had received previous treatment with an EGFR TKI.

Place in Therapy

Tagrisso provides an option for patients with EGFR mutations who have developed resistance to TKI treatments due to a common resistance mutation the T790M mutation. Tagrisso has been shown to provide significant benefits in mid-stage trials in patients for whom the only other alternative was chemotherapy causing this drug to be given conditional approval pending the results from a confirmatory Phase 3 trial.

Comparative Pricing

Drug	Estimated monthly cost
Tagrisso™	$9,300
erlotinib	$2,100
Giotrif®	$2,300
Iressa®	$2,300

Impact/Plan Management Suggestions

High Impact – Low utilization but high cost.

FIRST TIME GENERICS

First Time Generic Drugs (Notices of Compliance (NOCs) from June 08, 2016 to August 30, 2016)

Generic Name	Reference Drug (Brand)	Rank by ingredient cost in 2015	Manufacturer	Route of Administration	Approved Indications/ Comments
gatifloxacin	Zymar	588	Apotex Inc.	Ophthalmic	Bacterial conjunctivitis caused by susceptible strains of bacteria.
zidovudine	Retrovir O/L	1204	Aurobindo Pharma Ltd. (Unit III)	Oral	Treatment of HIV infection in combination with other antiretrovirals in individuals with difficulties swallowing solid dosage forms.
tadalafil	Cialis	62	Apotex Inc.	Oral	Erectile dysfunction; benign prostatic hyperplasia
miglustat	Zavesca	—	Sandoz Canada Inc.	Oral	Mild-moderate Type 1 Gaucher disease; Niemann-Pick Type C disease.
temsirolimus	Torisel	—	Genmed, A Division of Pfizer Canada Inc.	Intravenous	Metastatic Renal Cell Carcinoma (mRCC)
darifenacin	Enablex	629	Apotex Inc.	Oral	Overactive bladder.

Health Newsflash

A Quarterly Publication

New Drugs and Pipeline News Reviewed at the July to September 2016 DEC Meetings

NEW DRUGS AND PRODUCT LINE EXTENSIONS

New Drugs and Product Line Extensions (Notices of Compliance (NOCs) from June 08, 2016 to August 30, 2016)

Band name	Chemical name	Manufacturer	Dosage form	Type of Line Extension	Specifics/Comments
Simponi	golimumab	Janssen Inc.	Subcutaneous injection	New indication	Treatment of adults with severe active non-radiographic axial spondyloarthritis (nr-Ax SpA).
Inflectra	infliximab	Celltrion Healthcare Co Ltd	Intravenous injection	New indication	Adults with moderately to severely active Crohn's disease.
Dysport	abobotulinum-toxinA	Ipsen BioPharm Limited	Intramuscular injection	New indications	Cervical dystonia (spasmodic torticollis); upper limb focal spasticity
Harvoni	sofosbuvir-ledipasvir	Gilead Sciences Canada, Inc.	Tablet	New indications	Treatment of individuals with chronic hepatitis C virus genotype 1 infection including liver transplant patients without cirrhosis or with compensated or decompensated cirrhosis; decompensated cirrhosis irrespective of transplantation status; individuals with HIV-1 co-infection
Cortiment	budesonide	Ferring Inc.	Delayed and extended release tablet	New brand	Induction of remission in patents with active mild to moderate ulcerative colitis.
Brilinta	ticagrelor	AstraZeneca Canada Inc.	Tablet	New strength, New indication	For secondary prevention of atherothrombotic events in patients with a history of myocardial infarction at least one year ago and a high risk of developing an atherothrombotic event. The new 60mg tablet supports this new indication with the dose being 60mg twice daily with concurrent low-dose ASA therapy.
Apo-Zidovudine-Lamivudine-Nevirapine	zidovudine-lamivudine-nevirapine	Apotex Incorporated	Tablet	New drug combination	New fixed-dose combination of triple therapy of two nucleoside reverse transciptase inhibitors (NRTI), lamivudine and zidovudine, with a non-nucleoside reverse transcriptase inhibitor (NNRTI), nevirapine.
SmofKabiven Peripheral	amino acids with electrolytes, dextrose, lipid	Fresenius Kabi Canada Ltd.	Intravenous injection	New drug combination, new brand	Total parenteral nutrition
Rixubis	nonacog gamma	Baxalta Canada Corporation	Intravenous injection	New indication	Expansion of indication for Hemophilia B to include children.

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EXPRESS SCRIPTS®

NEW DRUGS AND PRODUCT LINE EXTENSIONS (continued)

New Drugs and Product Line Extensions (Notices of Compliance (NOCs) from June 08, 2016 to August 30, 2016)

Band name	Chemical name	Manufacturer	Dosage form	Type of Line Extension	Specifics/Comments
Monoprost	latanoprost	Thea Laboratories	Ophthalmic solution	New brand	Preservative-free version of latanoprost available in unit dose packaging.
Jardiance	empagliflozin	Boehringer Ingelheim (Canada) Ltd.	Tablet	New indication	To reduce the incidence of cardiovascular death in patients with type 2 diabetes and established cardiovascular disease.
Synjardy	empagliflozin-metfomin	Boehringer Ingelheim (Canada) Ltd.	Tablet	New drug combination	Fixed-dose combination of empaglifozin (Jardiance) with metformin. Available in the following strengths: 5/500mg; 5/850mg; 5/1,000mg; 12.5/500mg; 12.5/850mg; 12.5/1,000mg.
Selexid	pivmecillinam	Leo Pharma Inc.	Tablet	New strength	Treatment of acute uncomplicated cystitis and chronic/recurrent bacteriuria caused by susceptible gram-negative organisms.
Keytruda	pembrolizumab	Merck Canada Inc.	Intravenous injection	New strength	New 100mg/4ml intravenous solution as opposed to the currently available 50mg powder for reconstitution for intravenous use provides added convenience and reduces risk of dosing and reconstitution errors.
Remsima	infliximab	Celltrion Healthcare Co. Ltd.	Intravenous Injection	New indication	New indications for Crohn's disease and ulcerative colitis which follow those added to the other Remicade SEB Inflectra. Remsima is currently not marketed in Canada.
Afinitor	everolimus	Novartis Pharmaceuticals Canada Inc.	Tablet	New indication	For treatment of neuroendocrine tumours (NET) of gastrointestinal or lung origin. Added to existing indications: hormone receptor-positive, HER-2-negative breast cancer; pancreatic neuroendocrine tumours (PNET); renal cell carcinoma; subependymal giant cell astrocytoma (SEGA) associated with tuberous sclerosis complex (TSC); renal angiomyolipoma associated with TSC.
Coversyl Plus	perindopril-indapamide	Servier Canada Inc.	Tablet	New strength	New strength: 8mg perindopril + 1.25mg indapamide for treatment of mild to moderate essential hypertension. Added to existing available strengths of 2/0.625mg, 4/1.25mg, 8/2.5mg.

NEW DRUGS AND PRODUCT LINE EXTENSIONS (continued)

New Drugs and Product Line Extensions (Notices of Compliance (NOCs) from June 08, 2016 to August 30, 2016)

Band name	Chemical name	Manufacturer	Dosage form	Type of Line Extension	Specifics/Comments
Copaxone	glatiramer acetate	Teva Canada Limited	Subcutaneous injection	New strength	New strength of 40mg/ml which can be administered three times per week compared with once daily for the 20mg/ml strength. N.B. 20mg/ml and 40mg/ml are not interchangeable.
Alprolix	coagulation factor IX (recombinant), Fc fusion protein	Biogen Canada Inc.	Intravenous injection	New indication	Expansion of indication to include use for perioperative management (surgical prophylaxis) for hemophilia B (congenital factor IX deficiency or Christmas disease).
Invega Trinza	paliperidone palmitate	Janssen Inc.	Intramuscular injection	New formulation, New strength	New formulation is a 3-month depot antipsychotic injection (the only 3-month depot available).
Galexos	simeprevir	Janssen Inc.	Capsule	New indication	For use in patient with genotype 4 chronic hepatitis C virus infection in combination with peginterferon alfa (PegiFN) and ribavirin (RBV) in adults with compensated cirrhosis. Treatment requires 12-weeks of triple therapy followed by dual therapy with PegIFN+RBV for 12-36 weeks for a total treatment duration of 24-48 weeks.
Brenzys	etanercept	Samsung Bioepis, distributed by Merck Canada Inc.	Subcutaneous injection	Subsequent Entry Biologic (SEB) for Enbrel	First SEB available for the reference biologic Enbrel. Indicated for two of the five indications of Enbrel: Rheumatoid Arthritis (RA) and Ankylosing Spondylitis (AS). Not yet indicated for polyarticular juvenile idiopathic arthritis (JIA), psoriatic arthritis (PsA), or plaque psoriasis.

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