Health Newsflash

A Quarterly Publication

New Drugs and Pipeline News Reviewed at the October to December 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

Anthrasil™ (anthrax immune globulin)			
Dosage Form	**DIN & Strength**	**Manufacturer**	**AHFS Class**
Intravenous injection	02469588 – 60 Unit/vial	Emergent BioSolutions Canada Inc.	80:04.00– Antitoxins and Immune Globulins

Indication(s)

Anthrasil [Anthrax Immune Globulin Intravenous (Human)] is indicated for the treatment of adult and pediatric patients with toxemia associated with inhalational anthrax. Anthrasil is beneficial in combination with appropriate antibacterial drugs. [Health Canada has authorized sale of Anthrasil as an Extraordinary Use New Drug (EUND) for exposure to inhalational anthrax based on limited clinical testing in humans.]

Dose

The initial dose of Anthrasil in combination with appropriate antimicrobial therapy is 420 units (seven vials). An initial dose of 840 units (14 vials) may be considered, depending on the clinical status of the patient The dose for pediatric patients is based on body weight.

Therapeutic Alternatives

None

Clinical Notes

Anthrasil is a clear to opalescent sterile liquid of purified immune globulin G (IgG) fraction of human plasma containing polyclonal antibodies that bind the protective antigen (PA) component of Bacillus anthracis lethal and edema toxins. Anthrasil is prepared using plasma collected from healthy, screened donors who were immunized with BioThrax® (Anthrax Vaccine Adsorbed) to achieve high titers of anti-anthrax antibody (meeting minimum potency specifications) and purified by an anion-exchange column chromatography method.

Anthrasil acts against anthrax toxin and is not known to have direct antibacterial activity, so it is to be administered in combination with appropriate antimicrobial therapy.

Because it is not ethical or feasible to conduct placebo-controlled clinical trials in humans with inhalational anthrax, the effectiveness of Anthrasil is based on efficacy studies demonstrating a survival benefit in animal models of inhalational anthrax infection.

Nineteen adult patients have been treated with Anthrasil under expanded access use, including three patients with inhalational anthrax, one patient with gastrointestinal anthrax and 15 patients with injectional anthrax due to injection of anthrax-contaminated heroin. Patients were receiving antimicrobial therapy before, during and after Anthrasil administration.

In patients with inhalational anthrax, two out of three patients treated with Anthrasil plus antimicrobial therapy survived and one died from progression of anthrax disease, systemic candidiasis and multiorgan failure. Among the 15 patients with injectional anthrax treated with Anthrasil plus antibiotics, 10 survived and five died (two from progression of anthrax disease; the cause of death was not determined or available for three patients). The single patient with gastrointestinal anthrax treated with Anthrasil survived. Therapy for these systemic anthrax cases included aggressive supportive measures including mechanical ventilation and pulmonary/abdominal fluid drainage.

Inhalational anthrax is triggered when B. anthracis spores are inhaled and deposited in the lung.

Treatment of patients suspected of having systemic anthrax should be started urgently and should include intravenous (IV) antimicrobial combination therapy, an antitoxin such as anthrax immunoglobulin (Anthrasil), drainage of pleural effusions, supportive care, and consideration of adjunctive glucocorticoids. When selecting an antimicrobial regimen, the production of toxin, the potential for antimicrobial drug resistance, the frequent occurrence of meningitis, and the presence of latent spores must be taken into account.

Place in Therapy

Anthrasil is to be used adjunctively with antibiotic treatment for systemic anthrax infections.

Pricing

N/A

Impact

No impact – distribution is expected to be managed through government emergency drug stockpiles.

Dupixent™ (dupilumab)			
Dosage Form	**DIN & Strength**	**Manufacturer**	**AHFS Class**
Subcutaneous injection	02470365 – 150mg/ml (300mg/2ml PFS)	Sanofi-aventis Canada Inc.	84:92.00 – Miscellaneous Skin and Mucous Membrane Agents

Indication(s)

Dupixent™ (dupilumab) is indicated for the treatment of adult patients with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable.

Dupixent can be used with or without topical corticosteroids.

Dose

The recommended dose of Dupixent for adult patients is an initial dose of 600 mg (two 300 mg injections), followed by 300 mg given every other week.

Therapeutic Alternatives

No other drugs are officially indicated for the treatment of moderate-to-severe atopic dermatitis. The following drugs have been used off-label in this patient population:

Neoral (cyclosporine, off-label)*, methotrexate (off-label)*, Imuran (azathioprine, off-label)*

*generics available

Clinical Notes

Dupixent is a recombinant human IgG4 monoclonal antibody that inhibits interleukin-4 (IL-4) and interleukin-13 (IL-13) signaling by specifically binding to the IL-4Rα subunit shared by the IL-4 and IL-13 receptor complexes.

The efficacy of Dupixent was established in three Phase III, randomized, double-blind, placebo-controlled, multicenter, pivotal studies in adults with moderate to severe AD inadequately controlled by topical therapies. In each study, the primary efficacy endpoint was a score of 0 (clear) or 1 (almost clear) on the Investigator's Global Assessment (IGA) and a reduction of ≥ 2 points from baseline to Week 16; one study also assessed this endpoint at Week 52. SOLO 1 and SOLO 2 evaluated Dupixent as monotherapy; CHRONOS evaluated Dupixent in combination with topical corticosteroid therapy. In all three trials the primary endpoint was achieved in significantly larger proportions of patients receiving Dupixent than the comparator.

Place in Therapy

Dupixent has been shown to reduce the extent and severity of atopic dermatitis in patients with moderate to severe disease, for whom available therapies are limited.

Pricing

Drug	Estimated Annual Cost
Dupixient	$31,200

Impact

High Impact – high cost treatment that fills a current gap in care.

Galafold™ (migalastat)			
Dosage Form	**DIN & Strength**	**Manufacturer**	**AHFS Class**
Capsules	02468042 – 123mg/cap	Amicus Therapeutics UK Ltd.	92:92.00 – Other Misc. Ther. Agents

Indication(s)

Galafold (migalastat) is indicated for long-term treatment of adults with a confirmed diagnosis of Fabry disease and who have a confirmed α-Gal A amenable mutation.

Dose

The recommended dose of Galafold is 123 mg (1 capsule) once every other day at the same time of day.

Therapeutic Alternatives

Replagal (agalsidase alfa); Fabrazyme (agalsidase beta)

Clinical Notes

Fabry disease is a rare, inherited, genetic condition due to a deficiency of an enzyme called alpha-galactosidase A. As a result, the major glycosphingolipid substrates, globotriaosylceramide (Gb3) and globotriaosylsphingosine (LysoGb3) accumulate in plasma, urine and tissue lysosomes. Without sufficient levels of the enzyme alpha-galactosidase A, persons with Fabry Disease develop severe neuropathic pain, kidney disease, heart disease, stroke and/or premature death; often before the age of 60 years. Fabry Disease is estimated to affect approximately one out of every 40,000 males and up to twice as many females in Canada. Currently there are approximately 469 people living in Canada, with the largest number living in Nova Scotia. Treating symptoms was all that was available for people with Fabry Disease until 2001, when enzyme replacement therapy (ERT) was developed as a treatment for this rare condition. ERT provides the deficient enzyme and may be beneficial in Fabry Disease.

The genotype of α-Gal A determines the nature and extent of the clinical response to Galafold in Fabry disease patients. For amenable genotypes, the extent of the migalastat-induced accumulation of the α-Gal A protein can vary significantly and therefore, response to Galafold can differ according to the specific amenable mutation. For non-amenable genotypes, Galafold may result in a net loss of α-Gal A activity, and potentially worsening the disease condition.

The clinical efficacy and safety of Galafold have been evaluated in two completed Phase 3 pivotal trials and an ongoing open-label extension trial. The Phase 3 clinical studies were conducted in patients with Fabry disease having 43 (approximately 16%) of the amenable mutations listed in the product monograph. All patients received the recommended dosage of 123 mg Galafold every other day.

The first Phase 3 trial (ERT-experienced trial) was an 18-month randomized open-label active comparator trial that evaluated the efficacy and safety of Galafold compared to ERT (Replagal, agalsidase beta, or Fabrazyme, agalsidase alfa) in male and female patients with Fabry disease who were receiving ERT prior to trial entry and who had amenable mutations. At baseline, 53% of patients had neurologic disorders, 72% had cardiac disorders, and 75% of patients had renal disorders. Patients were randomized in a ratio of 1.5:1 to switch to Galafold or continue with ERT. After 18 months of treatment, patients in the ERT treatment arm switched to Galafold and patients in the Galafold treatment arm continued on the same treatment for a 12-month extension period.

The second Phase 3 trial (ERT-naïve trial) was a 6-month randomized double-blind placebo-controlled trial (through month 6) with an 18-month open-label period that evaluated the efficacy and safety of Galafold in male and female patients with Fabry disease who were naïve to ERT or had previously been on ERT and had stopped for at least 6 months prior to trial entry and who have amenable mutations. Patients were randomized in a ratio of 1:1 to receive either Galafold or placebo for 6 months (Stage 1), followed by Stage 2 in which patients in the Galafold arm continued to receive Galafold and patients in the placebo arm switched to Galafold for 6 months, followed by an open-label extension phase in which all patients from Stage 2 continued to receive Galafold treatment for 12 months.

In the ERT-experienced trial, renal function remained stable for up to 18 months of treatment with Galafold. In the ERT-naïve trial, no clinically significant differences in renal function were observed during the initial 6-month placebo-controlled period. In the open-label period, renal function remained stable over 18-24 months of Galafold treatment. There was also a statistically significant reduction in plasma lyso-Gb3 concentrations and kidney interstitial capillary GL-3 inclusions in patients with amenable mutations. In the ERT-experienced trial, plasma lyso-Gb3 levels remained low and stable for up to 18 months in patients with amenable mutations switched from ERT to Galafold, and in patients remaining on ERT.

Place in Therapy

This medication, if proven clinically beneficial, brings an alternative to ERT for patients with Fabry disease, it also serves as a more convenient oral therapy that potentially provides better patient adherence as well as less down time (infusion time) compared to the only other alternative for Fabry's disease. The place in therapy for Galafold will evolve over time.

Comparative Pricing

Drug	Estimated Annual Cost
Galafold	$310,250
Replagal	$252,350
Fabrazyme	$275,430

Impact

High impact – high-cost treatment with potential cost-shift from lower cost (but similarly high-cost) alternatives.

Prevymis™ (letermovir)			
Dosage Form	**DIN & Strength**	**Manufacturer**	**AHFS Class**
Tablet; Injection	02469375 – 240mg/tab 02469383 – 480mg/tab 02469367 – 240mg/vial 02469405 – 480mg/vial	Merck Canada Inc.	08:18.92 – Miscellaneous Antivirals

Indication(s)

Prevymis is indicated for the prophylaxis of cytomegalovirus (CMV) infection in adult CMV-seropositive recipients [R+] of an allogeneic hematopoietic stem cell transplant (HSCT).

Dose

The recommended dose is 480mg daily taken with or without food.

Pervymis should be started as early as day 0 (on the day of transplant) but no later than Day 28 post-transplant, and continued through Day 100 post-transplant.

Therapeutic Alternatives

Valcyte (ganciclovir),
Teva-Valganciclovir (valganciclovir)

Clinical Notes

Cytomegalovirus (CMV) is the leading source of illness and death in patients who have undergone allogeneic hematopoietic stem cell transplant (HSCT) as infection involves multiple organs leading to serious conditions like pneumonia, gastroenteritis, retinitis, often half of the patients undergoing HSCT transplants will develop clinically significant infections in the first 100 days post-transplant.

It is more common now to follow a prophylactic therapy strategy among those patients.

CMV is a member of the herpes virus family. This virus has a tendency to cause prolonged latent infections to several types of body cells like epithelial cells, hematopoetic cells and connective tissues. It has a wide spectrum of clinical presentation. While it generally presents as an asymptomatic infection, it can lead to serious disorders, particularly among high-risk populations with compromised immune systems such as those undergoing HSCT.

Prevymis has a different mechanism of action where it targets the viral terminase complex, a uniquely viral function, making target-related toxicities unlikely reducing the risk of adverse events.

The efficacy of Prevymis was evaluated through a randomized, double-blind placebo-controlled multi-site study that involved 565 patients (18-78 years) receiving HCSTrandomized at a ratio of 2:1 to receive either Prevymis or placebo. The most common reason for HCST was acute myeloid leukemia, and 12% of all subjects were positive for CMV DNA at baseline. The primary efficacy endpoint was the incidence of clinically significant CMV infections through week 24 post-transplant and this is defined as the occurrence of either CMV end organ disease or initiation of anti CMV therapy. Preyvmis has shown a superior efficacy compared to placebo with a difference of -23.5%.

Place in Therapy

This is a very selective antiviral agent offering a better safety profile over currently available treatments that are restricted by clinically significant toxicity (nephrotoxicity) and drug resistance. It also offers a once daily dosing regimen (orally or IV) with a good tolerability.

Comparative Pricing

Drug	Estimated cost per treatment
Prevymis	$18,100 - $25,100
Valcyte	$5,100
Teva-Valganciclovir	$1,200

Impact

High impact – new treatment with significantly higher cost than alternatives but potentially improved safety.

Shingrix™ (herpes zoster vaccine)			
Dosage Form	**DIN & Strength**	**Manufacturer**	**AHFS Class**
Intramuscular injection	02468425 – 50mcg/ 0.5ml	GlaxoSmithKline Inc.	80:12.00 – Vaccines

Indication(s)

Shingrix is indicated for prevention of herpes zoster (HZ, or shingles) in adults 50 years of age or older.

Dose

The primary vaccination schedule consists of two doses of 0.5 mL each; an initial dose at Month 0 followed by a second dose administered anytime between 2 and 6 months later. Administration of the second dose of Shingrix is important to ensure maximum vaccine efficacy and duration of protection against HZ disease.

The need for booster doses following the primary vaccination schedule has not been established.

Therapeutic Alternatives

Zostavax II (zoster vaccine)

Clinical Notes

Shingrix is a non-live subunit vaccine consisting of recombinant varicella zoster virus glycoprotein E (VZV gE) which is reconstituted at the time of use with an adjuvant suspension of AS01B.

Primary VZV infection results in varicella (chickenpox), after which VZV becomes latent in neurons of dorsal root and cranial nerve ganglia. HZ (or shingles) results from the reactivation of latent VZV in sensory ganglia.

Any person who has had varicella is at risk of developing HZ. Nearly all adult Canadians (≥90%) have had chickenpox and are therefore at risk for HZ. Age is the most important risk factor for the development of HZ with two-thirds of the cases occurring in those over 50 years of age. The risk and severity of HZ is greatest in the elderly, an age group predicted to grow in coming decades. This age-related risk may be explained by waning immunity over time including the loss of components of VZV-specific cell mediated immunity as a result of natural aging processes. The severity of illness associated with HZ and its complications also increases markedly with age. In Canada, it has been estimated that 30% of the population will develop HZ at some point in their lives. This number increases to almost 50% for those who live to 85 years of age.

HZ can be a severely debilitating disease that typically presents as an acute, painful, vesicular rash distributed along a single dermatome. HZ rash is preceded by prodromal pain in 70% to 80% of the cases, and can last up to a week or longer. The prodromal pain might also be associated with fever, malaise and headache. During the eruptive phase, acute local neurological pain occurs in up to 90% of immunocompetent individuals. The median duration of acute phase pain is 2 weeks and can be very severe, disabling, and interfere with daily activities. The rash typically heals in 2-4 weeks but may leave scars or pigmentation changes. HZ-associated pain can persist (then becoming known as post-herpetic neuralgia, PHN) for weeks, months or even years.

Shingrix was approved based on the results of two pivotal phase 3 trials. The Zoster Efficacy Study in Adults 50 Years of Age or Older (ZOE-50) was a randomized, placebo-controlled, phase 3 study in 18 countries to evaluate the efficacy and safety of Shingrix in older adults (≥50 years of age), stratified according to age group (50 to 59, 60 to 69, and ≥70 years). Participants received two intramuscular doses of the vaccine or placebo 2 months apart. The primary objective was to assess the efficacy of the vaccine, as compared with placebo, in reducing the risk of herpes zoster in older adults. A total of 15,411 participants who could be evaluated received either the vaccine (7,698 participants) or placebo (7,713 participants). During a mean follow-up of 3.2 years, herpes zoster was confirmed in 6 participants in the vaccine group and in 210 participants in the placebo group (incidence rate, 0.3 vs. 9.1 per 1,000 person-years) in the modified vaccinated cohort.

Overall vaccine efficacy against herpes zoster was 97.2% (95% confidence interval [CI], 93.7 to 99.0; P<0.001). Vaccine efficacy was between 96.6% and 97.9% for all age groups. Solicited reports of injection-site and systemic reactions within 7 days after vaccination were more frequent in the vaccine group. There were solicited or unsolicited reports of grade 3 symptoms in 17.0% of vaccine recipients and 3.2% of placebo recipients. The proportions of participants who had serious adverse events or potential immune-mediated diseases or who died were similar in the two groups.

The Zoster Efficacy Study in Adults 70 Years of Age or Older (ZOE-70) was a randomized, placebo-controlled, phase 3 trial conducted in 18 countries and involving adults 70 years of age or older. Participants received two doses of Shingrix or placebo (assigned in a 1:1 ratio) administered intramuscularly 2 months apart. Vaccine efficacy against herpes zoster and postherpetic neuralgia was assessed in participants from ZOE-70 and in participants pooled from ZOE-70 and ZOE-50. In ZOE-70, 13,900 participants who could be evaluated (mean age, 75.6 years) received either Shingrix (6,950 participants) or placebo (6,950 participants). During a mean follow-up period of 3.7 years, herpes zoster occurred in 23 Shingrix recipients and in 223 placebo recipients (0.9 vs. 9.2 per 1,000 person-years). Vaccine efficacy against herpes zoster was 89.8% (95% confidence interval [CI], 84.2 to 93.7; P<0.001) and was similar in participants 70 to 79 years of age (90.0%) and participants 80 years of age or older (89.1%). In pooled analyses of data from participants 70 years of age or older in ZOE-50 and ZOE-70 (16,596 participants), vaccine efficacy against herpes zoster was 91.3% (95% CI, 86.8 to 94.5; P<0.001), and vaccine efficacy against postherpetic neuralgia was 88.8% (95% CI, 68.7 to 97.1; P<0.001). Solicited reports of injection-site and systemic reactions within 7 days after injection were more frequent among Shingrix recipients than among placebo recipients (79.0% vs. 29.5%). Serious adverse events, potential immune-mediated diseases, and deaths occurred with similar frequencies in the two study groups.

Another study demonstrated the effectiveness of use of Shingrix in individuals who have already received the live HZ vaccine (HZL, Zostavax). Immune responses for individuals who had previously received Zostavax (five or more years earlier) were similar to those who had not been previously vaccinated and both demonstrated similarly marked increases in immune response compared to before vaccination.

Place in Therapy

The precise place in therapy for Shingrix remains to be established, particularly in relation to the other available live zoster vaccine, Zostavax. Shingrix was evaluated by the US Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices (ACIP) which recommended the vaccine for the prevention of herpes zoster and related complications for immunocompetent adults 50 and older, for the prevention of herpes zoster and related complications for immunocompetent adults who previously received Zostavax, and preferred over Zostavax for the prevention of herpes zoster and related complications.

Comparative Pricing

Drug	Estimated cost per treatment
Shingrix	$230
Zostavax II	$180

Impact

Intermediate impact – 30% higher cost than alternative but potentially twice as potent.

Tremfya™ (guselkumab)			
Dosage Form	**DIN & Strength**	**Manufacturer**	**AHFS Class**
Subcutaneous Injection	02469758 – 100mg/ml PFS	Janssen Inc.	84:92:00 – Miscellaneous Skin and Mucous Membrane Agents

Indication(s)

Tremfya is indicated for the treatment of adult patients with moderate to severe plaque psoriasis who are candidates for systemic therapy or oral therapy.

Dose

The recommended dose is 100mg given subcutaneously at week 0 and week 4, followed by a maintenance dosing once every 8 weeks thereafter.

Therapeutic Alternatives

Humira, Enbrel, Remicade, Inflectra, Stelara, Cosentyx, Taltz

Clinical Notes

The term psoriasis encompasses a set of chronic inflammatory dermatoses of which plaque psoriasis is the most common form. It is a chronic, relapsing, immune-mediated inflammatory disease characterized by red scaly patches covered with dry, thin scales that are often located on the scalp, trunk, buttocks, and limbs. Approximately 2-3% of the Canadian population is affected by psoriasis, 28% of patients have moderate-to-severe form of the disease.

This condition is also associated with significant comorbidities, including depression, anxiety, obesity and inflammatory bowel disease (IBD).

There is no cure for psoriasis but for patients with moderate-to-severe disease phototherapy, conventional systemic or biologics are prescribed, with the goal of achieving a complete or near complete skin clearance.

Guselkumab is a new targeted therapy and the first anti interleukin-23 agent (IL-23) that possesses high selectivity and affinity to the p19 subunit of the IL-23 where by inhibiting IL-23 it acts in the upstream of the psoriasis pathway reducing the expression of multiple cytokines involved in the pathogenesis of psoriasis. This upstream action results in a longer duration of clinical effect.

The efficacy and safety of Tremfya were determined through three 3 phase multicenter, randomized, double-blind studies (VOYAGE 1, VOYAGE 2 and NAVIGATE) in patients 18 years or older with moderate to severe plaque psoriasis with more than 10% BSA involvement, Investigator's Global Assessment (IGA) ≥ 3 and PASI≥ 12, and were candidates for systemic therapy or phototherapy for psoriasis and no concurrent therapies were allowed. All three studies involved 1,829 patients in total who were randomized to Tremfya or active comparator with adalimumab (VOYAGE) or ustekinumab (NAVIGATE). The endpoints in the trials were the proportion of patients who achieved an IGA score of 0 or minimum of 1 and the proportions of patients who achieved a PASI score of 90 at the end of the study period. Tremfya was superior to adalimumab in the VOYAGE trials. NAVIGATE, which was a switch trial, showed improved response with respect to IGA and PASI 90 in patients who switched from ustekinumab to Tremfya.

Place in Therapy

Tremfya is a targeted IL-23 therapy that has showed a significant efficacy with a longer duration of action and thus fewer injection times compared to currently available therapeutic options.

Comparative Pricing

Drug	Estimated annual cost (maintenance)
Tremfya	$19,890
Humira	$21,120
Stelara	$21,000
Inflectra	$12,600

Impact

Intermediate Impact – cost shift from less cost effective alternatives.

Trumenba™ (meningitis B vaccine)			
Dosage Form	**DIN & Strength**	**Manufacturer**	**AHFS Class**
Intramuscular injection	02468751 – 120mcg	Pfizer Canada Inc.	80:12.00 – Vaccines

Indication(s)

Trumenba is indicated for active immunization to prevent invasive meningococcal disease (IMD) caused by Neisseria meningitidis serogroup B in individuals 10 through 25 years of age.

Dose

Standard schedule for routine immunization: Two doses (0.5 mL each) administered at 0 and 6 months.

Schedule for individuals at increased risk of invasive meningococcal disease: Two doses (0.5 mL each) administered at least 1 month apart, followed by a third dose at least 4 months after the second dose.

Therapeutic Alternatives

Bexsero – difference in approved age range: 2 months - 17 years

Clinical Notes

Trumenba is a bivalent vaccine that consists of two purified Neisseria meningitidis serogroup B recombinant lipoprotein 2086 (rLP2086) antigens, one from each of the two factor H binding protein (fHBP) subfamilies (A and B). fHbp is found on the surface of meningococcal bacteria and is essential for bacteria to avoid host immune defences. Trumenba also contains aluminium phosphate, which is a known adjuvant but in this case functions as formulation stabiliser.

The efficacy of Trumenba has not been evaluated through clinical trials. Vaccine efficacy has been inferred by demonstrating the induction of serum bactericidal antibody responses to four meningococcal group B test strains. The studies assessed the proportions of subjects with a 4-fold or greater increase from baseline in antibody titer for each of the four strains, and the proportion of subjects who achieved a titer greater than or equal to 1:8 (3 strains) or 1:16 (1 strain) for the four strains combined (composite response). Antibodies were produced in sufficient quantities to provide protection against the 4 main test strains in between 80 and 90% of test subjects; 84% of those given the vaccine had protective antibodies against all 4 strains when tested.

Supportive studies were also carried out, which showed that 2 doses of the vaccine achieved a broadly similar antibody response to 3 doses, and that even though protective antibody levels declined over time they could be improved by an additional booster dose after both 2- and 3-dose treatments.

Place in Therapy

Trumenba offers an alternative to Bexsero for meningitis B immunization. At this time there is no evidence supporting the preference of one vaccine over the other; however, these vaccines are not interchangeable and a vaccination series started with one vaccine should be completed with the same product.

Comparative Pricing

Drug	Estimated Cost Per Treatment
Trumenba	$205 - $310
Bexsero	$205 - $410

Impact

High impact. Although SMA is a rare disease, the ultra-high cost of Spinraza can have serious impacts on payers. Intrathecal administration of the drug can be a challenge in the outpatient setting.

FIRST TIME GENERICS

First Time Generic Drugs (Notices of Compliance (NOCs) from August 30, 2017 to November 28, 2017)

Generic Name	Reference Drug (Brand)	Rank by ingredient cost in 2016	Manufacturer	Route of Administration	Approved Indications/ Comments
sevelamer carbonate	Renvela	671	Sanofi-aventis Canada Inc.	Oral	for the control of hyperphosphatemia in patients with end-stage renal disease (ESRD) undergoing dialysis
gefitinib	Iressa	508	Apotex Inc.	Oral	first line treatment of patients with locally advanced (not amenable to curative therapy) or metastatic non-small cell lung cancer
pinaverium	Dicetel	405	Apotex Inc.	Oral	treatment and relief of symptoms associated irritable bowel syndrome (IBS) abdominal pain, bowel disturbances and intestinal discomfort.
cefixime	Suprax	645	Sanofi-aventis Canada Inc.	Oral	treatment of bacterial infections such as: middle ear, upper respiratory tract and lower respiratory tract.
azacitidine	Vidaza	—	Celgene Inc.	Oral	the treatment of adult patients who are not eligible for hematopoetic stem cell transplant with either Intermediate-2 and high risk Myelodysplastic Syndrome or Acute Myeloid Leukemia (AML)
melphalan	Alkeran	1,409	Apotex Inc.	Oral	For the palliative treatment of multiple myeloma; the palliation of nonresectable epithelial carcinoma of the ovary.

Health Newsflash

A Quarterly Publication

New Drugs and Pipeline News Reviewed at the October to December 2017 DEC Meetings

NEW DRUGS AND PRODUCT LINE EXTENSIONS

New Drugs and Product Line Extensions (Notices of Compliance (NOCs) from August 30, 2017 to November 28, 2017)

Brand name	Chemical name	Manufacturer	Dosage form	Type of Line Extension	Specifics/Comments
Actemra SC	tocilizumab	Hoffmann-La Roche Ltd.	Subcutaneous injection	New indication	New indication: Giant cell arteritis Existing indication: Rheumatoid arthritis
Admelog	insulin lispro	Sanofi-aventis Canada Inc.	Subcutaneous injection	New biosimilar – Humalog	First biosimilar insulin for the reference biologic Humalog
Afinitor Disperz	everolimus	Novartis Pharmaceuticals Canada Inc.	Tablet for suspension	New indication	New indication: Adjunctive treatment of seizures associated with Tuberous Sclerosis Complex (TSC) in patients 2 years and older, with a definite diagnosis of TSC not satisfactorily controlled with other therapies. Existing indication: subependymal giant cell astrocytoma (SEGA) associated with TSC.
Akynzeo	netupitant/ palonosetron	Purdue Pharma	Capsule	New drug combination	Fixed-dose combination of drugs currently available as Aloxi and Emend for once-per-cycle treatment of chemotherapy-induced nausea and vomiting
Baca Respiclick	salbutamol	Teva Canada Ltd.	Dry-powder inhaler	New brand	Alternative brand to Ventolin HFA MDI.
Cuvposa	glycopyrrolate	Pediapharm Inc.	Oral solution	New dosage form	Ooral solution used to treat pediatric patients (3-18 years) with chronic severe drooling associated with neurologic disorders such as cerebral palsy.
Entuzity KwikPen	regular human insulin U-500	Eli Lilly Canada Inc.	Subcutaneous injection	New brand, New strength	500 Units per ml strength for individuals with diabetes who have high levels of insulin resistance and require high doses of insulin.
Faslodex	fulvestrant	AstraZeneca Canada Inc.	Intramuscular injection	New indication	New indication: Treatment of postmenopausal women with estrogen receptor-positive, human epidermal growth receptor 2 (HER2)-negative locally advanced or metastatic breast cancer who have not been previously treated with endocrine therapy. Existing indication: Second-line treatment after anti-estrogen therapy.
Haegarda	human C1-esterase inhibitor	CSL Behring Canada Inc.	Subcutaneous injection	New brand, New drug formulation	Subcutaneous form of C1-esterase inhibitor compared to existing intravenous forms, Cinryze, Berinert.

(continued next page)

EXPRESS SCRIPTS®

NEW DRUGS AND PRODUCT LINE EXTENSIONS (continued)

New Drugs and Product Line Extensions (Notices of Compliance (NOCs) from August 30, 2017 to November 28, 2017)

Brand name	Chemical name	Manufacturer	Dosage form	Type of Line Extension	Specifics/Comments
Humalog Junior KwikPen	insulin lispro	Eli Lilly Canada Inc.	Subcutaneous injection	New brand	New version of KwikPen to allow delivery of 0.5 Unit insulin doses.
Imbruvica	ibrutinib	Janssen Inc.	Capsule	New indication	New indication: Steroid dependent or refractory chronic graft versus host disease (cGVHD) Existing indication: Chronic Lymphocytic Leukemia (CLL); Mantle Cell Lymphoma (MCL); Waldenström's Macroglobulinemia (WM)
Keytruda	pembrolizumab	Merck Canada Inc.	Intravenous injection	New indications (2)	New indications: (1) Hodgkin Lymphoma – 2nd line after relapse or failure of autologous stem cell transplant and/or brentuximab vedotin [NOC/c] (2) Urothelial Carcinoma – 2nd line after progression or failure of platinum-containing chemotherapy Existing indications: melanoma, non-small cell lung cancer
Lenvima	lenvatinib mesylate	Eisai Ltd.	Capsule	New strengths, New indication	New strengths: 8mg/dose; 18mg/dose New indication: in combination with everolimus (Afinitor®) to treat patients with advanced renal cell carcinoma (RCC) following one prior VEGF-targeted therapy.
Mavenclad	cladribine	EMD Serono, a Division of EMD Inc., Canada	Tablet	New dosage form, New indication	Oral tablet formulation for treatment of adult patients with relapsing remitting multiple sclerosis. (intravenous cladribine is used for the treatment of Hairy Cell Leukemia)
Mifegymiso	mifepristone/ misoprostol	Linepharma International Ltd.	Kit containing oral and buccal tablets	New indication, New distribution	For medical termination of intra-uterine pregnancy with gestational age extended from 49 days to 63 days as measured from the first day of the last menstrual period. This product is fully publically funded in some provinces.

(continued next page)

NEW DRUGS AND PRODUCT LINE EXTENSIONS (continued)

New Drugs and Product Line Extensions (Notices of Compliance (NOCs) from August 30, 2017 to November 28, 2017)

Brand name	Chemical name	Manufacturer	Dosage form	Type of Line Extension	Specifics/Comments
Niastase RT	eptacog alfa	Novo Nordisk Canada Inc.	Intravenous injection	New indication	New indication: For treatment or prevention of bleeding in patients with congenital Factor VII deficiency. Existing indications: Treatment or prevention of bleeding episodes in patients with: hemophilia A/B with inhibitors to F-VIII or F-X; Glanzmann's thrombasthenia; acquired hemophilia.
Opdivo	nivolumab	Bristol-Myers Squibb Canada	Intravenous injection	New indication	New indication: Monotherapy treatment of adult patients with classical Hodgkin Lymphoma (cHL) that has relapsed or progressed following previous treatments. [NOC/c] Existing indications: unresectable or metastatic melanoma; metastatic non-small cell lung cancer (NSCLC); metastatic renal cell carcinoma (RCC); recurrent or metastatic squamous cell carcinoma of the head and neck (SCCHN)
Orfadin	nitisinone	Swedish Orphan Biovitrum AB (publ)	Oral suspension	New dosage form	Oral liquid suspension form added to the currently available line of oral capsules for treating patients with hereditary tyrosinemia type 1 (HT-1) who are unable to take capsules.
Panzyga	human immune globulin	Octapharma Canada Inc.	Intravenous injection	New indication	New indication: for treatment of moderate to severe Guillain-Barre syndrome (GBS) Existing indications: primary immune deficiency (PID); secondary immune deficiency (SID); immune thrombocytopenic purpura (ITP)
pms-Amitriptyline	amitriptyline	Pharmascience Inc.	Tablet	New strength	100mg
Renflexis	infliximab	Samsung Bioepis Co. Ltd.	Intravenous injection	New biosimilar – Remicade	This is the second biosimilar for the reference biologic drug Remicade to be approved in Canada.
Sitavig	acyclovir	Cipher Pharmaceuticals Inc.	Mucoadhesive buccal tablet	New dosage form	New dosage form specifically indicated for treatment of immunocompetent adults with recurrent herpes labialis (cold sores).

(continued next page)

NEW DRUGS AND PRODUCT LINE EXTENSIONS (continued)

New Drugs and Product Line Extensions (Notices of Compliance (NOCs) from August 30, 2017 to November 28, 2017)

Brand name	Chemical name	Manufacturer	Dosage form	Type of Line Extension	Specifics/Comments
Stivarga	regorafenib	Bayer Inc.	Tablet	New indication	New indication: Hepatocellular carcinoma (HCC) in those who have been previously treated with sorafenib. Existing indications: metastatic colorectal cancer (CRC); mestatic and/or unresectable gastrointestinal stroma tumors (GIST)
Suboxone	buprenorphine/naloxone	Indivior Canada Ltd.	Sublingual tablet	New strengths	12mg/3mg; 16mg/4mg
Triumeq	abacavir-dolutegravir-lamivudine	ViiV Healthcare ULC	Tablet	New indication	New indication: Extension of indication to include treatment of patient with HIV-1 infection aged 12 - 18 years.
Victoza	liraglutide	Novo Nordisk Canada Inc.	Subcutaneous injection	New indication	Now indicated to reduce the risk of cardiovascular death in patients with type 2 diabetes and existing cardiovascular disease.

NOC/c = marketing approval with conditions; VEGF = vascular endothelial growth-factor

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