Health Canada Santé Canada

Canada

Health Canada New Drug Authorizations: 2016 Highlights

New Active Substances, Biosimilars, and Generic Pharmaceuticals

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To obtain additional information, please contact:

Health Canada
Address Locator 0900C2
Ottawa, ON K1A 0K9
Tel.: 613-957-2991
Toll free: 1-866-225-0709
Fax: 613-941-5366
TTY: 1-800-465-7735
E-mail: publications@hc-sc.gc.ca

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Foreword

Health Canada is pleased to release *Health Canada New Drug Authorizations: 2016 Highlights*. It contains information on new active substances (NASs), biosimilars, and new generic pharmaceuticals authorized in 2016. This document identifies a subset of the drugs reviewed by Health Canada in 2016.

New for the 2016 edition are notations identifying drugs which are biologics (Schedule D Drugs) and those drugs which are considered Orphan Drugs by either the United States Federal Drug Administration (FDA) or the European Medicines Agency (EMA).

Prior to being given market authorization, a manufacturer must present substantive scientific evidence of a product's safety, efficacy and quality as required by the *Food and Drugs Act* and *Regulations*. New drugs are authorized for sale in Canada once they have successfully gone through the drug review process. This process is the means by which a drug application is reviewed by Health Canada scientists to assess the safety, efficacy and quality of the drug.

The drug review process helps provide access for Canadians to innovative new products as well as contributing to cost savings in the health care system through the authorization of lower cost generic and biosimilar medications. Throughout the process, the safety and well-being of Canadians is the paramount concern.

For more information on the drug review process, please see: http://www.hc-sc.gc.ca/dhp-mps/prodpharma/activit/fs-fi/reviewfs_examenfd-eng.php .

Health Canada New Drug Authorizations: 2016 Highlights will be published by Health Canada on an annual basis. This document is not meant to replace the Quarterly or Annual Submission Review Performance Reports, which provide detailed metrics about the timeliness of pre-market drug review processes against the performance service standard. Those reports will continue to be prepared and made available to the general public.

For any questions on the content of this document please contact BGTD.OPIC@hc-sc.gc.ca.

Please note that the indications provided here are intended to be plain-language summaries of the specific indications for which the drugs were authorized. To see the specific indications for each drug, we encourage you to visit the links provided, or visit the Product Monograph of the drug, available on the Drug Product Database.

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New Active Substances

A new active substance (NAS) is a drug that contains a medicinal ingredient not previously approved in a drug in Canada and that is not a variation of a previously approved medicinal ingredient. In 2016 Health Canada authorized **38** new active substances for the Canadian market. Of those **38**, **7** were issued marketing authorization with conditions, **10** were authorized with a priority review, and **1** was authorized for extraordinary use. The remaining **20** new active substances were authorized without a priority review nor were issued marketing authorization with conditions.

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B – Biologic (Schedule D Drug)
O – Orphan Drug (by the FDA or the EMA)

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New Active Substances Issued Marketing Authorization with Conditions

In 2016, Health Canada issued marketing authorization with conditions to **7** new active substances as outlined in Health Canada's Notice of Compliance with Conditions (NOC/c) Guidance.

A Notice of Compliance with Conditions may be granted for a drug product with promising clinical benefit, providing that it possesses an acceptable safety profile based on a benefit/risk assessment, and is found to be of high quality. Submissions that are granted NOC/c status are subject to shorter review targets

Health Canada's NOC/c guidance can be found at: http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demande/guide-ld/compli-conform/noccg_accd-eng.php

Alecensaro[O] (alectinib hydrochloride) *Hoffmann La Roche Limited* – Alecensaro is indicated as monotherapy for the treatment of patients with anaplastic lymphoma kinase (ALK)-positive, locally advanced (not amenable to curative therapy) or metastatic non-small cell lung cancer (NSCLC) who have progressed on or are intolerant to crizotinib.

Darzalex[BO] (daratumumab) *Janssen Inc* – Darzalex is used 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.

Ibrance (palbociclib) *Pfizer Canada Inc* – Ibrance is used in combination with letrozole for the treatment of postmenopausal women with estrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced breast cancer as initial endocrine-based therapy for their metastatic disease.

Lynparza[O] (olaparib) *AstraZeneca Canada Inc* – Lynparza is indicated as monotherapy for the maintenance treatment of adult patients with platinum-sensitive relapsed breast cancer susceptibility gene (*BRCA*)-mutated (germline or somatic) high grade serous ovarian, fallopian tube or primary peritoneal cancer who are in response (complete response or partial response) to platinum-based chemotherapy.

Praxbind[BO] (idarucizumab) *Boehringer Ingelheim (Canada) Ltd* – Praxbind is used as an antidote specific for dabigatran in patients treated with Pradaxa (dabigatran etexilate) when rapid specific reversal of the anticoagulant effects of dabigatran is required either for emergency surgery/urgent procedures or in situations of life-threatening or uncontrolled bleeding.

Tagrisso[O] (osimertinib, osimertinib mesylate) *AstraZeneca Canada Inc* – Tagrisso is used 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. Tagrisso will be available in 40 mg and 80 mg tablets.

Venclexta[O] (Venetoclax) *Abbvie Corporation* – Venclexta is used for the treatment of patients with chronic lymphocytic leukemia (CLL) who have received at least one prior therapy.

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New Active Substances Authorized with a Priority Review

In 2016, Health Canada authorized **10** new active substances with a priority review.

Priority review status may be granted to a drug submission for a serious, life-threatening or severely debilitating disease or condition. Submissions that are granted priority review status are subject to shorter review targets.

Health Canada's Priority Review guidance can be found at: http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demande/guide-ld/priorit/priordr-eng.php

Empliciti[BO] (elotuzumab) *Bristol-Myers Squibb Canada* – Empliciti is used in the treatment of multiple myeloma, in combination with lenalidomide and dexamethasone, in patients that have had disease progression after 1 or more prior therapies.

Epclusa (sofosbuvir, velpatasvir) *Gilead Sciences Canada* – Epclusa is used in the treatment of adults with chronic hepatitis C, caused by HCV genotypes 1, 2, 3, 4, 5, or 6 infections, without cirrhosis or with compensated cirrhosis and in combination with ribavirin in decompensated cirrhosis.

Kyprolis[O] (carfilzomib) *Amgen Canada Inc* – Kyprolis is used in combination with either lenalidomide and dexamethasone or dexamethasone alone for the treatment of patients with relapsed multiple myeloma who have received 1 to 3 prior lines of therapy. Kyprolis was previously authorized for use in combination with lenalidomide and dexamethasone for the treatment of these patients.

MDK-Nitisinone[O] (Nitisinone) *Mendelikabs Inc* – MDK-Nitisinone is used for the treatment of patients with hereditary tyrosinemia type 1 (HT-1), in combination with dietary restriction of tyrosine and phenylalanine.

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New Active Substances Authorized with a Priority Review continued

Ninlaro[O] (Ixazomib Citrate) *Takeda Canada Inc* – Ninlaro is used in combination with lenalidomide and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least one prior therapy.

Nitisinone Tablets[O] (nitisinone) *Cycle Pharmaceuticals Ltd* – Nitisinone Tablets are used for treatment of patients with hereditary tyrosinemia type 1 (HT-1), in combination with dietary restriction of tyrosine and phenylalanine.

Orfadin[O] (nitisinone) *Swedish Orphan Biovitrum AB (PUBL)* – Orfadin is indicated for the treatment of patients with hereditary tyrosinemia type 1 (HT-1) in combination with dietary restriction of tyrosine and phenylalanine.

Orkambi[O] (ivacaftor, lumacaftor) *Vertex Pharmaceuticals (Canada) Incorporated* – Orkambi is a combination drug consisting of lumacaftor and ivacaftor indicated to treat the most common mutation (F508del) affecting cystic fibrosis patients.

Ravicti[O] (glycerol phenylbutyrate) *Horizon Pharma Ireland Ltd* – Ravicti is used as a nitrogen-binding agent for chronic management of adult and pediatric patients ≥2 years of age with urea cycle disorders who cannot be managed by dietary protein restriction and/or amino acid supplementation alone.

Zepatier (grazoprevir, elbasvir) *Merck Canada Inc* – Zepatier is used for the treatment of genotype 1 or 4 chronic hepatitis C infected adults including treatment-naïve and prior treatment failures with or without compensated cirrhosis in a regimen with or without ribavirin. The submission was also to seek approval of Zepatier for the treatment of genotype 3 chronic hepatitis C infected treatment-naive adults with or without cirrhosis in a regimen with sofosbuvir.

O – Orphan Drug (by the FDA or the EMA)

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New Active Substance Authorized for Extraordinary Use

Health Canada recognizes that there are circumstances in which manufacturers cannot reasonably provide substantial evidence demonstrating the safety and efficacy of a therapeutic product as there are logistical or ethical challenges in conducting the appropriate human clinical trials. For these types of products, which may be needed as part of emergency preparedness in Canada, the regulations for Extraordinary Use New Drugs (EUND) allow for the possibility of a market authorization based primarily on animal data.

Once a product has received market authorization as an EUND, the sale of the product for that indication is restricted to federal, provincial and territorial, and municipal government(s).

Health Canada's Submission and Information Requirements for Extraordinary Use New Drugs (EUNDs) guidance can be found at: http://www.hc-sc.gc.ca/dhp-mps/brgtherap/applic-demande/guides/eund-dnue-eng.php

BAT[B] (Botulinum Antitoxin Serotype A, B, C, D, E, F, G) *Cangene Corporation* – BAT is used for the treatment of symptomatic botulism following documented or suspected exposure to botulinum neurotoxin serotypes A, B, C, D, E, F or G.

B – Biologic (Schedule D Drug)

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Other New Active Substances

In 2016, Health Canada authorized **20** new active substances without a priority review and with no conditions.

Drugs are authorized for sale in Canada once they have successfully gone through the drug review process. This process is the means by which a drug application is reviewed by Health Canada scientists to assess the safety, efficacy and quality of a drug.

Throughout the process, for all types of submissions, the safety and well-being of Canadians is the paramount concern. More information on how drugs are reviewed and authorized in Canada can be found at: http://www.hc-sc.gc.ca/dhp-mps/prodpharma/activit/fs-fi/reviewfs_examenfd-eng.php

Cardiovascular

Praluent[B] (alirocumab) *Sanofi-AventisCanada Inc* -- Praluent is used to reduce low density lipoprotein cholesterol (LDL-C) in patients with familial hypercholesterolemia or in patients with clinical atherosclerotic cardiovascular disease.

Lancora (ivabradine hydrochloride) *Servier Canada Inc* – Lancora is for the treatment of stable chronic heart failure with reduced left ventricular ejection fraction (≤35%) in adult patients with New York Heart Association (NYHA) Classes II or III who are in sinus rhythm with a resting heart rate ≥77 beats per minute, to reduce the incidence of cardiovascular mortality and hospitalisations for worsening heart failure.

Lixiana (edoxaban) *Daiichi Sankyo Inc* – Lixiana is used to prevent stroke and systemic embolic events in patients with atrial fibrillation, as well as to treat and prevent venous thromboembolism including deep vein thrombosis and pulmonary embolism.

Uptravi[O] (selexipag) *Actelion Pharmaceuticals Ltd* – Uptravi is used in the treatment of Pulmonary Arterial Hypertension (PAH) either in conjunction with other currently approved drugs or as monotherapy.

Zontivity (vorapaxar sulfate) *Merck Canada Inc* – Zontivity is used to reduce the incidence of atherothrombotic events (cardiovascular death, myocardial infarction, stroke and urgent coronary revascularisation) in patients with a history of myocardial infarction.

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Other New Active Substances (continued)

Dermatology

Blexten (bilastine) *Aralez Pharmaceuticals Trading DAC* – Blexten is used for the symptomatic treatment of seasonal allergic rhinitis (SAR) and chronic spontaneous urticaria (CSU).

Rupatadine (rupatadine fumarate) *Pediapharm Inc* – Rupatadine is used for the treatment of seasonal allergic rhinitis (SAR), perennial allergic rhinitis (PAR) and chronic spontaneous urticaria (CSU).

Taltz[B] (ixekizumab) *Eli Lilly Canada Inc* – Taltz is used for the treatment of adult patients with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

Imaging Agent

Dotarem (gadoterate meglumine) *Guerbet* -- Dotarem is a gadolinium-based contrast agent indicated for intravenous use with magnetic resonance imaging (MRI) in brain (intracranial), spine and associated tissues in adult and pediatric patients (2 years of age and older) to detect and visualize areas with disruption of the blood brain barrier (BBB) and/or anormal vascularity.

Infections

Sunvepra (asunaprevir) *Bristol-Myers Squibb* – Sunvepra is to be used in combination with other agents for the treatment of chronic hepatitis C virus genotypes 1 or 4 in adult patients with compensated liver disease, including cirrhosis.

Xtoro (finafloxacin) *Alcon Canada Inc* – Xtoro is used for the treatment of acute otitis externa (AOE) caused by susceptible strains of Staphylococcus aureus and Pseudomonas aeruginosa, with or without otowick, in patients age 1 year and older.

Neurology

Bridion (sugammadex) *Merck Canada Inc* – Bridion is indicated for reversal of moderate to deep neuromuscular blockade induced by rocuronium or vecuronium in adults undergoing surgery. Rocuronium and vecuronium are two skeletal neuromuscular relaxants used to facilitate surgical anaesthesia.

Brivlera (brivaracetam) *UCB Canada Inc* – Brivlera is an anti-epileptic drug for the management of partial-onset seizures in adults who are not satisfactorily controlled with conventional therapy. Brivlera solution for injection for intravenous use is an alternative when oral administration is temporarily not feasible.

Zinbryta[B] (daclizumab beta) *Biogen Canada Inc* – Zynbryta is used for the treatment of relapsing forms of multiple sclerosis (MS).

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Oncology/Hematology

Adynovate[B] (Antihemophilic factor (recombinant), pegylated) *Baxalta Canada Corporation* – Adynovate is used for the treatment of the hereditary bleeding disorder - hemophilia A. This product is Advate - a recombinant FVIII now on the market - with attached polyethylene glycol (PEG) molecules (PEGylation).

Afstlya[B] (Ionoctocog alfa) *CSL Behring Canada Inc* – Afstlya is used for control and prevention of bleeding episodes, routine prophylaxis to prevent or reduce the frequency of bleeding episodes and perioperative prophylaxis for previously treated children and adults with hemophilia A.

Cotellic[O] (cobimetinib fumurate) *Hoffman-La Roche Limited* – Cotellic is used in combination with vemurafenib for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600 mutation.

Idelvion[BO] (albutrepenonacog alfa) *CSL Behring Canada Inc* – Idelvion is used in the treatment and prophylaxis of bleeding in subjects of all ages suffering with severe congenital FIX deficiency.

Ophthalmology

Bepreve (bepotastine besilate) *Bausch & Lomb Inc* – Bepreve is used for the treatment of allergic conjunctivitis.

Pulmonary/Respiratory

Cinqair[B] (reslizumab) *Teva Canada Limited* – Cinqiar is used as add-on maintenance treatment of adult and adolescent patients (12 years of age and above) with severe eosinophilic asthma, whose symptom are not controlled despite the medium-to- high dose of inhaled corticosteroids.

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Biosimilars

In 2016, Health Canada authorized **1** new biosimilar and new indications for **2** previously authorized biosimilar drugs.

A biosimilar is a biologic drug that enters the market subsequent to a previously authorized biologic drug in Canada with a demonstrated similarity to the previously authorized biologic drug.

Health Canada's biosimilar guidance can be found at: http://www.hc-sc.gc.ca/dhp-mps/brgtherap/applic-demande/guides/biosimilars-biosimilaires-eng.php

Brenzys[B] (etanercept) *Samsung Bioepis Co., Ltd*—Brenzys is authorized for indications and clinical uses in Rheumatoid Arthritis and Ankylosing Spondylitis. The market application relied on comparisons made to demonstrate similarity to the Canadian authorized product, Enbrel (etanercept).

Inflectra[B] (Infliximab) *Celltrion Healthcare Co. Ltd*—Inflectra is authorized for indications and clinical uses in adult Crohn's disease, including fistulising Crohn's disease and adult ulcerative colitis. The market application relied on comparisons made to demonstrate similarity to the Canadian authorized product, Remicade (infliximab). This indication was authorized through a supplemental new drug submission.

Remsima[B] (Infliximab) *Celltrion Healthcare Co. Ltd*—Remsima is authorized for indications and clinical uses in adult Crohn's disease, including fistulising Crohn's disease and adult ulcerative colitis. The market application relied on comparisons made to demonstrate similarity to the Canadian authorized product, Remicade (infliximab). This indication was authorized through a supplemental new drug submission.

Generic Pharmaceuticals

In 2016, Health Canada authorized **150** new generic pharmaceuticals.

A generic drug is a copy of a brand name product, known as the 'reference product.' Generic drugs contain the same medicinal ingredients as the brand name drug, and are considered bioequivalent to the reference product.

More information on how Health Canada handles generic pharmaceuticals can be found at: http://www.hc-sc.gc.ca/hl-vs/iyh-vsv/med/med-gen-eng.php

B – Biologic (Schedule D Drug)