U.S. FOOD & DRUG ADMINISTRATION

ADVANCING HEALTH THROUGH INNOVATION

NEW DRUG THERAPY APPROVALS 2019

Impact | Innovation | Predictability | Access

CENTER FOR DRUG EVALUATION AND RESEARCH

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Introduction

Welcome to the FDA's Center for Drug Evaluation and Research's (CDER) annual report, *Advancing Health Through Innovation: New Drug Therapy Approvals*, reporting our Center's notable new drug approvals to the American public, and illustrating CDER's role in bringing innovative new drug therapies that are safe and effective to patients in need.

As with previous years, this year's notable new drug therapies include a variety of novel drugs — those never before approved or marketed in the United States. Novel drugs often represent important new therapies for advancing patient care.

Importantly, this report also goes beyond a discussion of novel approvals and includes an overview of an array of other notable approvals — for instance, new approvals for uses of already FDA-approved drugs. Please take particular note of these other approvals. You will find, as in past years, that many important advances in drug therapy approved in 2019 use an already FDA-approved drug to treat a new disease beyond that for which it was originally approved or to treat a new population of patients, such as children.

Our report emphasizes some of the many innovative ways we were able to evaluate safety and efficacy for these new therapies, as well as key regulatory tools we used to enhance our efficiency and expedite the review and approval of applications.

We also highlight the year's biosimilar approvals. Biosimilars have great potential for both patients and the entire health care system. As patents and exclusivity protections for biologics expire in the United States, we can expect many more biosimilars to be submitted for approval. More products on the market means greater competition that can lead to increased access to therapies and lower costs to patients.

The decisions we made on these approvals were generally completed by or before their goal dates as defined by Congressionally-mandated user fee programs. Most were approved in the United States before any other country in the world.

Throughout all of our approval evaluations, safety remains our top priority. Our annual Drug Safety Priorities report provides a valuable overview of the many ways we work to ensure safety for all of our approvals.

Keep in mind that this report focuses on CDER approvals. FDA's Center for Biologics Evaluation and Research (CBER) also approves many important therapies to advance and protect the health of the American public. For more information, please visit CBER's web page for 2019 Biological Approvals.

We trust this report will continue to promote greater understanding of the many ways CDER works to support innovation and improve treatments for patients.

Janet Woodcock, M.D.,
Director, Center for Drug Evaluation and Research

2019: Another Strong Year for Innovation and Advances

In 2019, FDA's Center for Drug Evaluation and Research's (CDER's) new drug therapy approvals helped a wide range of patients suffering from many different medical conditions gain new hope for improved quality of life, and in some cases, improved chances of surviving life-threatening illnesses.

Rare Diseases

CDER approved two notable new advances for patients with **cystic fibrosis** (CF): 1) the first triple combination therapy to treat patients with CF who have the most common form of the CF gene mutation, which is estimated to represent 90 percent of the cystic fibrosis population and, 2) a new use for an already FDA-approved CF drug to treat certain patients as young as 6 years of age, which previously was approved only for certain patients 12 years of age or older, Additionally, CDER approved a new drug to increase pain-free light exposure in patients with phototoxic reactions (sensitivity to sunlight) due to **erythropoietic protoporphyria**, a rare condition resulting from excess accumulation of a chemical that normally helps red blood cells deliver oxygen to the body. CDER also approved the first treatment for **neuromyelitis optica spectrum disorder**, a rare chronic disorder

CDER approved many new treatment options for patients in need.

dominated by inflammation of the optic nerve and spinal cord. CDER approved a new treatment for **tenosynovial giant cell tumor**, a rare painful condition in which non-cancerous tumors grow around joint areas and cause damage. Adding more to 2019's advances for patients with rare diseases, CDER approved a new medication to treat patients who have **sickle cell disease** (SCD); the drug was shown to raise hemoglobin levels which may predict for a reduction in the risk of stroke, a leading cause of disability and death in patients with SCD. Also to help patients with SCD, CDER approved a new medication to help prevent vasoocclusive crises, the most common complication of SCD, a very painful condition that results when tissues in the body do not receive enough oxygen. CDER also approved a new therapy which slows the rate of decline in lung function for patients with **systemic sclerosis-associated interstitial lung disease** (SSc-ILD), a rare disease for which there previously was no FDA-approved treatment. SSc-ILD is a serious and sometimes fatal disease that can damage the lungs, heart, kidneys and gastrointestinal tract. In addition, CDER approved a new drug for the treatment of certain patients with **Duchenne muscular dystrophy**.

Neurological and Psychiatric Disorders

In 2019, CDER approved two new treatments for certain adult patients with **multiple sclerosis**, a chronic and often debilitating disease of the central nervous system. Also, CDER approved a new treatment for adults with **depression** who have tried other medications without success. Additionally, FDA approved monoclonal antibody for the treatment of **episodic cluster headache**, an extremely painful and often debilitating condition. CDER also approved a new drug to treat patients with **Parkinson's disease** (PD) who experience "off" episodes, during which medications are not working well, causing an increase in PD symptoms, such as tremor and difficulty walking. CDER also approved two new drugs to help patients who suffer from **migraine**. CDER also approved a new drug to decrease the frequency of **partial onset seizures** in patients with epilepsy.

Infectious Diseases

CDER approved two new antibiotics effective against certain resistant **Gram-negative infections** — important advances because Gram-negative bacteria represent a growing danger of serious and potentially life-threatening infections. We also approved a new drug which, when used in combination with certain others, is effective against a form of **tuberculosis** that is resistant to many other therapies. In 2019, CDER also approved a new antibiotic for the treatment of patients with **community-acquired bacterial pneumonia** (pneumonia that someone gets outside of a hospital), a leading cause of illness and death worldwide. Also, to help patients with the HIV-1 virus, CDER approved the first FDA-approved two-drug, fixed-dose, complete regimen for HIV-infected adults who have never received treatment for HIV. Previously, the standard of care for patients who have never been treated is a three-drug regimen, so this important new **"drug sparing" regimen** eliminates additional toxicity and potential drug interactions from a third drug. We also approved a new therapy for the **prevention of HIV** in certain at-risk adults and adolescents to reduce the risk of infection from sexual exposure. This is only the second FDA-approved drug combination for HIV prevention.

Heart, Lung, Circulatory, and Endocrine Diseases

CDER approved two new drugs to treat adults with **cardiomyopathy** (heart disease) caused by a condition called transthyretin mediated amyloidosis. In addition, we approved the first anticoagulant therapy ever for pediatric patients as young as one month of age to reduce the recurrence of a condition called **symptomatic venous thromboembolism**, which can include blood clots in the deep veins of the legs and in the lungs and can lead to death. To help certain patients with diabetes, CDER approved a therapy to treat patients with **type 2 diabetes** as young as ten years of age, previously approved for use only in adults. Additionally, CDER approved a new nasal

powder to treat severe hypoglycemia, which typically occurs in people with diabetes who are using insulin. Also, for adult patients with **type 2 diabetes**, CDER approved, the first diabetes medication in the drug class, "glucagon-like peptide receptor agonist protein" approved for use in the U.S. that is taken orally and does not need to be injected.

Autoimmune Conditions

In 2019, CDER approved the first therapy to treat children with **systemic lupus erythematosus** — a serious chronic disease that causes inflammation and damage to various body tissues and organs. We also approved the first FDA-approved treatment for certain adults with a type of inflammatory arthritis called **non-radiographic axial spondyloarthritis**, an autoimmune condition that causes inflammation in the spine and other symptoms. 2019 also saw the first FDA approval of a treatment specifically for pediatric patients — ages 6 to 17 years of age — with **Lambert-Eaton myasthenic syndrome**, a disease that can cause muscle weakness in the body's limbs and eyes as well as those used for talking and swallowing, making walking, and self-care difficult. We also approved the first pediatric treatment **granulomatosis with polyangiitis** (GPA) and **microscopic polyangiitis** (MPA), in combination with glucocorticoids (steroid hormones); GPA and MPA are diseases in which a patient's small blood vessels become inflamed, reducing the amount of blood that can flow through them.

Women's and Men's Specific Health Issues

CDER approved a new biologic drug to treat **osteoporosis** in certain postmenopausal women at high risk of breaking a bone. Also, to help advance women's health, CDER approved a new drug to treat acquired, **generalized hypoactive sexual desire disorder**, or low sexual desire, in premenopausal women. We also approved the first FDA-approved drug specifically for the treatment of adult women with **postpartum depression**. To help advance men's health, CDER approved a new oral testosterone capsule to treat men with **low testosterone levels** due to specific medical conditions. Until this approval, testosterone replacement therapies have most commonly been applied to the skin or injected.

Cancers and Blood Disorders

2019 was another strong year for making new cancer and blood therapies available to patients in need. We approved new advances for certain patients with **prostate cancer bladder cancer, breast cancer,** and **lung cancer**. We also approved two new **bone marrow**

cancer therapies. Additionally, CDER approved another new cancer therapy that can be used to treat any kind of tumor that has a **specific genetic marker**, as opposed to where in the body the tumor originated --- only the third cancer therapy approved by the FDA to target treatment based on a specific characteristic of a tumor instead of its site of origin. Also to help advance cancer therapies, CDER approved a new drug to treat certain adult patients with **diffuse large B-cell lymphoma**, the most common type of non-Hodgkin lymphoma, a type of blood cancer. CDER also approved a new therapy for patients with **mantle cell lymphom**a, also a form of blood cancer. CDER also approved a new treatment for a certain type of **myelofibrosis**, in which the bone marrow is replaced by scar tissue and is not able to make healthy blood cells. Additionally, CDER approved the first FDA-approved therapy for the treatment of adult patients with **acquired thrombotic thrombocytopenic purpura**, a disorder that causes blood clots that can cut off oxygen and blood supply to the major organs and cause strokes and heart attacks that may lead to brain damage or death. We also approved a new treatment for certain patients with **acute hepatic porphyria**, in which enzyme deficiencies cause insufficient formation of a blood substance called heme in the liver followed by accumulation of toxins in the liver. Additionally, in 2019, CDER approved a first-in-class drug used for the treatment of certain adult patients who require red blood cell transfusions as a result of specific type of anemia caused by **beta-thalassemia**. We also approved a new therapy for adult patients with **chronic lymphocytic leukemia** or **small lymphocytic lymphoma**, similar blood cancers that occur in different parts of the body.

CDER's drug therapy approvals of 2019 will help advance patient care in many new areas.

Biosimilars

As in previous years, 2019 saw advances in the approval of **biosimilars**. CDER approved ten new biosimilars, which will further help to create competition, increase patient access, and potentially reduce the cost of important biological drug therapies. These new approvals can help patients suffering from a wide range of conditions, such as rheumatoid arthritis, various other forms of arthritis, plaque psoriasis, and a variety of cancers and blood disorders including breast cancer, metastatic stomach cancer, metastatic colorectal cancer, non-squamous non-small cell lung cancer, glioblastoma, metastatic renal cell carcinoma, cervical cancer, B-cell non-Hodgkin's lymphoma, chronic lymphocytic leukemia, granulomatosis with polyangiitis, and microscopic polyangiitis.

CDER's Drug Therapy Approvals of 2019

In 2019, CDER approved a wide variety of drug therapies to improve the health of the American public, including:

- **Novel drugs,** which are often among the more innovative products in the marketplace, and help advance clinical care by providing therapies never before marketed in the United States;
- **New and expanded uses** for already FDA-approved drugs;
- **Biosimilars,** which are highly similar to already FDA-approved therapeutic biological products. These approvals add consumer choice and spur marketplace competition;
- **New formulations** or new manufacturers of already FDA-approved products that can provide advantages over original products, such as being able to take the drug on an empty stomach instead of with food; and
- **New dosage forms** that can add value to already FDA-approved drugs, such as chewable tablets for patients unable to swallow pills.

This report summarizes these approvals and highlights examples, emphasizing those approvals that offer new and innovative treatments to patients in need.

As with all FDA-approved products, the new drug therapies discussed in this report have risks. **For more information about these drugs and for complete risk information, see the drugs' approval letters and FDA-approved labeling at Drugs@FDA.**

Novel Drugs

Novel drugs are often innovative products that serve previously unmet medical needs or otherwise significantly help to advance patient treatments. The active ingredient or ingredients in a novel drug have never before been approved in the United States. This report lists all of CDER's novel drug approvals of 2019 and also discusses those that CDER considers notable advances. In 2019, CDER approved 48 novel drugs, either as new molecular entities (NMEs) under New Drug Applications (NDAs), or as new therapeutic biologics under Biologics License Applications (BLAs).

CDER's Novel Drug Approvals of 2019

CDER's novel drug approvals for 2019 are listed alphabetically below by trade name.* See **Appendix A** in this report or visit online, CDER's Novel Drug Approvals for 2019, for the non-proprietary names, dosage forms, and what each drug is used for.

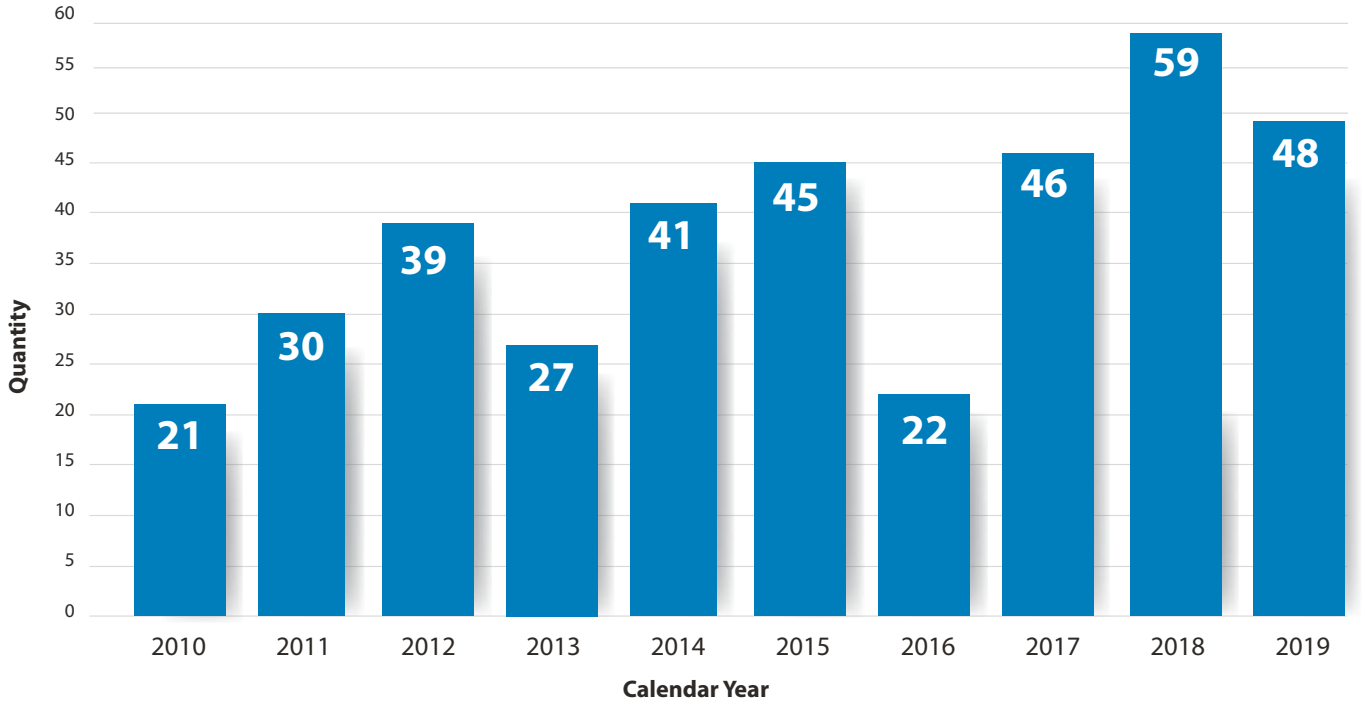
Accrufer	Enhertu	Mayzent	Reyvow	Vyleesi
Adakveo	Evenity	Nourianz	Rinvoq	Vyndaqel
Aklief	ExEm Foam	Nubeqa	Rozlytrek	Vyondys 53
Balversa	Fetroja	Oxbryta	Scenesse	Wakix
Beovu	fluorodopa F 18**	Padcev	Skyrizi	Xcopri
Brukinsa	Ga 68 DOTATOC**	Piqray	Sunosi	Xenleta
Cablivi	Givlaari	Polivy	TissueBlue	Xpovio
Caplyta	Ibsrela	pretomanid**	Trikafta	Zulresso
Dayvigo	Inrebic	Reblozyl	Turalio	
Egaten	Jeuveau	Recarbrio	Ubrelvy	

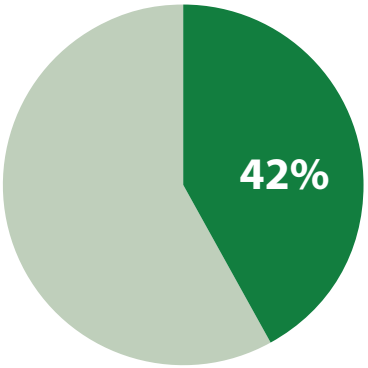
* This information is accurate as of December 31, 2019. In rare instances, it may be necessary for FDA to change a drug's NME designation or the status of its application as a novel BLA. For instance, new information may become available which could lead to a reconsideration of the original designation or status. If changes must be made to a drug's designation or the status of an application as a novel BLA, the agency intends to communicate the nature of, and the reason for, any revisions as appropriate.

** Product approved with no trade name

CDER's Annual Novel Drug Approvals: 2010–2019

In 2019, CDER approved 48 novel drugs. The 10-year graph below shows that from 2010 through 2018, CDER has averaged about 37 novel drug approvals per year.





CDER identified 20 of the 48 novel drugs approved in 2019 (42%) as first-in-class.

2019 saw the first FDA-approved drug specifically for the treatment of adult women with **postpartum depression.**

Impact of Novel Drug Approvals

Many of the novel drugs CDER approved in 2019 are notable for their potential positive impact and unique contributions to quality medical care and patient treatment.

First-in-Class

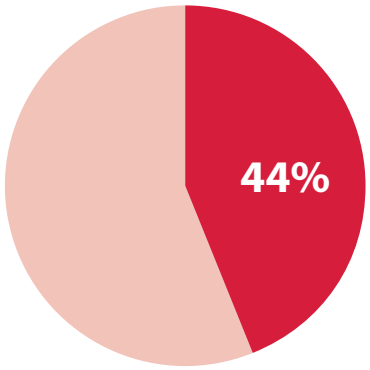
CDER identified 20 of the 48 novel drugs approved in 2019 (42%) as first-in-class, which is one indicator of the drug's potential for strong positive impact on the health of the American people. These drugs often have mechanisms of action different from those of existing therapies. Novel drugs approved in 2019 that FDA identified as first-in-class were: Adakveo, Balversa, Cablivi, Evenity, Givlaari, Ibsrela, Nourianz, Oxbryta, Padcev, Polivy, pretomanid, Reblozyl, Reyvow, Scenesse, Turalio, Vyleesi, Vyndaqel, Wakix, Xpovio, and Zulresso.

Examples of notable novel First-in-Class approvals for 2019 include:

- **Balversa** (erdafitinib) tablets, approved under FDA's accelerated approval program (see p. 22) a treatment for adult patients with locally advanced or metastatic **bladder cancer** that has a type of susceptible genetic alteration known as FGFR3 or FGFR2, and that has progressed during or following prior platinum-containing chemotherapy. Patients should be selected for therapy with Balversa using an FDA-approved companion diagnostic device. In 2019, the FDA also approved the therascreen FGFR RGQ RT-PCR Kit for use as a companion diagnostic with Balversa for this therapeutic indication.
- **Zulresso** (brexanolone) injection, for the treatment of **postpartum depression** (PPD) in adult women — the first drug approved by the FDA specifically for PPD. PPD is a major depressive episode that occurs following childbirth, although symptoms can start during pregnancy. As with other forms of depression, it is characterized by sadness and/or loss of interest in activities that one used to enjoy and a decreased ability to feel pleasure (anhedonia) and may present with symptoms such as cognitive impairment, feelings of worthlessness or guilt, or suicidal ideation.

Drugs for Rare Diseases

In 2019, 21 of CDER's 48 novel drug approvals (44%) were approved to treat rare or "orphan" diseases that affect 200,000 or fewer Americans. Patients with rare diseases often have few or no drugs available to treat their conditions. Novel drugs approved in 2019 with the orphan drug designation were: Adakveo, Brukinsa, Cablivi, Egaten, Ga 68 DOTATOC, Givlaari, Inrebic, Oxbryta, Polivy, pretomanid, Reblozyl, Rozlytrek, Scenesse, Sunosi, TissueBlue, Trikafta, Turalio, Vyndaqel, Vyondys 53, Wakix, and Xpovio.



21 of CDER's 48 novel drugs (44%) were approved to treat rare or "orphan" diseases.

Notable examples of novel approvals of 2019 that advance the care of patients with rare diseases include:

- **Scenesse** (afamelanotide), implants, to increase pain-free light exposure in patients with phototoxic reactions (sensitivity to sunlight) due to **erythropoietic protoporphyria**, a rare condition resulting from excess accumulation of a chemical that normally helps red blood cells deliver oxygen to the body; even brief sun exposure can result in painful skin lesions.
- **Turalio** (pexidartinib), capsules, for certain adult patients with **tenosynovial giant cell tumor**, a rare condition involving non-cancerous tumors around the joint areas. Although the tumors are non-cancerous, they can grow and cause damage to the surrounding tissue and structures of the body. Symptoms can include pain, swelling, and limitation of movement of the joint and can lead to significant disability if untreated. Surgery remains the primary treatment for this condition. However, pexidartinib is now the first FDA-approved drug to treat this condition in patients who are not candidates for surgery.

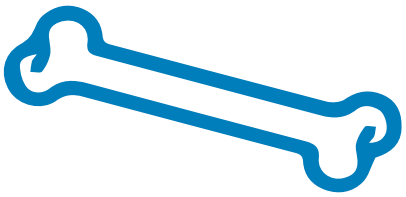
Patients with rare diseases often have few or no drugs available to treat their conditions.

Other Notable Novel Drug Approvals: Advances in Patient Care Across a Broad Range of Diseases

In addition to the noteworthy first-in-class and orphan-designated drugs mentioned above, the 2019 novel drug field also includes these notable examples — approved for the first time in the United States, and likely to significantly improve the care of patients with the conditions noted below:

- **Adakveo** (crizanlizumab-tmca) injection, to help prevent the most common complication of sickle cell disease — **vasoocclusive crisis** — a very painful condition that results when tissues in the body do not receive enough oxygen.
- **Beovu** (brolucizumab–dbll) injection, to treat patients with wet **age-related macular degeneration**, (AMD) which is the deterioration of the macula, a part of the retina of the eye, that enables clear vision. Wet AMD is a form of the disease in which new blood vessels grow in the eye and often leak. Macular degeneration is the leading cause of severe, irreversible vision loss in people over age 60.
- **Brukinsa** (zanubrutinib) capsules, approved under FDA's accelerated approval program (see p. 22), for the treatment of patients with **mantle cell lymphom**a (a form of blood cancer), a life-threatening condition — for adult patients who have received at least one other prior therapy to treat the condition. Mantle cell lymphoma usually responds well to initial treatment, but eventually returns or stops responding, and the cancer cells continue to grow. Clinical trials for this therapy showed that 84 percent of patients saw tumor shrinkage. For patients whose disease relapses or becomes refractory (resistant to treatment), secondary therapies may be successful in providing another remission, and this approval provides patients with another treatment option.
- **Cablivi** (caplacizumab-yhdp) injection, the first therapy specifically indicated, in combination with plasma exchange and immunosuppressive therapy, for the treatment of adult patients with **acquired thrombotic thrombocytopenic purpura** (aTTP), a life-threatening disorder that causes blood clotting. Patients with aTTP develop extensive blood clots in the small blood vessels throughout the body. These clots can cut off oxygen and blood supply to the major organs and cause strokes and heart attacks that may lead to brain damage or death. Patients can develop aTTP because of conditions such as cancer, HIV, pregnancy, lupus or infections, or after having surgery, bone marrow transplantation or chemotherapy.
- **Egaten** (triclabendazole) tablets, for the treatment of the tropical disease, **fascioliasis**, commonly known as liver fluke infestation, in patients aged 6 years and older. The approval marks the first FDA-approved drug for this neglected tropical disease, which can be transmitted to humans following consumption of larvae in contaminated water or food.
- **Enhertu** (fam-trastuzumab deruxtecan-nxki) injection, approved under FDA's accelerated approval program (see p. 22) for the treatment of patients with HER2 positive, locally advanced or metastatic **breast cancer** who have disease progression after other specific treatments.
- **Evenity** (romosozumab-aqqg) injection, to treat **osteoporosis** in postmenopausal women at high risk of fracture (breaking a bone). These are women with a history of osteoporotic fracture or multiple risk factors for fracture, or those who have failed or are intolerant to other osteoporosis therapies. More than 10 million people in the U.S. have osteoporosis, which is most common in women who have gone through menopause. People with osteoporosis have weakened bones that are more likely to fracture. Evenity is a monoclonal antibody that blocks the effects of the protein sclerostin and works mainly by increasing new bone formation. Evenity may increase the risk of heart attack, stroke and cardiovascular death so it is important to carefully select patients for this therapy, which includes avoiding use in patients who have had a heart attack or stroke within the previous year.

- **Fetroja** (cefiderocol) injection, an antibiotic aimed at countering multi-drug-resistant Gram-negative bacteria in patients with **complicated urinary tract infections**. This approval is an important advance because Gram-negative bacteria are generally more resistant to antibacterial medications because their cell structures make it difficult for the drug to penetrate the cell wall (see also Recarbrio, p. 22).
- **fluorodopa F 18** injection, a radioactive diagnostic agent for use in positron emission tomography to help diagnose adult patients with suspected **Parkinsonian syndromes**, a group of disorders, that includes Parkinson's disease, that may occur when there is a reduction in the ability of dopamine, an essential chemical in the body that works in the brain, to function normally.
- **Givlaari** (givosiran) injection, for certain patients with **acute hepatic porphyria**. Porphyria is the term used to describe a group of rare inherited blood disorders resulting from buildup of certain chemicals related to red blood cell proteins. Acute hepatic porphyrias are specific to porphyrias in which enzyme deficiencies cause insufficient formation of a blood substance called heme in the liver followed by accumulation of toxins in the liver.
- **Inrebic** (fedratinib) capsules, a new treatment for a certain type of **myelofibrosis**, a condition in which the bone marrow is replaced by scar tissue and is not able to make healthy blood cells.
- **Mayzent** (siponimod) tablets, to treat adults with relapsing forms of **multiple sclerosis** (MS), to include clinically isolated syndrome, a first episode of neurologic symptoms that lasts at least 24 hours and is caused by inflammation or damage to nerve cells. MS is a chronic, inflammatory, autoimmune disease of the central nervous system that disrupts communications between the brain and other parts of the body. Most people experience their first symptoms of MS between the ages of 20 and 48. MS is among the most common causes of neurological disability in young adults and occurs more frequently in women than in men.
- **Nourianz** (istradefylline) tablets, approved as an add-on treatment to levodopa/carbidopa in adult patients with **Parkinson's disease** experiencing "off" episodes. Off episodes occur when the effect of carbidopa/levodopa wears off and Parkinson's symptoms recur between doses. Off episodes are often sudden and unpredictable.



CDER approved a new biologic drug to treat osteoporosis in certain postmenopausal women at high risk of breaking a bone.

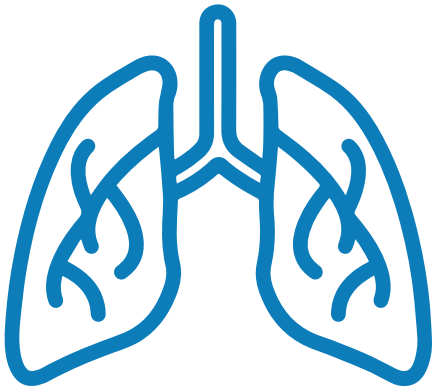
CDER approved a new therapy to help patients who experience "off episodes" related to Parkinson's disease.

CDER approved a new drug therapy that can help reduce the risk of stroke for patients with sickle cell disease.

- **Nubeqa** (darolutamide) tablets, a new treatment for men with a kind of **prostate cancer** that has not spread to other parts of the body but continues to grow even after the patient's testosterone is reduced to very low levels.
- **Oxbryta** (voxelotor) tablets, for the treatment of patients with **sickle cell disease**, a genetic condition that causes hemoglobin, the component of the red blood cell that carries oxygen, to become sickle (i.e., crescent) shaped, leading to a reduced amount of oxygen the blood can supply to vital tissues and organs of the body. These mis-shaped blood cells can also lodge into the smallest blood vessels, blocking blood flow and leading to excruciating pain and sometimes stroke — the leading cause of death in SCD. Voxelotor has been shown to raise hemoglobin levels in affected cells and may therefore reduce a patient's risk of stroke.
- **Padcev** (enfortumab vedotin-ejfv) injection, approved under FDA's accelerated approval program (see p. 22) to treat **refractory bladder cancer.** Refractory means a type of cancer that does not respond well to treatment.
- **Piqray** (alpelisib) tablets, used with the FDA-approved endocrine therapy fulvestrant, to treat postmenopausal women, and men, with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, PIK3CA-mutated, advanced or metastatic **breast cancer** (as detected by an FDA-approved test) following progression on or after an endocrine-based regimen. In 2019, the FDA also approved the companion diagnostic test, therascreen PIK3CA RGQ PCR Kit, to detect the PIK3CA mutation. Metastatic breast cancer is breast cancer that has spread beyond the breast to other organs in the body (most often the bones, lungs, liver or brain).
- **Polivy** (polatuzumab vedotin-piiq) injection, approved under FDA's accelerated approval program (see p. 22), in combination with the chemotherapy bendamustine and a rituximab product (a combination known as "BR"), to treat adult patients with **diffuse large B-cell lymphoma** (DLBCL) that has progressed or returned after at least two prior therapies. Polivy is a novel antibody-drug conjugate, and DLBCL is the most common type of non-Hodgkin lymphoma. Antibody-drug conjugates are an emerging

class of targeted immunotherapies for cancer. This type of therapy, unlike traditional chemotherapy, is intended to target specific cells. More than 18,000 people are diagnosed with DLBCL each year in the U.S. Although it can be cured, about 30 percent to 48 percent of patients suffer relapse.

- **pretomanid** tablets, a new therapy as part of a combination with bedaquiline and linezolid, in adults for the treatment of pulmonary extensively drug-resistant or treatment-intolerant or non-responsive multidrug-resistant **tuberculosis**. This is the second antibacterial drug product approved under the Limited Population Pathway for Antibacterial and Antifungal Drugs (LPAD) pathway, established by Congress under the 21st Century Cures Act. LPAD is designed to streamline development and approval of antibacterial drugs to treat serious or life-threatening infections in a limited population of patients with unmet need. In 2018, CDER utilized the LPAD pathway to approve Arikayce (amikacin liposome inhalation suspension), for the treatment of lung disease caused by a group of bacteria, Mycobacterium avium complex (MAC) in a limited population of patients with the disease who do not respond to conventional treatment (refractory disease).



CDER approved a new drug therapy effective against a form of tuberculosis that is resistant to many other therapies.

- **Reblozyl** (luspatercept-aamt) injection, a first-in-class drug called an erythroid maturation agent — designed to regulate late-stage red blood cell maturation — used for the treatment of certain adult patients who require red blood cell transfusions as a result of specific anemia caused by **beta-thalassemia**. This approval fills an important unmet medical need. Prior to this approval, the primary treatment option has been chronic transfusion of red blood cells which can be associated with complications such as iron overload.

- **Recarbrio** (imipenem, cilastatin, relebactam) injection, an antibiotic for adults with **complicated urinary tract infections** and **complicated intra-abdominal infections** — caused by certain susceptible Gram-negative bacteria — who have limited or no alternative therapies available. This approval is an important advance because Gram-negative bacteria are generally more resistant to antibacterial medications because their cell structures make it difficult for the drug to penetrate the cell wall. (See also Fetroja, p. 15).

CDER approved two new antibiotics effective against certain Gram-negative infections — an important advance because Gram-negative bacteria represent a growing danger of serious and potentially life-threatening infections.

CDER separately approved two different new drugs for the acute treatment of migraine.

- **Reyvow** (lasmiditan) tablets, for the acute treatment of **migraine** with or without aura (a sensory phenomenon or visual disturbance) in adults. (See also Ubrelvy, below).
- **Rozlytrek** (entrectinib) capsules, approved under FDA's accelerated approval program (see p. 22), to treat certain patients 12 years of age and older whose **metastatic solid tumors** have a genetic characteristic, or "biomarker," called "NTRK gene fusion-positive." Treatment with this drug for this purpose is known as being "tissue agnostic," meaning the therapy can be used for the treatment of any kind of tumor with this genetic characteristic, regardless of where in the body the tumor originated. This is the third FDA-approved tissue agnostic cancer treatment in two years. In 2017, CDER approved Keytruda (pembrolizumab) to treat patients whose cancers have a specific biomarker called MSI-H. In 2018, CDER approved Vitrakvi (larotrectinib) (under accelerated approval) for the treatment of patients with locally advanced or metastatic solid tumors with an "*NTRK* gene fusion" biomarker. At the same time, Rozlytrek was also approved for the treatment of **non-small cell lung cancer** whose tumors test positive for the genetic biomarker, "ROS1."
- **Skyrizi** (risankizumab–rzaa) injection, for the treatment of **moderate-to-severe plaque psoriasis** in adults who are candidates for systemic therapy or phototherapy. Plaque psoriasis is a chronic autoimmune condition that causes patches of thick, red, scaly skin. For mild cases (less than 3% of the body covered in rash), topical medications (i.e., those applied to the skin) are usually used. In moderate (3% to 10% body covered) or severe (more than 10% covered) cases, systemic treatment (inside the body) or phototherapy (exposure to ultraviolet light) is used.
- **Sunosi** (solriamfetol) tablets, to improve wakefulness in adult patients with excessive daytime sleepiness associated with **narcolepsy** or **obstructive sleep apnea**.
- **TissueBlue** (Brilliant Blue G) solution, used as a **dye** to stain a part of the retina of the eye called the internal limiting membrane to help surgeons better perform some types of eye surgery.

- **Trikafta** (elexacaftor, tezacaftor, and ivacaftor) tablets, to treat patients 12 years of age and older with **cystic fibrosis** (CF) who have at least one F488del mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene — the most common CF mutation, which is estimated to represent 90 percent of the cystic fibrosis population. Currently available therapies are effective for some patients with CF, but many patients have mutations that are ineligible for treatment.

CDER approved the first triple combination therapy to treat patients with cystic fibrosis which can be effective for about 90 percent of patients with this condition.

- **Ubrelvy** (ubrogepant) tablets, for the acute (active but short-term) treatment of **migraine** with or without aura (a sensory phenomenon or visual disturbance) in adults. It is not approved for the preventive treatment of migraine. (See also Reyvow, above).
- **Vyleesi** (bremelanotide) injection, to treat acquired **generalized hypoactive sexual desire disorder** (HSDD) in premenopausal women. HSDD is characterized by low sexual desire that causes marked distress or interpersonal difficulty and is not due to a co-existing medical or psychiatric condition, problems within the relationship or the effects of a medication or other drug substance. Acquired HSDD develops in a patient who previously experienced no problems with sexual desire. Generalized HSDD refers to HSDD that occurs regardless of the type of sexual activity, situation or partner. Vyleesi activates melanocortin receptors, but the mechanism by which it improves sexual desire and related distress is unknown. Patients self-inject Vyleesi under the skin of their abdomen or thigh, as needed.

CDER approved a new drug to treat acquired, generalized hypoactive sexual desire disorder, or low sexual desire, in certain premenopausal women.

- **Vyndaqel** (tafamidis meglumine) capsules, approved at the same time as Vyndamax (tafamidis) — both for the treatment of **cardiomyopathy** (heart disease) caused by the rare condition, transthyretin mediated amyloidosis (ATTR-CM) in adults. Vyndaqel and Vyndamax are the first FDA-approved treatments for ATTR-CM. The two drugs have the same active moiety (i.e., an almost identical active ingredient), tafamidis, but they are not substitutable on a milligram to milligram basis and their recommended doses differ. ATTR is caused by the buildup of abnormal deposits of specific proteins known as amyloid in the body's organs and tissues, interfering with their normal functioning. These protein deposits most frequently occur in the heart and the peripheral nervous system.

CDER approved two new drugs to treat adult patients with heart disease caused by the rare condition, transthyretin mediated amyloidosis.

CDER approved a new drug to treat patients with Duchenne muscular dystrophy who have a specific gene mutation — offering new hope to approximately 8 percent of patients with this condition.

- **Vyondys 53** (golodirsen) injection, approved under FDA's accelerated approval program (see p. 22) to treat patients with **Duchenne muscular dystrophy** (DMD) who have a confirmed mutation of the dystrophin gene that is amenable to exon 53 skipping. It is estimated that about eight percent of the population with DMD have this mutation. DMD is a rare genetic disorder characterized by progressive muscle deterioration and weakness. It is the most common type of muscular dystrophy.
- **Wakix** (pitolisant) tablets, a new therapy for the treatment of excessive daytime sleepiness in adults with **narcolepsy**, a chronic sleep disorder that causes overwhelming daytime drowsiness. This is the first FDA-approved drug to treat narcolepsy that is not a controlled substance.
- **Xcopri** (cenobamate) tablets, to decrease the frequency of **partial onset seizures** in patients with epilepsy.

CDER approved a new antibiotic to treat patients with community-acquired bacterial pneumonia, a leading cause of illness and death worldwide.

- **Xenleta** (lefamulin) tablets and injection, a first-in-class new antibiotic for the treatment of patients with **community-acquired bacterial pneumonia** — pneumonia that someone gets outside of a hospital, a leading cause of illness and death worldwide. This is the first FDA approval of a pleuromutilin that can be used systemically (ingested or injected into the body as opposed to being applied to the skin).
- **Xpovio** (selinexor) tablets, approved under FDA's accelerated approval program (see p. 22), in combination with the corticosteroid dexamethasone for the treatment of certain adult patients with **relapsed refractory multiple myeloma** (a type of bone marrow cancer) whose disease is resistant after unsuccessfully trying a specific number and types of therapies. While there is no cure for multiple myeloma, there are FDA-approved treatments to target the cancer and slow down the spread of the disease. Unfortunately, over time, patients can often exhaust all available treatments and still have their disease progress. This approval provides a treatment option for patients with multiple myeloma with no available therapy. Multiple myeloma is cancer that begins in plasma cells (white blood cells that produce antibodies) and may also be referred to as plasma cell myeloma. Abnormal plasma cells build up in the bone marrow, forming tumors in many bones of the body. As more antibodies are made, it can cause blood to thicken and keep the bone marrow from making enough healthy blood cells.

Novel Drugs have never before been approved or marketed in the United States and often represent important new therapies for advancing patient care.

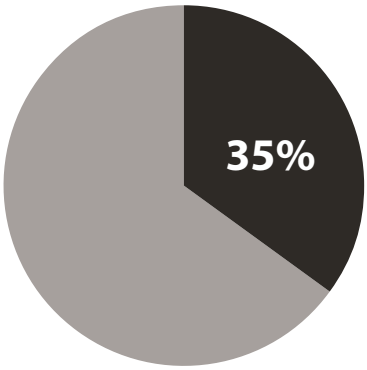
Innovation: Frequent Use of Expedited Development and Review Pathways

CDER used several regulatory pathways to enhance efficiency and expedite the development and approval of novel drugs in 2019. These pathways use a range of approaches, including more interactions between CDER staff and drug developers, greater program design flexibility, and shortened timelines for review of applications.

Fast Track

Fast Track-designated drugs have the potential to address unmet medical needs. CDER designated 17 of the 48 novel drugs (35%) in 2019 as Fast Track. Fast Track speeds new drug development and review by increasing the level of communication between FDA and drug developers, and by enabling CDER to review portions of a drug application ahead of the submission of the complete application.

Drugs designated with Fast Track status were: Cablivi, Caplyta, Egaten, Enhertu, Fetroja, Nubeqa, Oxbryta, pretomanid, Reblozyl, Recarbrio, Scenesse, Trikafta, Vyndaqel, Vyondys 53, Wakix, Xenleta, and Xpovio.

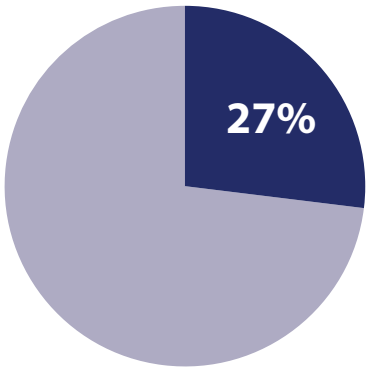


CDER designated 17 of the 48 novel drugs approved in 2019 (35%) as Fast Track.

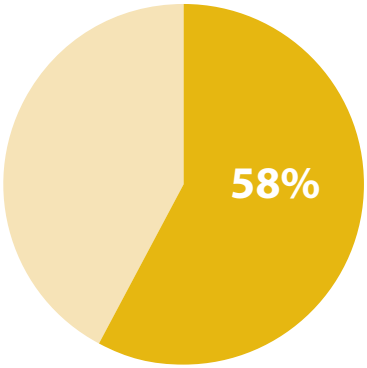
Breakthrough Therapy

Breakthrough therapies are drugs for serious or life-threatening diseases for which there is unmet medical need and for which there is preliminary clinical evidence demonstrating that the drug may result in substantial improvement on a clinically significant endpoint (usually an endpoint that reflects how the patient feels, functions or survives) over other available therapies. CDER designated 13 of the 48 novel drugs (27%) in 2019 as breakthrough therapies. A breakthrough therapy designation includes all the Fast Track program features, as well as more intensive FDA guidance on an efficient drug development program. Breakthrough therapy designation is designed to help shorten the development time of potentially important new therapies.

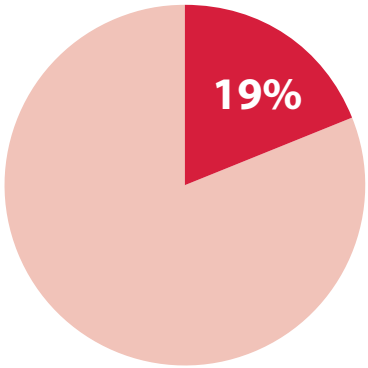
Drugs designated with Breakthrough therapy status were: Adakveo, Balversa, Brukinsa, Enhertu, Givlaari, Oxbryta, Padcev, Polivy, Rozlytrek, Trikafta, Turalio, Vyndaqel, and Zulresso.



CDER designated 13 of the 48 novel drugs approved in 2019 (27%) as Breakthrough therapies.



28 of the 48 novel drugs approved in 2019 (58%) were designated Priority Review.



CDER approved 9 of the 48 novel drugs approved by FDA in 2019 (19%) under the Accelerated Approval program.

Priority Review

A drug receives a Priority Review if CDER determines that the drug could potentially provide a significant advance in medical care. The drug is reviewed in an expedited time line: within eight months instead of the standard 12 months. Twenty-eight of the 48 novel drugs approved in 2019 (58%) were designated Priority Review. *Note, in some instances, priority review is assigned as a result of the sponsor redeeming a voucher for priority review under CDER's Priority Review Voucher program, which may mean the drug does not potentially provide a significant advance. Such drugs are not included in the list below.*

Drugs designated Priority Review were: Adakveo, Balversa, Brukinsa, Cablivi, Egaten, Enhertu, Fetroja*, Givlaari, Inrebic, Nubeqa, Oxbryta, Padcev, Piqray, Polivy, pretomanid*, Reblozyl, Recarbrio*, Rozlytrek, Scenesse, TissueBlue, Trikafta, Turalio, Vyndaqel, Vyondys 53, Wakix, Xenleta*, Xpovio, and Zulresso.

* Fetroja, Recarbrio, and Xenleta received Priority Review as Qualified Infectious Disease Products (QIDPs) as authorized by the Generating Antibiotics Incentives Now Act (GAIN Act), which provides incentives to help bring new antibacterial and antifungal drugs to market. These products may or may not have otherwise received the priority review designation. Pretomanid, also a QIDP-designated approval, received priority review as it met criteria needed for a priority review designation.

Accelerated Approval

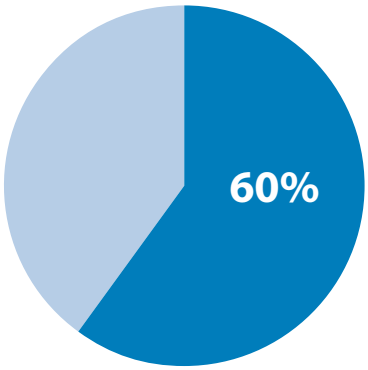
The Accelerated Approval program allows FDA more flexibility in what endpoints can be used to approve a drug that offers a benefit over current treatments for a serious or life-threatening illness. These accelerated approval endpoints may include ones that show benefits over a shorter duration of treatment (where longer term demonstration of benefit is needed for full approval) or are considered as "reasonably likely" to predict an important clinical benefit. Subsequent confirmatory trials must be conducted to support full approval. CDER approved nine of the 48 novel drugs (19%) in 2019 under the Accelerated Approval program. The application of accelerated approval brings drugs that can provide important advances to patients sooner than with traditional approvals.

The Novel drug approved in 2019 that received the Accelerated Approval designation were: Balversa, Brukinsa, Enhertu, Oxbryta, Padcev, Polivy, Rozlytrek, Vyondys 53, and Xpovio.

Overall Use of Expedited Development and Review Methods

Twenty-nine of the 48 novel drug approvals of 2019 (60%) were designated in one or more expedited categories of Fast Track, Breakthrough, Priority Review, and/or Accelerated Approval.

Novel drugs approved in 2019 using at least one expedited approval method were: Adakveo, Balversa, Brukinsa, Cablivi, Caplyta, Egaten, Enhertu, Fetroja, Givlaari, Inrebic, Nubeqa, Oxbryta, Padcev, Piqray, Polivy, pretomanid, Reblozyl, Recarbrio, Rozlytrek, Scenesse, TissueBlue, Trikafta, Turalio, Vyndaqel, Vyondys 53, Wakix, Xenleta, Xpovio, and Zulresso.



29 of the 48 novel drugs approved in 2019 (60%) were designated in one or more expedited categories of Fast Track, Breakthrough, Priority Review, and/or Accelerated Approval.

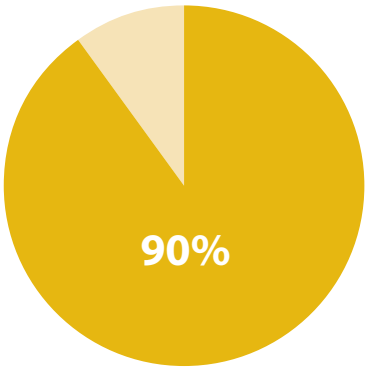
Predictability: Meeting PDUFA Goals

Under the Prescription Drug User Fee Act (PDUFA), sponsors are assessed user fees that provide FDA with the additional resources needed to maintain an efficient and effective review process. Throughout the year, CDER met or exceeded almost every PDUFA goal date for application review agreed to with the pharmaceutical industry and approved by Congress. In 2019, CDER met its PDUFA goal dates for 100% of the novel drugs approved (48 of 48).

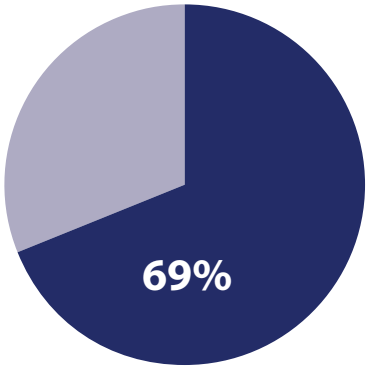
CDER met its PDUFA Goal Date for

100%

of the novel drugs approved in 2019.



CDER approved 43 of the 48 novel approvals of 2019 (90%) on the first cycle of review.



33 of the 48 novel drugs approved by CDER in 2019 (69%) were approved in the United States before receiving approval in any other country.

See Appendix B for a summary chart of designations for CDER's novel drug approvals.

Access: First Cycle Approval and Approvals Compared to Other Countries

First Cycle Approval

CDER approved 43 of the 48 novel drugs of 2019 (90%) on the "first cycle" of review, meaning without a "complete response" letter from FDA that requires re-submission with additional information, resulting in a delay to approval. From 2011 through 2018, CDER approved 309 novel drugs, of which 261 (84%) were approved on the first cycle. This high proportion of first-cycle approval reflects the extent to which CDER staff and drug developers work together to ensure that the studies supporting approval are well designed and that the application contains the information CDER needs to be able to fully review, and if appropriate, approve an application.

First cycle approval prevents delays in bringing valuable new therapies to market.

Novel drugs approved in 2019 on the first cycle were: Accrufer, Adakveo, Aklief, Balversa, Beovu, Brukinsa, Cablivi, Caplyta, Dayvigo, Egaten, Enhertu, ExEm Foam, Fetroja, Ga 68 DOTATOC, Givlaari, Ibsrela, Inrebic, Mayzent, Nubeqa, Oxbryta, Padcev, Piqray, Polivy, pretomanid, Reblozyl, Recarbrio, Reyvow, Rinvoq, Rozlytrek, Scenesse, Skyrizi, Sunosi, TissueBlue, Trikafta, Turalio, Ubrelvy, Vyleesi, Vyndaqel, Wakix, Xcopri, Xenleta, Xpovio, and Zulresso.

Approval in the United States Before Other Countries

Although regulatory processes differ widely between FDA and those of regulatory agencies in other countries, 33 of the 48 novel drugs approved in 2019 (69%) were approved in the United States before receiving approval in any other country.

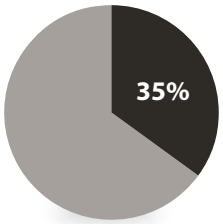
Novel drugs of 2019 approved first in the United States were: Adakveo, Aklief, Balversa, Beovu, Brukinsa, Caplyta, Dayvigo, Enhertu, Fetroja, Givlaari, Ibsrela, Inrebic, Mayzent, Nubeqa, Oxbryta, Padcev, Piqray, Polivy, pretomanid, Reblozyl, Recarbrio, Reyvow, Rinvoq, Sunosi, Trikafta, Turalio, Ubrelvy, Vyleesi, Vyondys 53, Xcopri, Xenleta, Xpovio, and Zulresso.

2019's Novel Drug Approvals

Expedited Review Pathway Usage

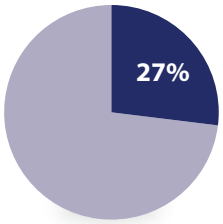
Fast Track (17 of 48)

Cablivi
Caplyta
Egaten
Enhertu
Fetroja
Nubeqa
Oxbryta
pretomanid
Reblozyl
Recarbrio
Scenesse
Trikafta
Vyndaqel
Vyondys 53
Wakix
Xenleta
Xpovio



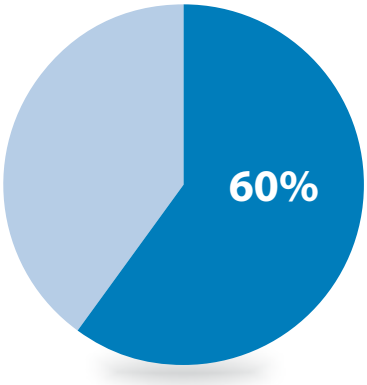
Breakthrough Therapy (13 of 48)

Adakveo
Balversa
Brukinsa
Enhertu
Givlaari
Oxbryta
Padcev
Polivy
Rozlytrek
Trikafta
Turalio
Vyndaqel
Zulresso



Used One or More Expedited Pathway (29 of 48)

Adakveo
Balversa
Brukinsa
Cablivi
Caplyta
Egaten
Enhertu
Fetroja
Givlaari
Inrebic
Nubeqa
Oxbryta
Padcev
Piqray
Polivy
pretomanid
Reblozyl
Recarbrio
Rozlytrek
Scenesse
TissueBlue
Trikafta
Turalio
Vyndaqel
Vyondys 53
Wakix
Xenleta
Xpovio
Zulresso



Priority Review (28 of 48)

Adakveo
Balversa
Brukinsa
Cablivi
Egaten
Enhertu
Fetroja
Givlaari
Inrebic
Nubeqa
Oxbryta
Padcev
Piqray
Polivy
pretomanid
Reblozyl
Recarbrio
Rozlytrek
Scenesse
TissueBlue
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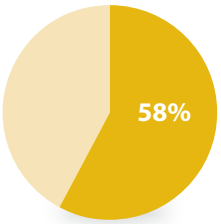
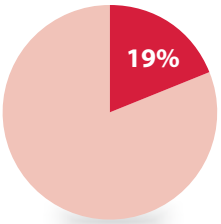
Turalio
Vyndaqel
Vyondys 53
Wakix
Xenleta
Xpovio
Zulresso

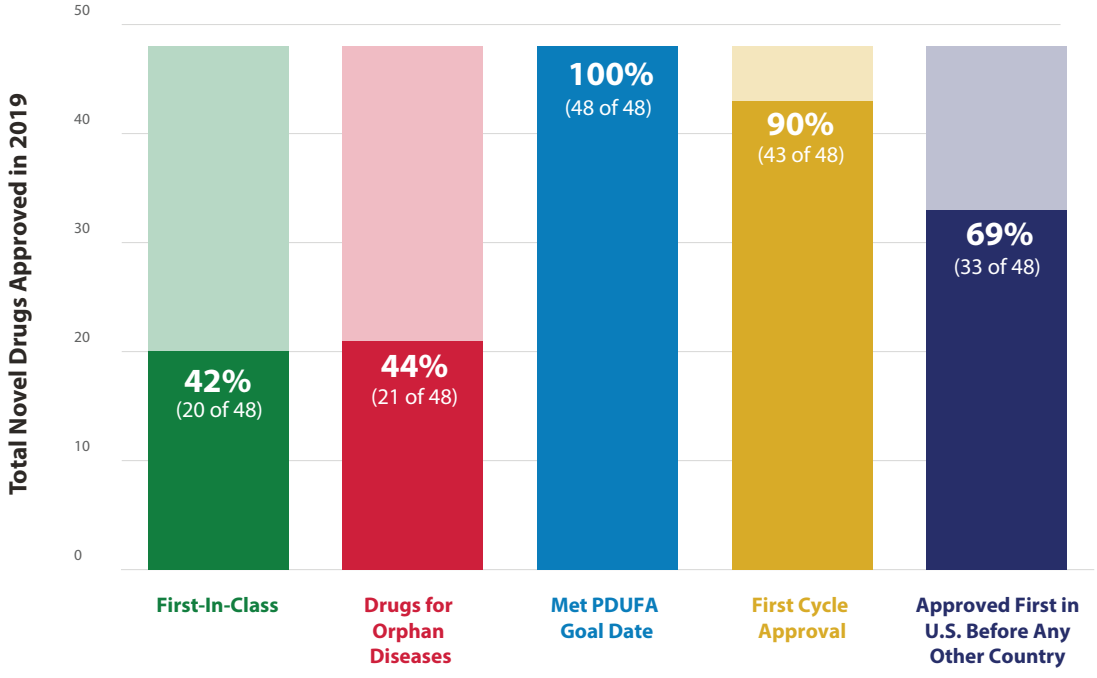


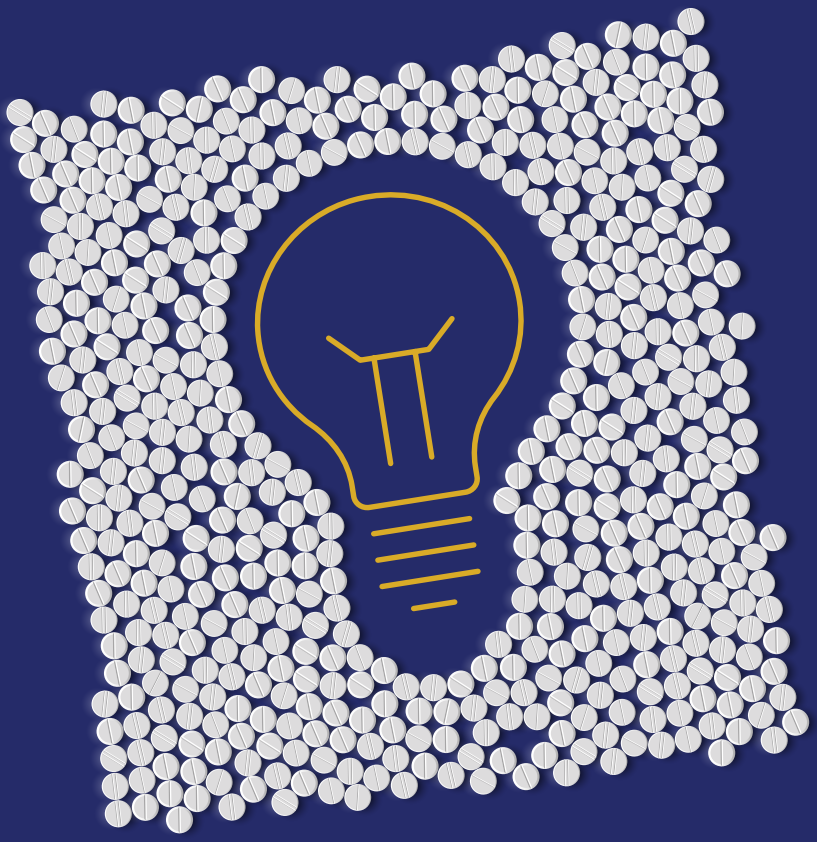
Accelerated Approval (9 of 48)

Balversa
Brukinsa
Enhertu
Oxbryta
Padcev
Polivy
Rozlytrek
Vyondys 53
Xpovio



Other Key Measures





New and Expanded Uses of Already FDA-Approved Drugs

After CDER approves a new drug, it is not uncommon for a manufacturer to submit an application with new data that demonstrate safety and effectiveness of the same product for an additional purpose or for use in a different population of patients. Applications to modify the use of an already-approved drug or to expand its use to other patients are known as "efficacy supplements."

New Uses

The products below are some notable approvals of 2019 for new uses of an already-FDA-approved drug:

- **Calquence** (acalabrutinib) capsules, originally approved in 2017 under the FDA's accelerated approval program to treat patients with mantle cell lymphoma (a form of blood cancer). In 2019, it was approved for the treatment of adults with **chronic lymphocytic leukemia** (CLL) or **small lymphocytic lymphoma** (SLL). CLL and SLL are similar cancers, but CLL occurs mainly in the blood and bone marrow, while SLL occurs mainly in the lymph nodes. This new approval provides a new treatment option for patients with CLL or SLL as an initial or subsequent therapy. The expanded approval for Calquence was part of an ongoing U.S., Australian and Canadian collaboration known as Project Orbis, which provides a framework for concurrent submission and review of oncology drug applications among the FDA's international partners. In addition, this review used the FDA's Real-Time Oncology Review (RTOR) and Assessment Aid pilot programs, which helped CDER approve this application four months prior to the FDA goal date.

- **Cimzia** (certolizumab pegol) injection, originally approved in 2008 to treat certain patient's with Crohn's disease, a chronic inflammatory bowel disease that can cause abdominal cramping and pain. It was approved in 2019 for treatment of adults with a certain type of inflammatory arthritis called **non-radiographic axial spondyloarthritis** (nr-axSpA), with objective signs of inflammation. This is the first time that the FDA has approved a treatment for nr-axSpA. Nr-axSpA causes inflammation in the spine and other symptoms. There is no visible damage seen on x-rays, so it is referred to as non-radiographic.

- **Descovy** (emtricitabine, tenofovir alafenamide fumarate) tablets, originally approved in 2016 for the treatment of patients over 12 years of age with HIV-1 infection. Its approval was expanded in 2019 to **reduce the risk of sexually acquired HIV-1-infection** in at-risk adults and adolescents, excluding people born female (assigned female at birth) who are at risk of getting HIV-1 infection from vaginal sex, because its effectiveness has not been studied. This is the second daily oral drug combination approved for pre-exposure prophylaxis (PrEP), or prevention of HIV infection. Until this approval, the only FDA-approved treatment to help prevent HIV-1 infection was Truvada (emtricitabine and tenofovir disoproxil fumarate).

- **Dupixent** (dupilumab) injection wasoriginally approved in 2017 for certain adult patients with eczema, a condition where patches of skin become inflamed, itchy, red, cracked, and rough. In March of 2019 the indication for eczema was expanded to include the treatment of adolescents age 12 and older. In October 2018, it was approved as an add-on maintenance treatment in patients 12 years of age and older with moderate to severe asthma, with an eosinophilic phenotype or with oral corticosteroid-dependent asthma. In June 2019, dupilumab was approved as add-on treatment for adult patients with inadequately controlled **chronic rhinosinusitis with nasal polyps**. Nasal polyps can lead to loss of smell and often patients require surgery to remove the polyps. This approval provides a treatment option for patients whose nasal polyps are not adequately controlled with intranasal steroids. It also reduces the need for nasal polyp surgery and oral steroids.
- **Emgality** (galcanezumab-gnlm) injection, originally approved in 2018 to prevent migraine, was approved in 2019 for the treatment of episodic cluster headache in adults. It is the first FDA-approved drug that reduces the frequency of attacks of **episodic cluster headache**, a form of headache that produces extreme pain and tends to occur in clusters, often at the same time(s) of the day, for several weeks to months. Cluster headache attacks may strike several times a day, generally lasting between 15 minutes and three hours.
- **Ofev** (nintedanib) capsules, originally approved in 2014 for the treatment of patients with idiopathic pulmonary fibrosis, a serious and sometimes fatal lung disease that results in scarring (fibrosis) of the lungs that gets worse and makes it hard for patients to breathe. In 2019, it was approved by the FDA to slow the rate of decline in pulmonary function in adults with **interstitial lung disease associated with systemic sclerosis or scleroderma**, (SSc-ILD). Scleroderma is a rare disease that causes tissue throughout the body, including the lungs and other organs, to thicken and scar. Interstitial lung disease or ILD is a condition affecting the interstitium, which is part of the lung's structure, and is one of the most common disease manifestations of scleroderma. SSc-ILD is a progressive lung disease in which lung function declines over time, and it can be debilitating and life-threatening. This is the first FDA-approved treatment for this rare lung condition.

Expanding approval of analready-FDA approved drug can be much less costly, and just as effective, as developing a completely new drug.

CDER approved the first FDA-approved drug that reduces the frequency of attacks of episodic cluster headaches, that produce extreme pain and tend to occur at the same time(s) of the day, for several weeks to months.

- **Otezla** (apremilast) tablets for oral ulcers associated with **Behcet's disease**. This is the first approved therapy for oral ulcers associated with this rare disease. Behcet's disease is an inflammatory condition that affects many parts of the body. The most common symptoms include painful mouth sores (ulcers), genital sores, rash, inflammation of parts of the eye, and arthritis. Severe manifestations occur rarely and include inflammation of the brain or spinal cord, blood clots, aneurysms, or blindness. Otezla was initially approved in 2014 for adult patients with active psoriatic arthritis and later that year for patients with moderate-to-severe plaque psoriasis who are candidates for phototherapy or systemic therapy.

- **Soliris** (eculizumab), injection for the treatment of certain adult patients with **neuromyelitis optica spectrum disorder** (NMOSD), an autoimmune disease of the central nervous system. This approval provides the first FDA-approved treatment for NMOSD, a debilitating disease that profoundly impacts patients' lives. In patients with NMOSD, the body's immune system mistakenly attacks healthy cells and proteins in the body, most often in the optic nerves and spinal cord. Individuals with NMOSD typically have attacks of optic neuritis, which causes eye pain and vision loss. Individuals also can have attacks resulting in transverse myelitis, which often causes numbness, weakness, or paralysis of the arms and legs, along with loss of bladder and bowel control. Most attacks occur in clusters, days to months to years apart, followed by partial recovery during periods of remission. Approximately 48 percent of patients with NMOSD have permanent visual impairment and paralysis caused by NMOSD attacks. Soliris was first approved by the FDA in 2007 for the treatment of patients with paroxysmal nocturnal hemoglobinuria (PNH), a rare acquired, life-threatening disease of the blood, characterized by destruction of red blood cells, blood clots, and impaired bone marrow function.

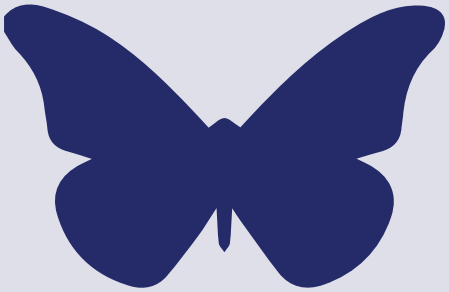
- **Ultomiris** (ravulizumab-cwvz) injection, originally approved in 2018 to treat patients with paroxysmal nocturnal hemoglobinuria, a sometimes-life-threatening blood disease that varies in intensity by individual. Its approval was expanded in 2019 to include treatment of patients one month of age and older with **atypical hemolytic uremic syndrome** to inhibit complement-mediated thrombotic microangiopathy, a condition that causes abnormal blood clots to form in small blood vessels in the kidneys. These clots can cause serious medical problems if they restrict or block blood flow.

- **Vascepa** (icosapent ethyl), capsules, originally approved in 2012 to help reduce severely elevated levels of triglycerides (500 milligrams per deciliter or higher), along with diet and exercise, in adult patients. High levels of triglycerides, a type of fat in the blood, can increase the risk of heart disease and heart attack or stroke (cardiovascular events). This drug's approval was expanded in 2019 as an adjunctive (secondary) therapy to **reduce the risk of cardiovascular events** among certain adults with elevated triglyceride levels of 150 milligrams per deciliter or higher. This is the first FDA approved drug to reduce cardiovascular risk among patients with elevated triglyceride levels as an add-on to maximally tolerated statin therapy. Statins are drugs used to treat elevated cholesterol levels and reduce the risk of cardiovascular events.

New Populations

The products listed below are notable approvals in 2019 of an already FDA-approved drug for use in an expanded population of patients:

- **Benlysta** (belimumab) intravenous (IV) infusion for treatment of children with **systemic lupus erythematosus** (SLE) — often referred to as simply "lupus" — a serious chronic disease that causes inflammation and damage to various body tissues and organs. This is the first time that the FDA has approved a treatment for pediatric patients with SLE. Benlysta has been approved for use in adult patients since 2011.
- **Darzalex** (daratumumab) injection, originally approved in2015 for the treatment of patients with multiple myeloma (a type of bone marrow cancer) who were previously treated unsuccessfully with three other specific therapies. It was approved in 2019 to be used combination with certain other already FDA-approved medications for the treatment of patients **newly diagnosed with multiple myeloma** who are ineligible for a bone marrow transplant.
- **Entresto** (sacubitril and valsartan) tablets, first approved by CDER in 2015 to reduce the risk of cardiovascular death or heart failure hospitalization in adult patients with chronic heart failure and reduced ejection fraction (a measure of how much blood the heart pumps with each beat). In 2019, CDER approved this drug for the treatment of certain patients aged one year and older with **heart failure** (the tablets can be made into an oral suspension for patients unable to swallow the tablet).



CDER approved the first treatment for children with systemic lupus erythematosus.

- **Fragmin** (dalteparin sodium), a low molecular weight heparin product, sometimes called a "blood thinner." It was originally approved in 1994 to avoid blockages in blood vessels to help prevent or avoid complications of unstable angina and a certain type of myocardial infarction. It was also approved at that time to prevent deep vein thrombosis (DVT) following certain types of surgery and for the extended treatment of symptomatic venous thromboembolism (VTE) to reduce the recurrence in patients with cancer. In 2019, Fragmin became the first ever drug approved for anticoagulation in pediatric patients and it was approved to reduce the recurrence of symptomatic **venous thromboembolism** (VTE) in pediatric patients one month of age and older. VTE can include deep vein thrombosis (blood clot in the deep veins of the leg) and pulmonary embolism (blood clot in the lungs), which can lead to death. Most children who have VTE are fighting a serious underlying primary illness such as cancer or congenital heart disease. Prior to this approval, there were no FDA-approved therapies to treat VTE in pediatric patients. VTE usually develops as a secondary complication of underlying clinical conditions such as a venous catheter, cancer, infection, congenital heart disease, and trauma or surgery. Pediatric VTE is associated with an increased risk of in-hospital mortality, recurrent VTE and post-thrombotic syndrome (damage to vein).
- **Kadcyla** (ado-trastuzumab emtansine) injection, originally approved in 2013 for the treatment of certain patients with HER2-positive, metastatic breast cancer (breast cancer that has spread to other parts of the body), was approved in 2019 for use in certain patients with **HER2-positive early breast cancer**. This approval represents a significant treatment advance, as the drug is now approved to be available for some patients much sooner than previously, which can help reduce the risk of disease recurrence. CDER rapidly reviewed and approved the application under the FDA's Real-Time Oncology Review (RTOR) and Assessment Aid pilot programs, leading to an approval 12 weeks after the drug's application was submitted.
- **Rituxan** (rituximab) injection, first approved by FDA in 1997 to treat patients with non-Hodgkin's lymphoma, a type of blood cancer. It was subsequently approved by the FDA for a variety of other uses, including, in 2011, use as a treatment for adults with the rare vascular diseases, **granulomatosis with polyangiitis** (GPA) and **microscopic polyangiitis** (MPA), in combination with glucocorticoids

CDER approved a new use for an already FDA-approved cystic fibrosis drug to treat certain patients as young as 6 years of age, which previously was approved only for certain patients 12 years of age or older.

(steroid hormones). In 2019 it was approved for use in children as young as age two. This is the first approved pediatric treatment for these rare vasculitis diseases, in which a patient's small blood vessels become inflamed, reducing the amount of blood that can flow through them.

- **Sovaldi** (sofosbuvir) and **Harvoni** (ledipasvir/sofosbuvir), first approved in 2013 and 2014 respectively, each to treat certain adults infected with the **hepatitis C** virus (HCV). In 2017, both drugs were also approved to treat children aged 12 to 17 years (Sovaldi for genotypes 2 or 3 and Harvoni for genotypes 1, 4, 5, or 6). In 2019, CDER expanded these approvals to include children aged 3 to 17 years.
- **Symdeko** (tezacaftor/ivacaftor; ivacaftor) tablets for treatment of pediatric patients ages 6 years and older with **cystic fibrosis** who have certain genetic mutations. In 2018, the FDA approved Symdeko to treat patients ages 12 and older who had the same specific genetic mutations. Cystic fibrosis is a serious genetic disorder that results in the formation of thick mucus that builds up in the lungs, digestive tract and other parts of the body. It leads to severe respiratory and digestive problems as well as other complications such as infections and diabetes.
- **Victoza** (liraglutide) injection, originally approved in 2010 to treat adult patients with **type 2 diabetes**, it was approved in 2019 for the treatment of pediatric patients 10 years or older with type 2 diabetes. This is the first non-insulin drug approved to treat type 2 diabetes in pediatric patients since metformin was approved for pediatric use in 2000. The expanded indication provides an additional treatment option at a time when an increasing number of children are being diagnosed with this disease. Type 2 diabetes is the most common form of diabetes, occurring when the pancreas cannot make enough insulin to keep blood sugar at normal levels. Although type 2 diabetes primarily occurs in patients over the age of 45, the prevalence rate among younger patients has been rising dramatically over the past couple of decades. Liraglutide improves blood sugar levels by creating the same effects in the body as the glucagon-like peptide (GLP-1) receptor protein in the pancreas.

CDER approved the first non-insulin drug approved to treat type 2 diabetes in pediatric patients since metformin was approved for pediatric use in 2000.

Additional Approvals

In addition to the many notable novel drug and efficacy supplement approvals of 2019, CDER approved a variety of other therapies. Among these are **biosimilars**, and **new formulations**, **manufacturers**, **combinations**, or **dosage forms** of already FDA-approved drugs, as well as others. Below are notable examples of these various types of approvals.

Biosimilars

Biosimilars expand treatment options and bring competition to the U.S. marketplace.

An FDA-approved biosimilar is a biological product that is highly similar to and has no clinically meaningful differences in terms of safety, purity and potency (safety and effectiveness) from an already FDA-approved product, called the reference product. Biological products are highly complex, and often used to treat patients with serious and life-threatening conditions. The law allowing FDA to approve biosimilars was designed to create competition, increase patient access, and potentially reduce cost of important therapies.

In 2019, CDER approved ten new biosimilars:

- **Avsola** (infliximab-axxq), the fourth biosimilar to Remicade (infliximab), approved for a variety of uses including, Crohn's disease, pediatric Crohn's disease, ulcerative colitis, pediatric ulcerative colitis, rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, plaque psoriasis. CDER approved Inflectra (infliximab-dyyb) in 2016, and Ixifi (infliximab-qbtx) and Renflexis (infliximab-abda) in 2017.
- **Eticovo** (etanercept-ykro), the second biosimilar to Enbrel (etanercept). It is approved to treat the same conditions as Enbrel, which include rheumatoid arthritis, various other forms of arthritis and plaque psoriasis. CDER approved the first Enbrel biosimilar, Erelzi (etanercept-szzs), in 2016.
- **Hadlima** (adalimumab-bwwd) and **Abrilada** (adalimumab-afzb) respectively the fourth and fifth biosimilars to Humira (adalimumab). These drugs are tumor necrosis factor (TNF) inhibitors that suppress the immune system. They are approved for a variety of uses, including rheumatoid arthritis, juvenile idiopathic arthritis in patients 4 years and older, ankylosing spondylitis, adult Crohn's disease, ulcerative colitis, psoriatic arthritis, and plaque psoriasis. CDER approved Amjevita (adalimumab-atto), the first biosimilar to Humira, in 2016. The second, Cyltezo (adalimumab-adbm), was approved in 2017, and the third, Hyrimoz (adalimumab-adaz), was approved in 2018.
- **Ontruzant** (trastuzumab-dttb), **Trazimera** (trastuzumab-qyyp), and **Kanjinti** (trastuzumab-anns) respectively, the third, fourth, and fifth biosimilars to Herceptin (trastuzumab), to treat patients with breast or metastatic stomach cancer (gastric or gastroesophageal junction adenocarcinoma) whose tumors overexpress the HER2 gene. CDER approved the first Herceptin biosimilar, Ogivri (trastuzumab-dkst), in 2017 and the second, Herzuma (trastuzumab-pkrb), in 2018.
- **Ruxience** (rituximab-pvvr), the second biosimilar to Rituxan (rituximab), approved to treat adult patients with CD-20-positive, B-cell non-Hodgkin's lymphoma, a type of blood cancer, to be used as a single agent or in combination with chemotherapy, and to treat CD-20-positive, chronic lymphocytic leukemia (a type of blood cancer) in combination with chemotherapy. Ruxience is also the first biosimilar approved to treat adult patients with granulomatosis with polyangiitis (sometimes called

Wegener's granulomatosis, inflammation of blood vessels and other internal parts of the body), and microscopic polyangiitis (blood vessel inflammation). CDER approved the first biosimilar to Rituxan, Truxima (rituximab-abbs), in 2018.

- **Ziextenzo** (pegfilgrastim-bmez), the third biosimilar to Neulasta (pegfilgrastim) approved to treat patients with cancer receiving myelosuppressive chemotherapy. CDER approved the first and second biosimilars to Neulasta, Fulphila (pegfilgrastim-jmdb) and Udenyca (pegfilgrastim-cbqv), in 2018.
- **Zirabev** (bevacizumab-bvzr), the second biosimilar to Avastin (bevacizumab). Zirabev is a monoclonal antibody used to prevent the growth of certain types of tumors. It is FDA-approved for the following indications currently approved for U.S.-licensed Avastin: metastatic colorectal cancer; non-squamous non-small cell lung cancer; glioblastoma (cancer originating in the brain); metastatic renal cell carcinoma (a type of kidney cancer that has spread to other parts of the body), and cervical cancer. CDER approved the first Avastin biosimilar, Mvasi (bevacizumab-awwb), in 2017.

CDER has now approved a total of 26 biosimilars for nine different reference products since 2015. This includes at least one biosimilar for each of these top selling biological drugs in the United States: Humira, Rituxan, Enbrel, Herceptin, Avastin, Remicade, and Neulasta. Two biological reference products (Humira and Herceptin) now have five biosimilars; one (Remicade) has four biosimilars; one reference product (Neulasta) has three biosimilars, four reference products (Avastin, Enbrel, Neupogen, and Rituxan) have two biosimilars and one reference product (Epogen/Procrit) has one biosimilar. Multiple biosimilars for an FDA-approved reference product can strengthen market competition. An increase in market competition may lead to significantly reduced costs for both patients and our healthcare system.

New Formulations and Other Notable Approvals

A new formulation of a drug is one in which the product's active ingredient is already FDA-approved. New formulations of already-approved drugs can offer significant advances in therapy. Below are **notable new formulations** as well as other notable non-novel drug approvals of 2019, including, but not limited to, those with a **new combination of active ingredients** or a **new manufacturer** of an already FDA-approved drug.

- **Dovato** (dolutegravir and lamivudine), a combination of two previously approved drugs. It is a complete regimen for the treatment of **human immunodeficiency virus type 1** (HIV-1) infection in adults with no antiretroviral treatment history and with no known or suspected substitutions associated with resistance to the individual components of Dovato. This is the first FDA-approved two-drug, fixed-dose, complete regimen for HIV-infected adults who have never received treatment for HIV. Currently, the standard of care for patients who have never been treated is a three-drug regimen. With this approval, patients who have never been treated have the option of taking a two-drug regimen in a single tablet while eliminating additional toxicity and potential drug interactions from a third drug.

CDER approved the first FDA-approved two-drug, fixed-dose, complete regimen for HIV-infected adults who have never received treatment for HIV.

- **Hemady** (dexamethasone) tablets. Dexamethasone is a widely used anti-inflammatory steroid, originally approved in 1958, and now available in many dosage forms used to treat many different conditions such as allergic disorders, skin conditions, ulcerative colitis, arthritis, lupus, psoriasis, and breathing disorders. This new formulation, a 20 mg tablet of dexamethasone, was approved for the first time in 2019 to be used in combination with other medications to treat patients with **multiple myeloma** (a type of bone cancer) [see Darzalex, p. 29, and Xpovio, p. 20].

- **Ruzurgi** (amifampridine), for the treatment of **Lambert-Eaton myasthenic syndrome** (LEMS) in patients 6 to less than 17 years of age. This is the first FDA approval of a treatment specifically for pediatric patients with LEMS. The other treatment approved for LEMS is approved for use only in adults. LEMS is a rare autoimmune disorder that affects the connection between nerves and muscles and causes weakness and other symptoms in affected patients. In people with LEMS, the body's own immune system attacks the neuromuscular junction (the connection between nerves and muscles) and disrupts the ability of nerve cells to send signals to muscle cells. LEMS may be associated with other autoimmune diseases, but more commonly occurs in patients with cancer such as small cell lung cancer, where its onset precedes or coincides with the diagnosis of cancer. LEMS can occur at any age. The prevalence of LEMS specifically in pediatric patients is not known, but the overall prevalence of LEMS is estimated to be three per million individuals worldwide.

2019 saw the first FDA approval of a treatment specifically for pediatric patients — ages 6 to 17 years of age — with Lambert-Eaton myasthenic syndrome.

CDER approved a new nasal spray treatment for adults with **depression** who have tried other medications without success.

- **selenious acid** injection, which provides a **source of selenium**, an essential trace element that is to be added to parenteral nutrition (feeding through an intravenous line) for adults and children who cannot be given food or medication by mouth. The body needs selenious acid to make certain proteins. It helps to maintain metabolic processes, including defense against oxidative stress, regulation of thyroid hormone metabolism, and how vitamin C and other molecules contribute to optimal human health. Inadequate selenium intake can lead to selenium deficiency which has been known to be associated with conditions such as enlargement of the heart, muscle weakness and nail changes. Prior to this approval, selenious acid injection was marketed in different forms, but was not FDA-approved.
- **Spravato** (esketamine) nasal spray, closely related chemically to the drug ketamine, originally approved in 1970 under the trade name Ketalar as an injectable anesthetic for certain diagnostic and surgical procedures. Esketamine was approved in 2019 as a nasal spray, to be used in conjunction with an oral antidepressant, for the treatment of **depression** in adults who have tried other antidepressant medicines but have not benefited from them (treatment-resistant depression). Patients with major depressive disorder who, despite trying at least two antidepressant treatments given at adequate doses for an adequate duration in the current episode, have not responded to treatment are considered to have treatment-resistant depression.

New Dosage Forms and New Dosing Regimes

New dosage forms and new dosing regimens for already FDA-approved drugs can improve patient health by helping to increase patient adherence to therapy, ensure a proper dose is taken, and improve quality of life for patients who must use the medication on a prolonged basis. Notable approvals in this category include:

- **Avaclyr** (acyclovir) ophthalmic ointment, for the treatment of a type of inflammation of the cornea of the eye called **acute herpetic keratitis** in patients with herpes simplex virus (HSV) 1 or 2 infection caused by recurrent HSV infection in the cornea. With the discontinuation of all other ophthalmic antiviral ointments several years ago, this is now the only available FDA-approved ophthalmic antiviral ointment.

- **Baqsimi** (glucagon), nasal powder, approved to treat patients with diabetes ages four and older who have **severe hypoglycemia** — which occurs when a patient's blood sugar level falls to a point where he or she becomes confused or unconscious or suffers from other symptoms that require assistance from another person to treat. Until this approval, people suffering from a severe hypoglycemic episode had to be treated with a glucagon injection that first had to be mixed in a several-step process. This new way to administer glucagon may simplify the process, which can be critical during an episode, especially since the patient may have lost consciousness or may be having a seizure.
- **Corlanor** (ivabradine), originally approved in 2015 in tablet form for the treatment of to reduce the risk of hospitalization for worsening heart failure in certain patients with stable, symptomatic chronic heart failure. In 2019, CDER approved a new dosage form of an oral solution for the treatment of certain pediatric patients ages six months and older with stable symptomatic heart failure due to **dilated cardiomyopathy**.
- **Jatenzo** (testosterone undecanoate), an oral testosterone capsule to treat men with certain forms of **hypogonadism**. These men have low testosterone levels due to specific medical conditions, such as genetic disorders like Klinefelter syndrome or tumors that have damaged the pituitary gland. It should not be used to treat men with "age-related hypogonadism," in which testosterone levels decline due to aging, even if these men have symptoms that appear to be related to low testosterone. Until this approval, testosterone replacement therapies have most commonly been applied to the skin or injected.
- **Mavenclad** (cladribine) oral tablets, to treat certain relapsing forms of **multiple sclerosis** (MS) in adults, and generally recommended for patients who have had an inadequate response to, or are unable to tolerate, an alternate drug indicated for the treatment of MS. MS is a chronic, inflammatory, autoimmune disease of the central nervous system that disrupts communications between the brain and other parts of the body. Cladribine was originally approved in 1993, under the trade name Leustatin, as an injectable drug to treat a type of blood cancer called hairy cell leukemia.

CDER approved a new oral testosterone capsule to treat men with non-age-related low testosterone levels due to specific medical conditions. Until this approval, therapy for such conditions have most commonly been applied to the skin or injected.

- **Mavyret** (glecaprevir and pibrentasvir) tablets, originally approved in 2017 as a therapy with eight week's duration to treat adults with **chronic hepatitis C virus** (HCV) genotypes 1–6 without cirrhosis (liver disease) or with mild cirrhosis. It was the first treatment of eight weeks duration approved for all HCV genotypes 1–6 in adult patients without cirrhosis who have not been previously treated (treatment-naïve). In 2019, CDER expanded the approval of this drug's eight-week duration therapy to include patients ages 12 years and older or weighing at least 99 pounds who have HCV genotype 1–6 infection and compensated cirrhosis and who are treatment-naïve. This is now the first eight-week treatment approved for all treatment-naïve adult and certain pediatric patients with HCV genotypes 1–6 both without cirrhosis and with compensated cirrhosis. Standard treatment length for patients with compensated cirrhosis was previously 12 weeks or more.
- **Rybelsus** (semaglutide) tablets, to improve control of blood sugar in adult patients with **type 2 diabetes**, along with diet and exercise. This is the first medication in the drug class, "glucagon-like peptide (GLP-1) receptor protein" approved for use in the United States that does not need to be injected. GLP-1 drugs are non-insulin treatments for people with type 2 diabetes. This new formulation of semaglutide can make it easier for patients to control their condition without injections. Semaglutide injectable, was originally approved by the FDA in 2017 under the trade name Ozempic — as an adjunct to diet and exercise to improve glycemic control (blood sugar levels) in adults with type 2 diabetes.

As with all FDA-approved products, the new drug therapies discussed in this report have risks. **For more information about these drugs and for complete risk information, see the drugs' approval letters and FDA-approved labeling at Drugs@FDA.**

Conclusion

CDER's staff consists of individuals with a range of expertise, including physicians, safety evaluators, chemists, biologists, biostatisticians, nurses, pharmacists, pharmacologists, epidemiologists, legal and regulatory experts, and many more. They work together to bring safe and effective drug therapies to the American public as efficiently as possible.

These therapies come in the form of novel drugs never before marketed in the United States, other new drugs that add important medical value, already FDA-approved products approved for new uses and for administration to new populations of patients, and new dosage forms of products designed to offer advantages over earlier versions.

More important than the quantity of the new therapies is their medical value and the important new roles these drugs are serving to advance patient care.

Also noteworthy is the efficiency with which these drugs were reviewed and approved. CDER used a variety of expedited development and regulatory review tools to help speed these drugs to market.

In all cases, CDER maintains its rigorous standards for demonstration of safety and efficacy while striving for efficiency of review of applications for new drug therapies.

Our drug therapy approvals of 2019 will help many patients in need for years to come. However, CDER's mission goes well beyond critically reviewing the safety and efficacy of drug applications we receive from industry. We also look to advance the science and technology that can lead to future innovative drugs — many of which may not yet even be conceived. We are working to develop more innovative and efficient approaches for the development and study of the drug therapies that will emerge from these technological advances.

Although our regulatory work extends to many scientific, clinical, and technological areas, we cannot accomplish all that is necessary on our own. CDER works collaboratively with a wide range of stakeholders across the medical community, including academia, industry, patients and their caregivers, patient advocacy groups, state and other federal agencies, and more. Listening has become an important component of our work. We strive to ensure that we understand the needs of our key constituencies and that we are providing the most benefit for patients and the strongest possibilities for improved public health in America.

Although not a comprehensive compilation of our approvals for the year, this report serves to provide a wide variety of valuable examples of the many ways CDER approves new drug therapies to enhance patient health.

Appendix A:
CDER's Novel Approvals of 2019 (In alphabetical order)

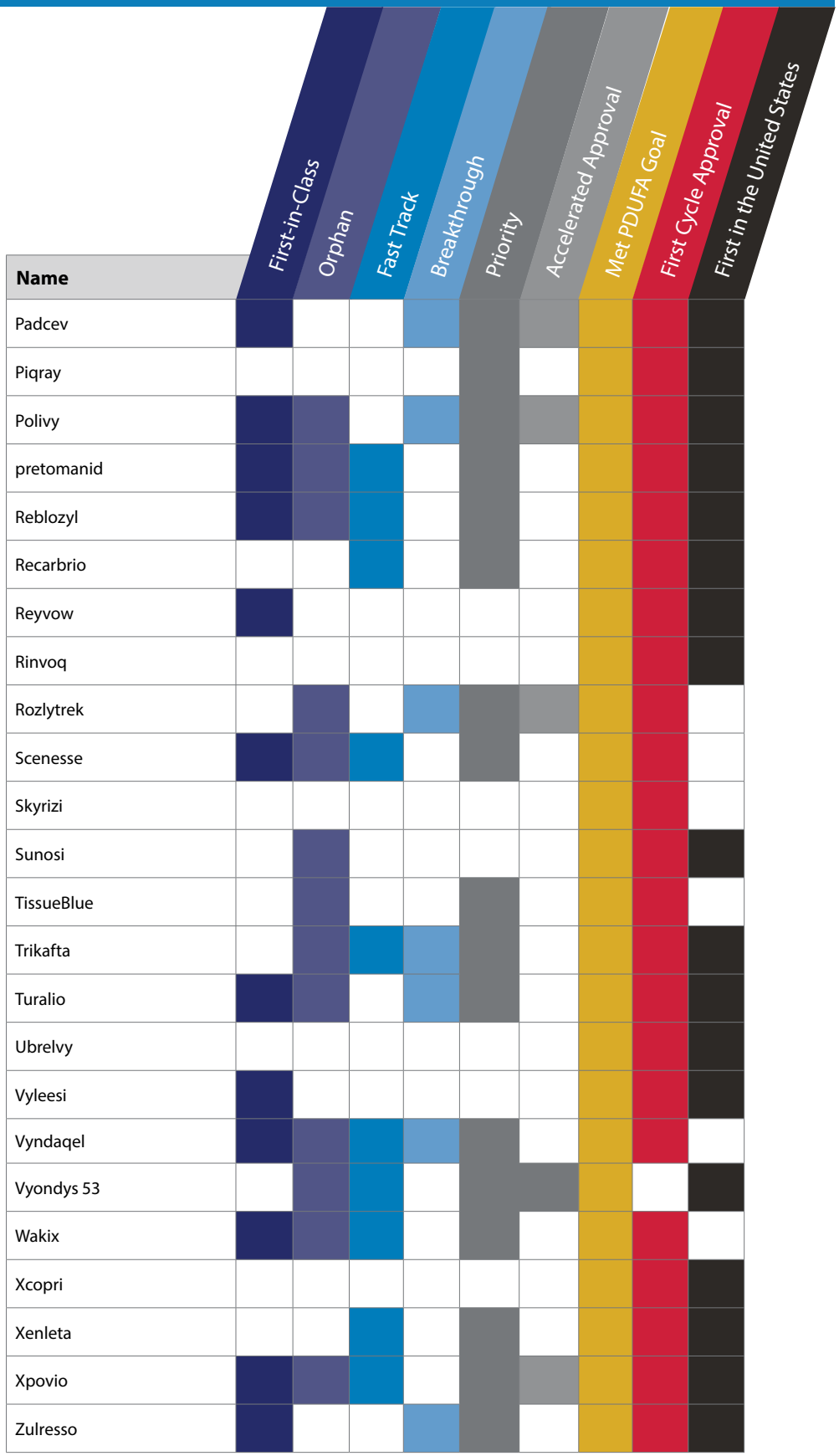
For information about vaccines, allergenic products, blood and blood products, cellular and gene therapy products go to 2019 Biological License Application Approvals.

Approval Date	Trade Name	Active Ingredient(s)	Summary of FDA-approved use on Approval date (see Drugs@FDA for complete indication)	Dosage Form
7/25/19	Accrufer	ferric maltol	Iron deficiency anemia	Capsule
11/15/19	Adakveo	crizanlizumab-tmca	Reduce vasoocclusive crises in sickle cell disease	Injection
10/4/19	Aklief	trifarotene	Acne vulgaris	Cream
4/12/19	Balversa	erdafitinib	Locally advanced or metastatic bladder cancer	Tablet
10/7/19	Beovu	brolucizumab-dbll	Wet age-related macular degeneration	Injection
11/14/19	Brukinsa	zanubrutinib	Mantle cell lymphoma	Capsule
2/6/19	Cablivi	caplacizumab-yhdp	Acquired thrombotic thrombocytopenic purpura	Injection
12/20/19	Caplyta	lumateperone	Schizophrenia	Capsule
12/20/19	Dayvigo	lemborexant	Insomnia	Tablet
2/13/19	Egaten	triclabendazole	Fascioliasis	Tablet
12/20/19	Enhertu	fam-trastuzumab deruxtecan-nxki	Metastatic breast cancer	Injection
4/9/19	Evenity	romosozumab-aqqg	Osteoporosis	Injection
11/7/19	ExEm Foam	air polymer-type A	Diagnostic agent for fallopian tube assessment	Foam
11/14/19	Fetroja	cefiderocol	Complicated urinary tract infection	Injection
10/10/19		fluorodopa F 18	Diagnostic agent for Parkinsonian syndromes	Injection
8/21/19		Ga 68 DOTATOC	Diagnostic agent for neuroendocrine tumors	Injection
11/20/19	Givlaari	givosiran	Acute hepatic porphyria	Injection
9/12/19	Ibsrela	tenapanor	Irritable bowel syndrome with constipation	Tablet
8/16/19	Inrebic	fedratinib	Certain types of myelofibrosis	Capsule
2/1/19	Jeuveau	prabotulinumtoxinA-xvfs	Improve appearance of glabellar lines (lines between eyebrows)	Injection
3/26/19	Mayzent	siponimod	Relapsing forms of multiple sclerosis	Tablet
8/27/19	Nourianz	istradefylline	Parkinson's disease "off" episodes	Tablet
7/30/19	Nubeqa	darolutamide	Non-metastatic prostate cancer	Tablet
11/25/19	Oxbryta	voxelotor	Sickle cell disease	Tablet

Approval Date	Trade Name	Active Ingredient(s)	Summary of FDA-approved use on Approval date (see Drugs@FDA for complete indication)	Dosage Form
12/18/19	Padcev	enfortumab vedotin-ejfv	Refractory bladder cancer	Injection
5/24/19	Piqray	alpelisib	Advanced or metastatic breast cancer	Tablet
6/10/19	Polivy	polatuzumab vedotin-piiq	Relapsed or refractory diffuse large B-cell lymphoma	Injection
8/14/19		pretomanid	Treatment-resistant forms of tuberculosis	Tablet
11/8/19	Reblozyl	luspatercept-aamt	Anemia associated with beta thalassemia	Injection
7/16/19	Recarbrio	imipenem, cilastatin, relebactam	Complicated urinary tract infections and complicated intra-abdominal infections	Injection
10/11/19	Reyvow	lasmiditan	Migraine with or without aura	Tablet
8/16/19	Rinvoq	upadacitinib	Moderately to severely active rheumatoid arthritis	Tablet
8/15/19	Rozlytrek	entrectinib	Metastatic non-small cell lung cancer and locally advanced or metastatic solid tumors with a specific genetic defect	Capsule
10/8/19	Scenesse	afamelanotide	Increase pain-free light exposure in patients with erythropoietic protoporphyria	Implant
4/23/19	Skyrizi	risankizumab-rzaa	Moderate-to-severe plaque psoriasis	Injection
3/20/19	Sunosi	Solriamfetol	Excessive daytime sleepiness in patients with narcolepsy or obstructive sleep apnea	Tablet
12/20/19	TissueBlue	brilliant blue G	Dye used in eye surgery	Ophthalmic Solution
10/21/19	Trikafta	elexacaftor, tezacaftor, ivacaftor	Cystic Fibrosis	Tablet
8/2/19	Turalio	pexidartinib	Symptomatic tenosynovial giant cell tumor	Capsule
12/23/19	Ubrelvy	ubrogepant	Migraine	Tablet
6/21/19	Vyleesi	bremelanotide	Hypoactive sexual desire disorder in premenopausal women	Injection
5/3/19	Vyndaqel	tafamidis meglumine	Cardiomyopathy caused by transthyretin-mediated amyloidosis	Capsule
12/12/19	Vyondys 53	golodirsen	Duchenne muscular dystrophy	Injection
8/14/19	Wakix	pitolisant	Excessive daytime sleepiness in patients with narcolepsy	Tablet
11/21/19	Xcopri	cenobamate	Partial-onset seizures	Tablet
8/19/19	Xenleta	lefamulin	Community-acquired bacterial pneumonia	Tablet/Injection
7/3/19	Xpovio	selinexor	Relapsed or refractory multiple myeloma	Tablet
3/19/19	Zulresso	brexanolone	Postpartum depression	Injection

Appendix B:
Novel Drug Designation Summary
(In alphabetical order)

Name	First-in-Class	Orphan	Fast Track	Breakthrough	Priority	Accelerated Approval	Met PDUFA Goal	First Cycle Approval	First in the United States
Accrufer									
Adakveo									
Aklief									
Balversa									
Beovu									
Brukinsa									
Cablivi									
Caplyta									
Dayvigo									
Egaten									
Enhertu									
Evenity									
ExEm Foam									
Fetroja									
fluorodopa F 18									
Ga 68 DOTATOC									
Givlaari									
Ibsrela									
Inrebic									
Jeuveau									
Mayzent									
Nourianz									
Nubeqa									
Oxbryta									



Name
Padcev
Piqray
Polivy
pretomanid
Reblozyl
Recarbrio
Reyvow
Rinvoq
Rozlytrek
Scenesse
Skyrizi
Sunosi
TissueBlue
Trikafta
Turalio
Ubrelvy
Vyleesi
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