Pediatric Labeling of Orphan Drugs

Required by Section 505 of the FDA Reauthorization Act of 2017 (Public Law 115-52)

Report to Congress

Department of Health and Human Services
Food and Drug Administration

Department of Health and Human Services
Food and Drug Administration

TABLE OF CONTENTS

EXECUTIVE SUMMARY 1
I. BACKGROUND 2
II. ASSESSMENT 4
A. Methods 4
B. Findings 5
III. CONCLUSION AND POLICY RECOMMENDATION 8

EXECUTIVE SUMMARY

The FDA Reauthorization Act of 2017 (FDARA)(Public Law 115-32), enacted on August 18, 2017, required in section 505, that the Secretary of Health and Human Services report by August 18, 2019, on the lack of information in the labeling of drugs for indications that have received an orphan designation under section 526 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 360bb) with respect to the use of such drugs in pediatric populations.[1] Section 505 of FDARA states that;

> *"Not later than 2 years after the date of the enactment of this Act, the Secretary of Health and Human Services shall submit to the Committee on Health, Education, Labor and Pensions of the Senate and the Committee on Energy and Commerce of the House of Representatives, and make publicly available, including through posting on the internet website of the Food and Drug Administration, a report on the lack of information in the labeling of drugs for indications that have received an orphan designation under section 526 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360bbb) with respect to the use of such drugs [in] pediatric populations."*

The report must include:

> *"(A) a list of drugs for which—*
> *(i) an indication was granted an orphan designation under section 526 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360bbb);*
> *(ii) an application described under section 505B(a)(1) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355c(a)(1)) for such indication was submitted to the Secretary of Health and Human Services on or after April 1, 1999; and*
> *(iii) the labeling for such indication lacks important pediatric information, including information related to safety, dosing, and effectiveness;*
> *(B) a description of the lack of information referred to in subparagraph (A)(iii) for each drug for an indication on such list; and*
> *(C) Federal policy recommendations to improve the labeling of drugs for indications that have received an orphan designation under such section 526 with respect to the use of such drugs [in] pediatric populations."*

This report, submitted in accordance with the requirements under FDARA, contains information on drugs granted an orphan designation which lack pediatric information for the orphan indication. The Food and Drug Administration (FDA) evaluated all drugs that were approved for an orphan indication between April 1, 1999 and August 31, 2018.[2] FDA identified 548 orphan indications that were approved during the review period.

[1] For the purposes of this report, references to drugs include drugs approved under section 505 of the FD&C Act (21 U.S.C. 355) and biological products licensed under section 351 of the Public Health Service Act (42 U.S.C. 262).

[2] Some drugs were approved for multiple orphan indications during the review period. FDA assumed for purposes of this report that an orphan indication is a new indication as described in section 505B(a)(1) of the FD&C Act.

FDA identified 548 orphan indications that were approved during the review period. FDA identified 200 orphan indications that did not warrant pediatric labeling (adult only indications or indications for which pediatric studies were impossible or highly impracticable). It should be noted that several products that received orphan designations are not appropriate for use in the pediatric population, and pediatric trials for some indications are impossible or highly impracticable. Of the total of 548 orphan indications, FDA deemed 348 indications (64 percent) to be relevant to children, thus warranting pediatric use information in the labeling for the indication. Of these 348 indications, 221 (64 percent) indications for which pediatric use information was considered to be appropriate were fully labeled (i.e., the labeling contains adequate efficacy, safety, dosing, and age-appropriate formulation information to support its use in the full range of affected pediatric patients) for pediatric use. Information used to support appropriate pediatric labeling was derived from a variety of sources. In addition to data from pediatric trials conducted by the sponsor for the orphan indication, other sources that contributed to pediatric labeling information included, where appropriate, published literature, extrapolation of efficacy from adults or other pediatric populations, safety data obtained from pediatric trials for other indications, pharmacokinetic modeling and simulation data, and studies conducted under the Animal Rule.[3]

FDA identified 127 orphan indications that were not fully labeled for the pediatric population. Some drugs were approved for multiple orphan indications. The 127 orphan indications missing pediatric information in labeling corresponded to 98 drugs approved for one or more orphan indications (19 of the 98 drugs were approved for more than one orphan indication). Approximately two-thirds (81) of these indications had no pediatric information at all, while the remainder had some pediatric labeling. For those indications that had some pediatric information, in general, the incomplete labeling was not specifically related to efficacy or safety data. Rather, for those indications, the labeling did not address use in specific populations, generally the youngest populations where it would be appropriate to use the indicated drug and, therefore, to study that indication.

While a significant number of drugs with orphan designation are appropriately labeled in children, there is a public health need for additional pediatric information in labeling for over one-third of approved orphan indications that are relevant in the pediatric population. FDA supports ensuring that information to support labeling is obtained for all appropriate pediatric age groups.

I. BACKGROUND

Overview

[3] The regulations that set forth the pathway for approval of drugs and biological products when human efficacy studies are not ethical or feasible can be found at 21 CFR 314.600 through 314.650 (drugs) or 21 CFR 601.90 through 601.95 (biological products). These regulations collectively are commonly referred to as "the Animal Rule."

In the United States, there have been legislative and regulatory approaches to address pediatric development of medicines since 1997. The Best Pharmaceuticals for Children Act (BPCA), as amended and codified in section 505A of the FD&C Act, provides incentives for sponsors to do pediatric studies, but is a voluntary program. The Pediatric Research Equity Act (PREA), as amended and codified in section 505B of the FD&C Act, establishes requirements for sponsors to conduct pediatric development studies under certain circumstances, but does not offer incentives to do so. Both acts were made permanent in 2012, with modifications, in Title V of the Food and Drug Administration Safety and Innovation Act (FDASIA).[4]

To incentivize sponsors to conduct pediatric studies of drugs when the Agency believes the studies may produce benefits in pediatric populations, the BPCA authorizes FDA to issue Written Requests (WR), which outline the studies FDA is requesting of the drug sponsor for a specific drug for one or more conditions or indications, possibly including indications not approved in adults or children. FDA grants 6 months of additional marketing exclusivity to sponsors who "fairly respond" to the WR and meet certain other requirements. PREA authorizes FDA to require sponsors of certain new drug applications, biologics license applications, or supplements to either application, to submit pediatric assessments or molecularly targeted pediatric cancer investigations (as appropriate) regarding the drug's safety, effectiveness, dosing, and administration in pediatric populations. However, PREA (including subsection 505B(a)(1)(A), i.e., the requirement to submit pediatric assessments for a drug with a new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration) does not apply to drugs for indications for which orphan designation has been granted.[5] Together, BPCA and PREA have led to over 770 prescription product labeling changes to incorporate pediatric-specific information.

In addition to BPCA and PREA, there are various additional programs, including incentive programs, intended to facilitate and encourage development of new drugs for prevention and treatment of certain pediatric diseases. These programs include orphan-drug designation and the associated benefits under the Orphan Drug Act for rare disease therapies;[6] the rare disease priority review voucher program described in section 529 of the FD&C Act;[7] and various programs intended to facilitate and expedite development and review of new drugs to address unmet medical needs in the treatment of serious or life-threatening conditions: fast track designation, accelerated approval, breakthrough

[4] FDASIA, Pub. L. 112-144. 126 Stat 993 (July 9, 2012). We note that section 505A of the FD&C Act is often referred to as "BPCA" and section 505B of the FD&C Act as "PREA," a convention we will adopt here.

[5] Section 505B(k)(1) of the FD&C Act. Section 505B(a)(1)(B) requires pediatric studies of drugs intended for the treatment of an adult cancer and directed at a molecular target FDA determines to be substantially relevant to the growth or progression of a pediatric cancer. This requirement exists even when the drug for the adult indication has received an orphan designation (see section 505B(k)(2)), or when the adult cancer indication does not occur in the pediatric population as long as the drug is directed at a molecular target determined to be substantially relevant to a pediatric cancer.

[6] Public Law 97-414, as amended, codified at sections 526-528 of the FD&C Act (21 U.S.C. 360aa-360ee).

[7] This rare pediatric disease priority review voucher program may be used alone or in combination with other programs. It is intended to stimulate new drug development for rare pediatric diseases by offering additional incentives for obtaining FDA approval of these products.

therapy designation, regenerative medicine advanced therapy designation, and priority review designation.[8]

II. ASSESSMENT

A. Methods

FDA assembled a working group to conduct the review of labeling for orphan drugs that included staff from the Office of Pediatric Therapeutics, Division of Pediatric and Maternal Health, the Center for Drug Evaluation and Research (CDER), and the Center for Biologics Evaluation and Research (CBER). Because some drugs were approved for multiple orphan indications, the group organized the review process by approved orphan indication rather than by specific drug. After identifying the indications that needed additional pediatric information, the group compiled the corresponding list of drugs (see Appendix 1).

The working group identified 548 approved orphan indications for the period of April 1, 1999, to August 31, 2018. The list of approved orphan indications was reviewed to identify approved indications that were not relevant in or feasible to label for children. These consisted of approved indications for diseases or conditions in one of the following categories:

- A disease or condition that only affects adults
- A disease or condition in which pediatric clinical trials are impossible or highly impracticable

The working group consulted the relevant review divisions in CDER and CBER when it was unclear whether a given indication was relevant in the pediatric population.[9] The working group also consulted the review divisions regarding the appropriate pediatric age range for use of a given drug for the approved orphan indication, including any factors (toxicity, formulation, etc.) that would preclude its use in a portion or all of the age range of affected pediatric patients.

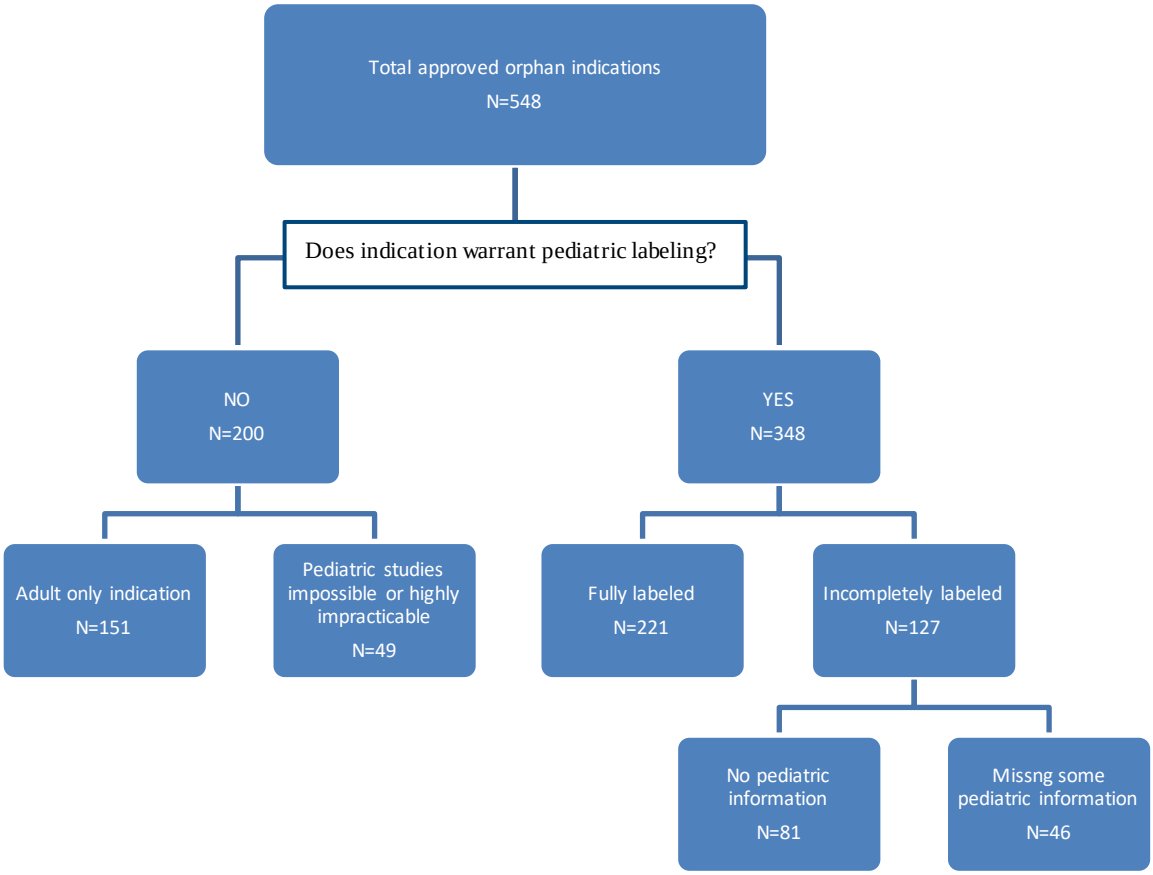
The working group determined that 200 of 548 (36 percent) approved orphan indications were not relevant in or feasible to study in children, including 151 indications for adult diseases or conditions and 49 indications for which pediatric trials were impossible or

[8] These programs often benefit sponsors of pediatric rare diseases, which are often serious or life-threatening conditions where there is considerable unmet need. For more information, you may refer to the FDA Guidance, Expedited Programs for Serious Conditions – Drugs and Biologics, *available at* http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM358301.pdf; FDA Guidance, Expedited Programs for Regenerative Medicine Therapies for Serious Conditions, *available at* https://www.fda.gov/regulatory-information/search-fda-guidance-documents/expedited-programs-regenerative-medicine-therapies-serious-conditions.

[9] For example, some of the indications were in diseases that have been reported in only a handful of children worldwide.

highly impracticable. The labeling for the remaining 348 approved orphan indications (64 percent) was reviewed for any clinical information related to the use of the drug in the pediatric population (i.e., efficacy, dosing, safety, age range for which the drug was approved and age-appropriate formulation information). In considering the appropriate age range to be included in pediatric labeling, the working group consulted the relevant review division to obtain clinical information to support the determination of the appropriate pediatric age range included in the review.[10] Figure 1 summarizes the review process.

Figure 1: Orphan Indication Pediatric Labeling Review Process



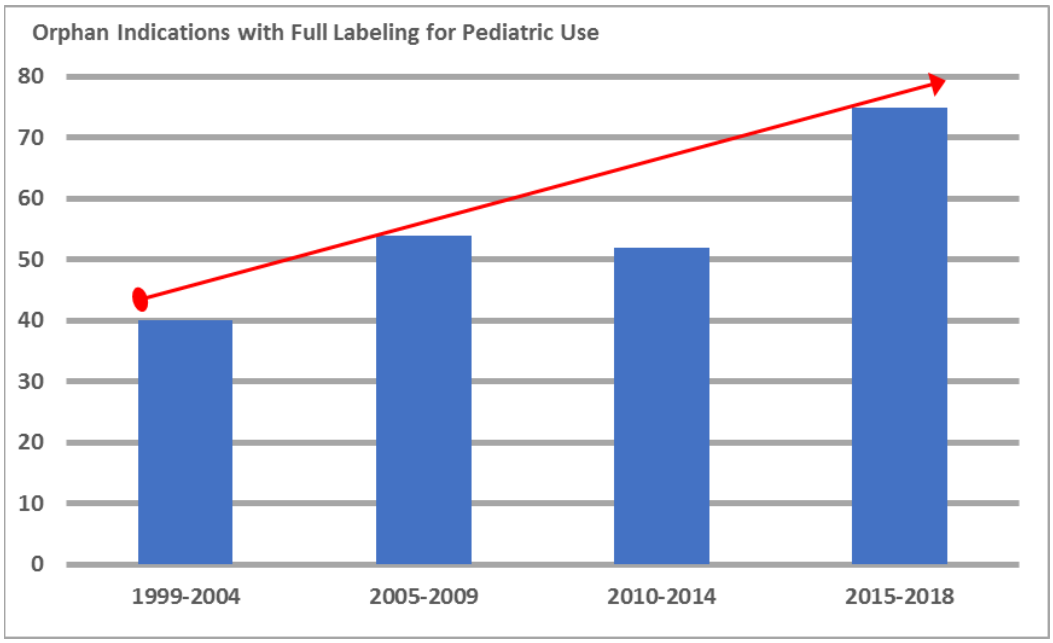
B. Findings

The working group identified 348 approved orphan indications for which pediatric labeling was warranted. Of these 348 indications, 221 indications (64 percent) were

[10] The agency lowered the age for waiver of pediatric studies after some orphan products were approved.

considered fully labeled for pediatric use (i.e., the labeling contains adequate efficacy, safety, dosing, and age-appropriate formulation information to support its use in the full age range of affected pediatric patients). The working group identified an increase in the number of approvals of orphan drugs that are fully labeled for pediatric use – most notably within the past 2-3 years (see Figure 2). Of these 221 indications, 198 indications (90 percent) were labeled for use in the full age range of affected pediatric patients at the time of original approval of the product. An additional 23 orphan indications (10 percent) were not labeled for use in the full age range of pediatric patients at the time of the original approval, but they were subsequently approved to extend the indicated population to the full age range of affected pediatric patients. Labeling for all but one of the extended indications was based on data from clinical trials completed after the original approval date; one indication was extended based on extrapolation of efficacy from adults and pharmacokinetic modeling and simulation data.

Figure 2: Orphan Indications with Appropriate Labeling for Pediatric Use, 1999 to 2018



Of the 348 approved orphan indications for which pediatric information was considered to be warranted, the working group identified 127 (36 percent) indications that were missing important pediatric information. The working group did not find any labeling that lacked a specific labeling component (e.g., efficacy, safety, or dosing). Of the 127 indications lacking pediatric information in labeling, 81 indications contained no pediatric information in labeling (64 percent); 46 indications (36 percent) did not address the full age range of affected pediatric patients in labeling. In the latter category, labeling

most commonly did not address use of the indicated drug in infants and young children affected by the indicated disease or condition.

Some drugs were approved for multiple orphan indications. The 127 orphan indications missing pediatric information in labeling corresponded to 98 drugs approved for one or more orphan indications (19 of the 98 drugs were approved for more than one orphan indication). Appendix 1 lists approved orphan indications that are lacking pediatric information in labeling under the corresponding drug name.

The working group reviewed the clinical development programs for all indications that currently are not fully labeled for pediatric use. The group found that there were ongoing studies or that the agency had issued a WR for pediatric studies to address labeling for 29 of 127 (23 percent) indications.

The working group found that the information used to support appropriate pediatric labeling was derived from a variety of sources. In addition to data from pediatric trials conducted, other sources that contributed to pediatric labeling information included, where appropriate, published literature, extrapolation of efficacy from adults or other pediatric populations, safety data obtained from pediatric trials for other indications, pharmacokinetic modeling and simulation data, and studies conducted under the Animal Rule.[11]

In summary, during the 1999-2018 review period, 127 of 348 (36 percent) of approved orphan indications that were relevant to pediatrics were missing important pediatric use information, either having no pediatric information at all or missing some information. Indications that contained pediatric labeling addressed all necessary components of labeling (efficacy, safety, dosing, and limitations of use where appropriate) but did not always address the full age range of affected pediatric patients. Most of the indications that were missing pediatric information did not contain any pediatric information (81 indications); indications that were partially labeled for pediatrics (46 indications) most commonly did not contain information on use of the drug in infants and young children. The 127 orphan indications missing pediatric information in labeling corresponded to 98 drugs approved for one or more orphan indications (19 of the 98 drugs were approved for more than one orphan indication).

Exclusively pediatric diseases or diseases in which pediatric patients comprised a majority of the overall disease population were most likely to be fully labeled for pediatrics. Conversely, indications for diseases or conditions where pediatric patients were a low percentage of the overall populations were less likely to be fully labeled for pediatrics. For some of these indications, as previously mentioned, there are ongoing studies to address this gap in pediatric labeling information. Other factors that impacted pediatric labeling were disease-specific.

[11] See https://www.fda.gov/regulatory-information/search-fda-guidance-documents/product-development-under-animal-rule.

III. CONCLUSION AND POLICY RECOMMENDATION

FDA has seen an increase over time in the number of approved orphan products with indications (some products were approved for multiple indications) that are fully labeled for pediatric use. During the review period for this report, 221 indications relevant to the pediatric population were fully labeled for pediatric use; most of these indications (90 percent) included appropriate pediatric labeling at the time of the original orphan product approval. This increase is most notable over the last 3 years.

However, 127 indications relevant to the pediatric population lacked pediatric information, either having no pediatric information at all (81 indications; 23 percent of all indications relevant in the pediatric population) or missing information for some relevant pediatric age ranges (46 indications; 13 percent of all indications relevant in the pediatric population), especially for the youngest populations.

While a significant number of drugs with orphan designation are appropriately labeled in children, there is a public health need for additional pediatric information in labeling for over one-third of approved orphan indications that are relevant in the pediatric population. FDA supports ensuring that information to support labeling is obtained for all appropriate pediatric age groups. The Agency will continue to work with stakeholders to achieve this goal.

Drug	Trade Name	Approved Orphan Indication	Orphan Indication Approval Date	Orphan Designation	Orphan Designation Date	Scope of Pediatric Information Lacking for Approved Orphan Indication	
						Information needed for a portion of the pediatric age range	Pediatric information lacking for entire age range
Acid alpha-glucosidase; alglucosidase alfa (recombinant human)	Lumizyme	Patients 8 years and older with late (non-infantile) onset Pompe disease (GAA deficiency) who do not have evidence of cardiac hypertrophy. The safety and efficacy of Lumizyme have not been evaluated in controlled clinical trials in infantile-onset patients, or in late (non-infantile) onset patients less than 8 years of age.	24-May-10	Treatment of glycogen storage disease type II	19-Aug-97	**X**	
		Patients with Pompe disease (acid alpha-glucosidase (GAA deficiency))	01-Aug-14	Treatment of glycogen storage disease type II	19-Aug-97	**X**	
Ambrisentan	Letairis	Treatment of pulmonary arterial hypertension (WHO group I) in patients with WHO class II or III symptoms to improve exercise capacity and delay clinical worsening	15-Jun-07	Treatment of pulmonary arterial hypertension	16-Jul-04		**X**
Aripiprazole	Abilify	Treatment of Tourette's disorder	12-Dec-14	Treatment of Tourette's syndrome	25-Jan-06	**X**	
Bedaquiline	Sirturo	Part of combination therapy in adults (greater than or equal to 18 years) with pulmonary multi-drug resistant tuberculosis (MDR-TB)	28-Dec-12	Treatment of active tuberculosis	10-Jan-05		**X**
Belatacept	Nulojix	Prophylaxis of organ rejection in adult patients receiving kidney transplants	15-Jun-11	Prophylaxis of organ rejection in renal allograft recipients	20-Feb-08		**X**
Benznidazole	n/a	Pediatric patients 2 to 12 years of age for the treatment of Chagas disease (American trypanosomiasis), caused by *Trypanosoma cruzi*	29-Aug-17	Treatment of Chagas disease	14-Apr-14	**X**	

Bevacizumab	Avastin	Treatment of glioblastoma with progressive disease following prior therapy	05-May-09	Treatment of malignant glioma	26-May-06		**X**
Binimetinib	Mektovi	In combination with encorafenib, for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation, as detected by an FDA-approved test	27-Jun-18	Treatment of Stage IIB-IV melanoma positive for the BRAF mutation	19-Nov-13		**X**
Brentuximab vedotin	Adcetris	The treatment of patients with Hodgkin lymphoma after failure of autologous stem cell transplant (ASCT) or after failure of at least two prior multi-agent chemotherapy regimens in patients who are not ASCT candidates	19-Aug-11	Treatment of Hodgkin's lymphoma	30-Jan-07		**X**
		Treatment of patients with classical Hodgkin lymphoma at high risk of relapse or progression as post-autologous hematopoietic stem cell transplantation (auto-HSCT)	17-Aug-15	Treatment of Hodgkin's lymphoma	30-Jan-07		**X**
		Treatment of adult patients with previously untreated Stage III or IV classical Hodgkin lymphoma (cHL), in combination with chemotherapy	20-Mar-18	Treatment of Hodgkin's lymphoma	30-Jan-07		**X**
Cannabidiol	Epidiolex	Treatment of seizures associated with Dravet syndrome (DS) in patients 2 years of age and older	25-Jun-18	Treatment of Dravet syndrome	14-Nov-13	**X**	
Carbamazepine, intravenous	Carnexiv	Replacement therapy for oral carbamazepine formulations, when oral administration is temporarily not feasible, in adults with the following seizure types: (1) Partial seizures with complex symptomatology; (2) Generalized clonic-tonic seizures; (3) Mixed seizures which include the above, or other partial or generalized seizures	07-Oct-16	Treatment of epilepsy patients who cannot take anything by mouth (NPO)	27-Jun-13		**X**

Ceramide trihexosidase/alpha -galactosidase A	Fabrazyme	For use in patients with Fabry disease to reduce globotriaosylceramide (GL-3) deposition in capillary endothelium of the kidney and certain other cell types	24-Apr-03	Treatment of Fabry's disease	19-Jan-88	**X**	
Cerliponase alfa	Brineura	To slow the progression of loss of ambulation in symptomatic pediatric patients 3 years of age and older with late infantile neuronal ceroid lipofuscinosis type 2 (CLN2), also known as tripeptidyl peptidase 1 (TPP1) deficiency	27-Apr-17	Treatment of neuronal ceroid lipofuscinosis type 2	01-Apr-13	**X**	
Cinacalcet	Sensipar	Treatment of hypercalcemia in adult patients with primary hyperparathyroidism for whom parathyroidectomy would be indicated on the basis of serum calcium levels, but who are unable to undergo parathyroidectomy	21-Nov-14	Treatment of hypercalcemia in patients with primary hyperparathyroidism for whom parathyroidectomy would be indicated on the basis of serum calcium levels, but who are unable to undergo surgery	30-Apr-10		**X**
		Treatment of severe hypercalcemia in patients with primary hyperparathyroidism who are unable to undergo parathyroidectomy	25-Feb-11	Treatment of hypercalcemia in patients with primary hyperparathyroidism for whom parathyroidectomy would be indicated on the basis of serum calcium levels, but who are unable to undergo surgery	30-Apr-10		**X**
Cysteamine enteric coated	Procysbi	For management of nephropathic cystinosis in adults and children ages 6 years and older	30-Apr-13	Treatment of cystinosis	24-Oct-06	**X**	
		Treatment of nephropathic cystinosis in adult and pediatric patients 2 years of age and older	14-Aug-15	Treatment of cystinosis	24-Oct-06	**X**	
		Treatment of nephropathic cystinosis in adults and pediatric patients 1 year of age and older	22-Dec-17	Treatment of cystinosis	24-Oct-06	**X**	

Dabrafenib	Tafinlar	Treatment of patients with unresectable or metastatic melanoma with BRAF V600E mutation as detected by an FDA approved test	29-May-13	Treatment of Stage IIb through IV melanoma	12-Jan-11		**X**
		TAFINLAR (dabrafenib) in combination with trametinib for treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test. This indication is based on the demonstration of durable response rate	08-Jan-14	Treatment BRAF V600 mutation positive Stage IIB through IV melanoma	20-Sep-12		**X**
		In combination with trametinib, for the adjuvant treatment of patients with melanoma with BRAF V600E or V600K mutations, as detected by an FDA-approved test, and involvement of lymph node(s), following complete resection	30-Apr-18	Treatment of Stage IIb through IV melanoma	20-Sep-12		**X**
Dalfampridine	Ampyra	Treatment to improve walking in patients with multiple sclerosis	22-Jan-10	Relief of symptoms of multiple sclerosis	02-Jun-87		**X**
Dasatinib	Sprycel	Treatment of adults with Philadelphia chromosome-positive acute lymphoblastic leukemia with resistance or intolerance to prior therapy	28-Jun-06	Treatment of Philadelphia-positive acute lymphoblastic leukemia	18-Nov-05		**X**
Deferiprone	Ferriprox	Treatment of patients with transfusional iron overload due to thalassemia syndromes when current chelation therapy is inadequate	14-Oct-11	Treatment of iron overload in patients with hematologic disorders requiring chronic transfusion therapy	12-Dec-01		**X**
Deflazacort	Emflaza	Treatment of Duchenne Muscular Dystrophy in patients 5 years of age and older	09-Feb-17	Treatment of Duchenne muscular dystrophy	16-Aug-13	**X**	
Dichlorphenamide	Keveyis	Treatment of primary hyperkalemic periodic paralysis, primary hypokalemic period paralysis, and related variants	07-Aug-15	Treatment of primary periodic paralyses	02-Sep-10		**X**

Dinutuximab	Unituxin	For use in combination with granulocyte-macrophage colony-stimulating factor (GM-CSF), interleukin-2 (IL-2) and 13-cis-retinoic acid (RA), for the treatment of pediatric patients with high-risk neuroblastoma who achieve at least a partial response to prior first-line multiagent, multimodality therapy	10-Mar-15	Treatment of neuroblastoma	20-Dec-10	**X**	
Ecallantide	Kalbitor	Treatment of acute attacks of hereditary angioedema in patients 16 years of age and older	01-Dec-09	Treatment of angioedema	04-Feb-03	**X**	
		Treatment of acute attacks of hereditary angioedema (HAE) in patients 12 years of age and older	28-Mar-14	Treatment of angioedema	04-Feb-03	**X**	
Eliglustat	Cerdelga	Long-term treatment of adult patients with Gaucher disease type 1 who are CYP2D6 extensive metabolizers (EMs), intermediate metabolizers (IMs), or poor metabolizers (PMs) as detected by an FDA-cleared test	19-Aug-14	Treatment of Type I Gaucher disease	17-Sep-08		**X**
Eltrombopag	Promacta	Treatment of patients with severe aplastic anemia who have had an insufficient response to immunosuppressive therapy	26-Aug-14	Treatment of aplastic anemia	08-Nov-13		**X**
Enasidenib	Idhifa	Treatment of adult patients with relapsed or refractory acute myeloid leukemia with an isocitrate dehydrogenase-2 (IDH2) mutation as detected by an FDA-approved test	01-Aug-17	Treatment of acute myelogenous leukemia	12-Jun-14		**X**
Encorafenib	Braftovi	In combination with binimetinib, for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation, as detected by an FDA-approved test	27-Jun-18	Treatment of Stage IIB-IV melanoma positive for the BRAF mutation	19-Nov-13		**X**

Epoprostenol	Flolan	Treatment of pulmonary hypertension associated with the scleroderma spectrum of disease in NYHA Class III and Class IV patient who do not respond adequately to conventional therapy	14-Apr-00	Treatment of secondary pulmonary hypertension due to intrinsic precapillary pulmonary vascular disease	22-Mar-99		**X**
Eteplirsen	Exondys 51	Treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 51 skipping	19-Sep-16	Treatment of Duchenne muscular dystrophy	23-Oct-07	**X**	
Evolocumab	Repatha	As an adjunct to diet and other LDL-lowering therapies (e.g., statins, ezetimibe, LDL apheresis) in patients with HoFH who require additional lowering of LDL-C	27-Aug-15	Treatment of homozygous familial hypercholesterolemia	12-Sep-13	**X**	
Glycopyrrolate	Cuvposa	To reduce chronic drooling in patients aged 3 - 16 with neurologic conditions associated with problem drooling (e.g. cerebral palsy)	28-Jul-10	Treatment of pathologic (chronic moderate to severe) drooling in pediatric patients	09-Jun-06	**X**	
Ibrutinib	Imbruvica	Treatment of adult patients with chronic graft versus host disease (cGVHD)	02-Aug-17	Treatment of chronic Graft versus Host disease	23-Jun-16		**X**
Icatibant	Firazyr	Treatment of acute attacks of hereditary angioedema in adults 18 years of age and older	25-Aug-11	Treatment of angioedema	25-Nov-03		**X**
Icodextrin 7.5% with electrolytes peritoneal dialysis solution	Extraneal	For use as a single daily exchange for the long (8-16 hour) dwell during continuous ambulatory peritoneal dialysis (CAPD) or automated peritoneal dialysis (APD) for the management of chronic renal failure	20-Dec-02	Treatment of those patients having end stage renal disease and requiring peritoneal dialysis treatment	18-Jul-97		**X**
Idursulfase	Elaprase	Indicated for patients with Hunter syndrome (mucopolysaccharidosis II, MPS II). Idursulfase has been shown to improve walking capacity in these patients.	24-Jul-06	Long term enzyme replacement therapy for patients with mucopolysaccharidosis II (Hunter Syndrome)	28-Nov-01	**X**	
Iloprost inhalation solution	Ventavis	Treatment of pulmonary arterial hypertension (WHO Group I) in patients with NYHA Class III or IV symptoms	29-Dec-04	Treatment of pulmonary arterial hypertension	17-Aug-04		**X**

Inotuzumab ozogamicin	Besponsa	Treatment of adults with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL)	17-Aug-17	Treatment of B-cell acute lymphoblastic leukemia	25-Mar-13		**X**
Ipilimumab	Yervoy	For the adjuvant treatment of patients with cutaneous melanoma with pathologic involvement of regional lymph nodes of more than 1 mm, who have undergone complete resection including total lymphadenectomy	28-Oct-15	Treatment of high risk Stage II, Stage III, and Stage IV melanoma	03-Jun-04		**X**
Isavuconazonium sulfate	Cresemba	Treatment of invasive aspergillosis in patients 18 years of age and older	06-Mar-15	Treatment of invasive aspergillosis	06-May-13		**X**
		Treatment of invasive mucormycosis in patients 18 years of age and older	06-Mar-15	Treatment of zygomycosis	25-Oct-13		**X**
Ivacaftor	Kalydeco	Treatment of cystic fibrosis (CF) in patients age 6 years and older who have a *G551D* mutation in the CFTR gene	31-Jan-12	Treatment of patients with cystic fibrosis	20-Dec-06	**X**	
		Treatment of cystic fibrosis (CF) in patients age 6 years and older who have one of the following mutations in the *CFTR* gene: *G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N,* or *S549R*	21-Feb-14	Treatment of patients with cystic fibrosis	20-Dec-06	**X**	
		Treatment of cystic fibrosis (CF) in patients age 6 years and older who have an *R117H* mutation in the *CFTR* gene	29-Dec-14	Treatment of patients with cystic fibrosis	20-Dec-06	**X**	
		Treatment of cystic fibrosis (CF) in patients ages 2 to less than 6 years who have one of the following mutations in the *CFTR gene*: *G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N, S549R*, or *R117H*	17-Mar-15	Treatment of patients with cystic fibrosis	20-Dec-06	**X**	
		Treatment of cystic fibrosis (CF) in patients age 2 years and older who have one mutation in the *CFTR* gene that is responsive to ivacaftor based on clinical and/or in vitro assay data	17-May-17	Treatment of patients with cystic fibrosis	20-Dec-06	**X**	

		Treatment of cystic fibrosis (CF) in patients age 2 years and older who have one mutation in the *CFTR* gene that is responsive to ivacaftor based on clinical and/or in vitro assay data	31-Jul-17	Treatment of patients with cystic fibrosis	20-Dec-06	**X**	
Ivosidenib	Tibsovo	Treatment of adult patients with relapsed or refractory acute myeloid leukemia (AML) with a susceptible isocitrate dehydrogenase-1 (IDH1) mutation as detected by an FDA-approved test	20-Jul-18	Treatment of acute myeloid leukemia (AML)	09-Jun-15		**X**
Lanadelumab-flyo	Takhzyro	Prophylaxis to prevent attacks of hereditary angioedema (HAE) in patients 12 years and older	23-Aug-18	Treatment of angioedema	26-Nov-13	**X**	
Lanreotide acetate	Somatuline Depot	Treatment of adults with carcinoid syndrome; when used, it reduces the frequency of short-acting somatostatin analog rescue therapy	15-Sep-17	Treatment of carcinoid syndrome	08-Sep-11		**X**
Ledipasvir/ sofosbuvir	Harvoni	Treatment of chronic hepatitis C virus (HCV) in pediatric patients 12 years of age and older or weighing at least 35 kg with genotype 1, 4, 5, or 6 without cirrhosis or with compensated cirrhosis	07-Apr-17	Treatment of chronic hepatitis C virus (HCV) infection in pediatric patients	12-Oct-16	**X**	
Letermovir	Prevymis	Prophylaxis of cytomegalovirus (CMV) infection and disease in adult CMV-seropositive recipients [R+] of an allogeneic hematopoietic stem cell transplant (HSCT)	08-Nov-17	Prevention of human cytomegalovirus viremia and disease in at risk populations	12-Dec-11		**X**
Levocarnitine (oral solution)	Carnitor	Prevention and treatment of carnitine deficiency in patients with end stage renal disease who are undergoing dialysis	15-Dec-99	Treatment of manifestations of carnitine deficiency in patients with end stage renal disease who require dialysis	06-Sep-88		**X**
L-glutamine	Nutrestore	Treatment of short bowel syndrome in patients receiving specialized nutritional support when used in conjunction with a recombinant human growth hormone that is approved for this indication	10-Jun-04	For use with human growth hormone in the treatment of short bowel syndrome (nutrient malabsorption from the gastrointestinal tract resulting from an inadequate absorptive surface)	06-Mar-95		**X**

Lomitapide	Juxtapid	Adjunct to a low-fat diet and other lipid-lowering treatments, including LDL apheresis where available, to reduce low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC), apolipoprotein B (apo B), and non-high-density lipoprotein cholesterol (non-HDL-C) in patients with homozygous familial hypercholesterolemia (HoFH)	21-Dec-12	Treatment of homozygous familial hypercholesterolemia	23-Oct-07		**X**
Lumacaftor/ ivacaftor	Orkambi	Treatment of cystic fibrosis in patients age 12 years and older who are homozygous for *F508del* mutation in the *CFTR* gene	02-Jul-15	Treatment of cystic fibrosis	30-Jun-14	**X**	
		Treatment of cystic fibrosis (CF) in patients age 6-11 years old who are homozygous for the *F508del* mutation in the *CFTR* gene	28-Sep-16	Treatment of cystic fibrosis	30-Jun-14	**X**	
		Treatment of cystic fibrosis (CF) in patients age 2 through 5 years old who are homozygous for the *F508del* mutation in the *CFTR* gene	07-Aug-18	Treatment of cystic fibrosis	30-Jun-14	**X**	
Macimorelin acetate	Macrilen	Diagnosis of adult growth hormone deficiency	20-Dec-17	Diagnosis of growth hormone deficiency	14-May-07		**X**
Macitentan	Opsumit	Treatment of pulmonary arterial hypertension (PAH, WHO Group 1) to delay disease progression. Disease progression included: death, initiation of intravenous (IV) or subcutaneous prostanoids, or clinical worsening of PAH (decreased 6-minute walk distance, worsened PAH symptoms and need for additional PAH treatment)	18-Oct-13	Treatment of pulmonary arterial hypertension	03-Sep-09		**X**
Metreleptin	Myalept	Adjunct to diet as replacement therapy to treat the complications of leptin deficiency in patients with congenital or acquired generalized lipodystrophy	24-Feb-14	Treatment of metabolic disorders secondary to lipodystrophy	22-Aug-01	**X**	

Midostaurin	Rydapt	Treatment of adult patients with newly diagnosed acute myeloid leukemia (AML) that is FLT3 mutation-positive as detected by an FDA approved test, in combination with standard cytarabine and daunorubicin induction and cytarabine consolidation	28-Apr-17	Treatment of acute myeloid leukemia	07-Jul-09		**X**
Mifepristone	Korlym	Indicated to control hyperglycemia secondary to hypercortisolism in adult patients with endogenous Cushing's syndrome who have type 2 diabetes mellitus or glucose intolerance and have failed surgery or are not candidates for surgery	17-Feb-12	Treatment of the clinical manifestations of endogenous Cushing's syndrome	05-Jul-07		**X**
Migalastat hydrochloride	Galafold	Treatment of adults with a confirmed diagnosis of Fabry disease and an amenable galactosidase alpha gene (*GLA*) variant based on in vitro assay data	10-Aug-18	Treatment of Fabry Disease	25-Feb-04		**X**
Miglustat	Zavesca	Treatment of mild to moderate Type I Gaucher disease in adults for whom enzyme replacement therapy is not a therapeutic option (e.g., due to constraints such as allergy, hypersensitivity, or poor venous access)	31-Jul-03	Treatment of Gaucher disease	29-May-98		**X**
Miltefosine	Impavido	Treatment of visceral leishmaniasis due to *Leishmania donovani*; cutaneous leishmaniasis due *to Leishmania braziliensis, Leishmania guyanensis,* and *Leishmania panamensis*; and mucosal leishmaniasis due to *Leishmania braziliensis*	19-Mar-14	Treatment of leishmaniasis	10-Oct-06	**X**	
Mipomersen	Kynamro	Adjunct to lipid-lowering medications and diet to reduce low density lipoprotein-cholesterol (LDL-C), apolipoprotein B (apo B), total cholesterol (TC), and non-high density lipoprotein-cholesterol (non-HDL-C) in patients with homozygous familial hypercholesterolemia (HoFH)	29-Jan-13	Treatment of homozygous familial hypercholesterolemia	23-May-06		**X**

Moxidectin	[moxidectin]	Treatment of onchocerciasis due to *Onchocerca volvulus* in patients aged 12 years and older	13-Jun-18	Treatment of onchocerciasis volvulus in children and adults	29-Sep-10	**X**	
Nitisinone (oral suspension)	Orfadin	Treatment of hereditary tyrosinemia type 1 in combination with dietary restriction of tyrosine and phenylalanine	22-Apr-16	Treatment of tyrosinemia type 1	16-May-95	**X**	
Nivolumab	Opdivo	Treatment of patients with unresectable or metastatic melanoma and disease progression following ipilimumab and, if BRAF V600 mutation positive, a BRAF inhibitor	22-Dec-14	Treatment of Hodgkin lymphoma	23-Jan-13		**X**
		Treatment of patients with BRAF V600 wild-type, unresectable or metastatic melanoma	30-Sep-15	Treatment of Stage IIb to IV melanoma	09-Oct-14		**X**
		Classical Hodgkin lymphoma that has relapsed or progressed after autologous hematopoietic stem cell transplantation (HSCT) and post-transplantation brentuximab vedotin	17-May-16	Treatment of Stage IIb to IV melanoma	07-Aug-14		**X**
		Treatment of adult patients with Classical Hodgkin lymphoma that has relapsed or progressed after 3 or more lines of systemic therapy that includes autologous HSCT	25-Apr-17	Treatment of Hodgkin lymphoma	07-Aug-14		**X**
		Adjuvant treatment of patients with melanoma with involvement of lymph nodes or metastatic disease who have undergone complete resection	20-Dec-17	Treatment of Stage IIb to Stage IV melanoma	23-Jan-13		**X**
Obeticholic acid	Ocaliva	Treatment of primary biliary cholangitis (PBC) in combination with ursodeoxycholic acid (UDCA) in adults with an inadequate response to UDCA, or as monotherapy in adults unable to tolerate UDCA	27-May-16	Treatment of primary biliary cirrhosis	09-Apr-08		**X**
Olaratumab	Lartruvo	In combination with doxorubicin, for the treatment of adult patients with soft tissue sarcoma (STS) with a histologic subtype for which an anthracycline-containing	19-Oct-16	Treatment of soft tissue sarcoma	09-Oct-14		**X**

		regimen is appropriate and which is not amenable to curative treatment with radiotherapy or surgery					
Oxybate	Xyrem	Treatment of cataplexy associated with narcolepsy	17-Jul-02	Treatment of narcolepsy	07-Nov-94	**X**	
		Treatment of excessive daytime sleepiness in patients with narcolepsy	18-Nov-05	Treatment of narcolepsy	07-Nov-94	**X**	
Paricalcitol	Zemplar	Adult and pediatric patients 10 years and older for the prevention and treatment of secondary hyperparathyroidism associated with: (1)Chronic kidney disease (CKD) Stages 3 and 4; (2) CKD Stage 5 in patients on hemodialysis or peritoneal dialysis	18-Oct-16	Treatment of pediatric hyperparathyroidism	27-Oct-15	**X**	
Pasireotide	Signifor	Treatment of adult patients with Cushing's disease for whom pituitary surgery is not an option or has not been curative	14-Dec-12	Treatment of Cushing's disease	24-Jul-09		**X**
		Treatment of patients with Cushing’s disease for whom pituitary surgery is not an option or has not been curative	29-Jun-18	Treatment of Cushing's disease	24-Jul-09		**X**
Pegvaliase-pqpz	Palynziq	Indicated to reduce blood phenylalanine concentrations in adult patients with phenylketonuria (PKU) who have uncontrolled blood phenylalanine concentrations greater than 600 micromol/L on existing management	24-May-18	Treatment of hyperphenylalaninemia	08-Mar-95		**X**
Plerixafor	Mozobil	In combination with granulocyte-colony stimulating factor (G-CSF) to mobilize hematopoietic stem cells to the peripheral blood for collect and subsequent autologous transplantation in patients with non-Hodgkin's lymphoma and multiple myeloma	15-Dec-08	For use to improve the yield of progenitor cells in the apheresis product for subsequent stem cell transplantation	10-Jul-03		**X**
Quinine sulfate	Qualaquin	Treatment of uncomplicated *Plasmodium falciparum* malaria	12-Aug-05	Treatment of malaria	03-Jun-04	**X**	

Rifaximin	Xifaxan	Reduction in the risk of overt hepatic encephalopathy (HE) recurrence in patients greater than or equal to 18 years of age	24-Mar-10	Treatment of hepatic encephalopathy	10-Feb-98		**X**
Riociguat	Adempas	Treatment of adults with pulmonary arterial hypertension (PAH) WHO Group 1, to improve exercise capacity, WHO functional class and to delay clinical worsening	08-Oct-13	Treatment of pulmonary arterial hypertension	19-Sep-13		**X**
		Treatment of adults with persistent/recurrent chronic thromboembolic pulmonary hypertension (CTEPH) WHO Group 4, after surgical treatment, or inoperable CTEPH, to improve exercise capacity and WHO functional class	08-Oct-13	Treatment of chronic thromboembolic pulmonary hypertension	19-Sep-13		**X**
Rituximab	Rituxan	For the use of Rituxan (rituximab) in combination with glucocorticoids for the treatment of patients with Wegener's Granulomatosis (WG) and Microscopic Polyangiitis (MPA))	19-Apr-11	Treatment of patients with anti-neutrophil cytoplasmic antibody-associated vasculitis (Wegener's Granulomatosis, Microscopic Polyangiitis, and Churg-Strauss Syndrome)	14-Feb-06		**X**
Romiplostim	Nplate	Treatment of thrombocytopenia in patients with chronic immune (idiopathic) thrombocytopenic purpura (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy	22-Aug-08	Treatment of immune thrombocytopenic purpura	27-Mar-03		**X**
Selexipag	Uptravi	Treatment of pulmonary arterial hypertension (PAH, WHO Group I) to delay disease progression and reduce the risk of hospitalization for PAH	21-Dec-15	Treatment of pulmonary arterial hypertension	30-Apr-10		**X**
Sofosbuvir	Sovaldi	Treatment of pediatric patients 12 years of age and older or weighing at least 35 kg with genotype 2 or 3 chronic hepatitis C virus (HCV) infection without cirrhosis or with compensated cirrhosis in combination with ribavirin	07-Apr-17	Treatment of pediatric chronic hepatitis C virus infection	25-Oct-16	**X**	

Somatropin [rDNA]	Zorbtive	Treatment of short bowel syndrome in patients receiving specialized nutritional support	01-Dec-03	For use alone or in combination with glutamine in the treatment of short bowel syndrome	06-Mar-95		**X**
Stiripentol	Diacomit	Treatment of seizures associated with Dravet syndrome (DS) in patients 2 years of age and older taking clobazam	20-Aug-18	Treatment of Dravet syndrome	30-Oct-08	**X**	
Synthetic human secretin	Chirhostim	Stimulation of pancreatic secretions, including bicarbonate, to aid in the diagnosis of pancreatic exocrine dysfunction, stimulation of gastrin secretion to aid in the diagnosis of gastrinoma, and stimulation of pancreatic secretions to facilitate the identification of the ampulla of Vater and accessory papilla during endoscopic retrograde cholangiopancreatography (ERCP)	09-Apr-04	For use in the diagnosis of gastrinoma associated with Zollinger-Ellison syndrome	16-Jun-99		**X**
Synthetic porcine secretin	Secreflo	Use in secretin stimulation testing for stimulation of pancreatic secretions, including bicarbonate, to aid in the diagnosis of pancreatic exocrine dysfunction	04-Apr-02	For use in conjunction with diagnostic, therapeutic, or combined diagnostic/ therapeutic procedures for pancreatic disorders to increase pancreatic fluid secretion	07-Mar-00		**X**
		For use in secretin stimulation testing for: Stimulation of pancreatic secretions to facilitate the identification of the ampulla of Vater and accessory papilla during endoscopic retrograde cholangio-pancreatography (ERCP)	01-Nov-02	For use in the evaluation of exocrine pancreas function	18-Jun-99		**X**
Tacrolimus	Envarsus Xr	Prophylaxis of organ rejection in kidney transplant patients converted from tacrolimus immediate-release formulations in combination with other immunosuppressants	10-Jul-15	Prophylaxis of organ rejection in patients receiving allogeneic kidney transplant	20-Dec-13		**X**
Tadalafil	Adcirca	Treatment of pulmonary arterial hypertension (WHO Group I) to improve exercise ability	22-May-09	Treatment of pulmonary arterial hypertension	18-Dec-06		**X**

Tafenoquine	Krintafel	Indicated for the radical cure (prevention of relapse) of *Plasmodium vivax* malaria in patients aged 16 years and older who are receiving appropriate antimalarial therapy for acute *P. vivax* infection	20-Jul-18	Treatment of malaria	15-Jan-13	**X**	
Taliglucerase alfa	Elelyso	Use as long-term enzyme replacement therapy in patients with Type 1 Gaucher disease	01-May-12	Treatment of Gaucher's disease	03-Sep-09	**X**	
Tasimelteon	Hetlioz	Treatment of non-24-hour sleep-wake disorder	31-Jan-14	Non-24-hour sleep-wake disorder in blind individuals without light perception	19-Jan-10		**X**
Technetium Tc 99m tilmanocept	Lymphoseek	Guiding sentinel lymph node biopsy, using a hand-held gamma counter in patients with clinically node negative squamous cell carcinoma of the oral cavity	13-Jun-14	Use in sentinel lymph node detection (SLN) with a hand-held gamma-counter, with scintigraphic imaging, in patients with cancer of the head and neck	17-Sep-14		**X**
Technetium Tc99m sulfur colloid injection, lyophilized	Technetium Tc99m Sulfur Colloid	Localization of lymph nodes draining a primary tumor in patients with melanoma when used with a hand-held gamma counter	13-Aug-12	For localization of sentinel lymph nodes in patients with melanoma	17-Mar-09	**X**	
Teduglutide [rDNA origin]	Gattex	Treatment of adult patients with short bowel syndrome (SBS) who are dependent on parenteral support	21-Dec-12	Treatment of short bowel syndrome	29-Jun-00		**X**
Telotristat etiprate	Xermelo	Treatment of carcinoid syndrome diarrhea in combination with somatostatin analog (SSA) therapy in adults inadequately controlled by SSA therapy	28-Feb-17	Treatment of carcinoid syndrome in patients with neuroendocrine tumors	09-Mar-12		**X**
Tezacaftor/ ivacaftor	Symdeko	Treatment of patients with cystic fibrosis (CF) aged 12 years and older who are homozygous for the *F508del* mutation or who have at least one mutation in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene that is responsive to tezacaftor/ivacaftor based on *in vitro* data and/or clinical evidence	12-Feb-18	Treatment of cystic fibrosis (CF)	15-Jun-17	**X**	

Tinidazole	Tindamax	Treatment of intestinal amebiasis and amebic liver abcess caused by E. histolytica in both adults and pediatric patients older than three years of age. It is not indicated for the treatment of asymptomatic cyst passage.	17-May-04	Treatment of amebiasis	20-Aug-03	**X**	
		Treatment of giardiasis caused by *G. duodenalis* (also termed *G. lamblia*) in both adults and pediatric patients older than three years of age	17-May-04	Treatment of giardiasis	18-Apr-02	**X**	
Tolvaptan	Jynarque	Indicated to slow kidney function decline in adults at risk of rapidly progressing autosomal dominant polycystic kidney disease (ADPKD)	23-Apr-18	Treatment of autosomal dominant polycystic kidney disease	06-Apr-12		**X**
Trametinib	Mekinist	Treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations as detected by an FDA approved test	29-May-13	Treatment of Stage IIb through Stage IV melanoma	20-Dec-10		**X**
		MEKINIST (trametinib) in combination with dabrafenib for treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test. This indication is based on the demonstration of durable response rate	08-Jan-14	Treatment of Stage IIb through IV melanoma	20-Sep-12		**X**
		In combination with dabrafenib, for the adjuvant treatment of patients with melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test, and involvement of lymph node(s), following complete resection	30-Apr-18	Treatment of Stage IIb through IV melanoma	20-Sep-12		**X**
Treprostinil	Remodulin	Treatment of pulmonary arterial hypertension	21-May-02	Treatment of pulmonary arterial hypertension	04-Jun-97		**X**

Treprostinil (inhalational)	Tyvaso	Treatment of pulmonary arterial hypertension (WHO Group I) in patients with NYHA Class III symptoms, to increase walk distance	30-Jul-09	Treatment of pulmonary arterial hypertension	17-Jun-10		**X**
Velaglucerase-alfa	VPRIV	Long-term enzyme replacement therapy (ERT) for pediatric and adult patients with type I Gaucher disease	26-Feb-10	Treatment of Gaucher disease	08-Jun-09	**X**	
Vemurafenib	Zelboraf	Treatment of unresectable or metastatic melanoma with the BRAFV600E mutation as detected by an FDA-approved test	17-Aug-11	Treatment of patients with IIb to Stage IV melanoma positive for the BRAF(v600) mutation	20-Dec-10		**X**
vinCRIStine sulfate LIPOSOME injection	Marqibo	Treatment of adult patients with Philadelphia chromosome-negative (Ph-) acute lymphoblastic leukemia (ALL) in second or greater relapse or whose disease has progressed following two or more anti-leukemia therapies	09-Aug-12	Treatment of acute lymphoblastic leukemia	08-Jan-07		**X**
von Willebrand factor (rhVWF) recombinant	Vonvendi	On-demand treatment and control of bleeding episodes in adults (age 18 and older) diagnosed with von Willebrand disease (VWD)	08-Dec-15	Treatment of von Willebrand disease	23-Nov-10		**X**
		For use in adults (age 18 and older) diagnosed with von Willebrand disease (VWD) for perioperative management of bleeding	13-Apr-18	Treatment of von Willebrand disease	23-Nov-10		**X**