

Emerging pediatric technologies

Pediatric Technology Watch | 2018 Volume 2



Table of contents

Introduction	3
Market watch.....	3
Economic watch	4
Overall projected price changes	4
Technology watch.....	5
Currently available products	5
Products in clinical trials.....	6
Products in development	7
Supplier watch	8
FUJIFILM Medical Systems U.S.A, Inc., a Vizient-contracted supplier	8
Pharmaceutical watch	9
New drugs.....	9
New indications.....	11
New formulations	11
References.....	13

Disclaimer: Vizient® staff attends clinical sessions at important scientific meetings throughout the year. The staff meets with suppliers, reviews new technologies and monitors data from pertinent clinical trials. The information is consolidated into this overview of product and practice trends in the various pediatric segments. This document is intended to educate nonclinical hospital staff by offering insights into new and innovative technologies. Vizient staff members have no personal financial connections with the suppliers and no conflicts of interest in the development of this document. The products and trends presented are for educational purposes. Vizient does not endorse any of the products described in this document.

Introduction

Children require specialized, compassionate and comprehensive care that supports every stage of their lives. The Vizient® Pediatric Technology Watch is intended to educate and provide insights into new and innovative technologies that support delivery of the highest-quality

pediatric care. This issue highlights the latest products and pharmaceuticals available in the market as well as emerging technologies. The Pediatric Technology Watch also features Vizient pricing projections for both products and pharmaceuticals.

Market watch

In 2017, the global pediatric health care products market was valued at approximately \$88 billion, with North America accounting for the leading share of the market. The market is projected to grow at a rate of approximately 5.5 percent between 2018 and 2026.

Factors in the growth of the pediatric health care products market include the rise in pediatric chronic health conditions, the surge in demand for pediatric diagnostic and imaging technology, the rise in child-bearing age among women, favorable reimbursement scenarios and governmental initiatives. These factors have also created opportunities for players operating in the market.¹

More specifically, the pediatric medical device market is growing at a faster rate than ever before. This growth can be attributed to many of the same factors driving the

global health care products market, with the launch of new pediatric medical technologies such as seizure monitors, wireless pulse oximeters and heart monitors driving the market during the forecast period.²

While children and adults suffer from many of the same diseases and conditions, their device needs can vary considerably due to their size, rates of growth, critical development periods, anatomy, physiological differences, etc.³ In many cases, adult medical devices are used in children due to the absence of pediatric-specific devices.

The Food and Drug Administration (FDA) has recognized the need for medical devices for the pediatric population and is responding with initiatives that support the development of safe and effective pediatric medical devices.⁴

Economic watch

Price projections affecting the pediatric market

Overall projected price changes

Vizient expects overall national market prices for supplies to increase 1.6 percent over the next 18 to 24 months. (Table 1). Table 2 shows projected change in drug prices over the next 18 months.

Table 1. Projected supply price changes over the next 18 to 24 months

Category	National price inflation projection (%)
Cardiology	1.5
Cardiac rhythm management	-0.5
Drug-eluting stents	-1.1
Neurosurgical	3.3
Orthopedic supplies	0.7
Joint implant	-2.2
Spinal	-0.4
Trauma	1.0
IV solutions	4.0
Medical/surgical supplies	0.6
Laboratory	0.3
Imaging equipment	-0.5
Medical equipment	0.5
Medical gases	2.8
Purchased services	1.9
Information technology (IT) hardware	-2.1

Category	National price inflation projection (%)
IT software	-1.2
IT services	5.0
Printing and forms	1.9
Office supplies	1.3
Furniture	1.6
Water	3.9
Electricity	1.4
Natural gas	2.1
Telephone	1.0
Internet	0.5
Food overall	2.0
Overall projected price change	1.6

Source: Vizient Budget Impact Projections Report, third quarter 2018.

Table 2. Projected drug price changes

Product group	Estimated price change weighted by Vizient purchases (%)
Contract purchases	1.04
Noncontract purchases	3.88
Total weighted average drug price inflation estimate	4.92

Source: Vizient Drug Price Forecast, July 2018.

Note that the Vizient market price projections are forecasts, not predictions. Forecasts are point-in-time estimates of price changes and are subject to changes in market conditions.

Technology watch

New innovative technology in the pediatric pipeline

Innovation in the pediatric market is increasing. While a need for pediatric medical devices has existed for many years, product development has lagged. Increasingly, more and more entrepreneurs are focusing their attention on pediatrics across a wide spectrum of products, indications and patient populations. Funding is also becoming available

to assist these young companies in completing clinical trials and bringing these products to market. The hope is that new device development efforts continue. Innovation will help health care providers improve their care of pediatric patients.

Currently available products

MiniMed 670G hybrid closed-loop system (Medtronic)

The MiniMed 670G system is a combination of an insulin pump and a continuous glucose monitor. The device is now approved for use in patients 7 years and older. The system is intended for continuous delivery of insulin for the management of type 1 diabetes mellitus. The system uses multiple components, including the pump, an infusion port and a sensor. The Guardian sensor, which has a seven-day lifespan, communicates with the insulin pump to provide accurate measurements, as well as closed-loop continuous monitoring of blood glucose. FDA approval was based on positive results from a pediatric clinical trial, which demonstrated the device's safety in 105 children between 7 and 13 years of age with type 1 diabetes. The study established a two-week baseline period in an open-loop mode (traditional pump therapy) and studied data from a three-month in-home period of the hybrid-closed-loop mode. The clinical results showed the percentage of time children spend in the optimal glycemic range of 70-180 mg/dl increased from 56.2 percent to 65 percent. A1C levels were also reduced from 7.9 percent to 7.5 percent. There were no incidences of diabetic ketoacidosis in the study phase and no severe hypoglycemic or serious device-related adverse events. The FDA expanded usage of the device in June 2018.⁵

Masters HP mechanical heart valve (Abbott Vascular)

(Humanitarian-exempt device)

The Masters HP 15-mm rotatable mechanical heart valve is the world's smallest mechanical heart valve that will allow surgeons to treat babies and toddlers in need of a valve replacement.⁶ The 15-mm device is a therapy intended to allow younger patients to live long enough to get another valve implanted. The device features a rotatable, bi-leaflet mechanical valve designed for implantation in the mitral or aortic position. The valve has pyrolytic carbon leaflets and an orifice ring, an 85-degree leaflet opening angle

to improve flow and reduce turbulence, and a controlled torque mechanism for rotation and intraoperative adjustment. A sewing cuff contains additional suture markers for more accurate placement. The device was cleared by the FDA in March 2018.⁷

CGM G6 (Dexcom)

The CGM G6 is a continuous glucose monitor that provides real-time, dynamic glucose information every five minutes, up to 288 readings in a 24-hour period. The device requires no fingersticks for calibration. The system consists of three parts: a small sensor that is worn on the body and is about 30 percent thinner than its predecessor; a low-profile transmitter that is incorporated into the 10-day sensor unit; and a receiver. The system works with any Apple and Android smart device. The monitor provides customizable alerts to warn the patient of approaching glucose highs and lows. The monitor is indicated for use with patients with diabetes ages 2 and up. The FDA cleared the device in March 2018.

MyoPro 2 orthosis (Myomo)

The MyoPro 2 is a powered orthosis (brace) designed to restore function to arms and hands paralyzed or weakened by neurological or neuromuscular disease, injury or other condition. In adolescents and children, this most often means cerebral palsy (CP) or brachial plexus injury (BPI). It works by reading the faint nerve signals (myoelectric signals) from the surface of the skin, then activating small motors to move the arm and hand as the user intends.⁸ The user is in complete control of their hand and arm movement. While there are orthotic products to support weak legs, the MyoPro 2 is the only product to help restore function for those who still have their arms and hands but are unable to use them.⁹ The MyoPro 2 was launched to the U.S. market in June 2017. In June 2018, the device's indicated use was expanded to include adolescent patients.

Products in clinical trials

IncuBlanket non-electric warming system (Warmilu)

The IncuBlanket is a non-electric warming system. The blanket uses a safe, reusable and durable heat pack that regulates warmth. With a click of the activator disk, the pack begins to warm up, and stays warm for four to six hours when used by itself and five to eight hours when used in conjunction with another insulator product. It is available in three sizes — preterm, newborn and infant. The patented technology was demonstrated to be safe and effective in a small patient study. The device is constructed of all non-toxic and food-grade materials. It can be reused by boiling or autoclaving over 100 times. The company is in the process of filing for FDA clearance.

Dynamic spinal alignment brace (Green Sun Medical)

Green Sun Medical is developing a dynamic scoliosis brace that applies continuous corrective pressure to the spine and allows physicians to monitor the performance of the brace remotely.⁹ The dynamic bracing system is designed to treat adolescent idiopathic scoliosis and kyphosis patients. The braces are made of rings connected by soft fabric that apply continuous pressure on the spine meant not only to slow down spine curvature but correct it. The brace is flexible enough that patients wearing it can move easily and bend over, something that isn't possible in a rigid brace. The brace is Bluetooth enabled, providing real data on how and when it is being worn and how effective the therapy is. The pressure sensors and Bluetooth-enabled device allow doctors to adjust the pressure on the brace as needed to correct the deformities. A study began in late 2017 to determine the device's effectiveness in being a substitute to the rigid brace and to study if it is effective in correcting spinal curvature. In March 2018, the device won first place at the South by Southwest (SXSW) Impact Pediatric Health Pitch Competition in Austin, Texas. It has not been cleared by the FDA for use in the U.S.

Amplatzer duct occluder II AS (Abbott Vascular)

The Amplatzer Duct Occluder II AS is the expansion of the occluder family designed for closure of the small patent ductus arteriosus (PDA). The ADO II AS device conforms to the smallest ducts while achieving complete closure from a pulmonary or aortic artery approach.¹⁰ The device provides a nonsurgical treatment option for closing the PDA defect in newborns and preterm infants. The wire mesh device is placed nonsurgically through a catheter inserted through the leg and guided through vessels to the heart, where it is placed to seal the duct.¹¹ The new device is similar to

the existing Amplatzer Duct Occluder II products but in a smaller sizes. Data collected during the ADO II AS trial across all trial sites will be used to seek FDA approval. The ADO II AS device is currently approved for use in more than 50 countries outside the United States.¹² It has not been cleared by the FDA for use in the U.S.

ADO II AS pediatric clinical trial (NCT03055858)¹³

Evan Zahn, MD (U.S., Cedars-Sinai Medical Center) (member), principal investigator

Size: 50 patients

Single arm, prospective, multicenter, nonrandomized, open-label U.S. study

The ADO II AS trial is a single-arm, prospective, multicenter, non-randomized clinical investigation designed to characterize the safety and effectiveness of the ADO II AS device in patients with a PDA who are more than 3 days old.¹⁴ Co-primary endpoints are the rate of major complications through 180 days after an attempted implant, and the rate of effective closure of the ductus arteriosus among patients with a successful implant at six months. The secondary endpoint is the rate of significant obstruction of the pulmonary artery or aorta through six months.¹¹ The clinical trial implanted its first patient in September 2017. The ADO II AS IDE trial will enroll a maximum of 50 patients at up to 10 children's hospitals within the U.S. No additional clinical data is available.

Magnamosis magnetic compression anastomosis system (Magnet-in-Me)

Magnamosis is a device consisting of two magnets designed to connect pieces of intestine between the attractive force of the magnets – without the use of staples or sutures. The procedure involves placing a parabolic magnet endoscopically in the lumen of each structure to be joined, and then allowing the attractive force between the magnets to create a compression anastomosis by tissue remodeling.¹⁵ It is believed the anastomosis will form after four to six days and the magnets will be expelled naturally through the large intestine. The device is supplied single-use and sterile. It is comprised of a matched pair of self-centering rare earth magnets encased in medical-grade polycarbonate.¹⁶ The geometry of the magnets' mating surfaces applies force on the inside of the mated rings to produce compression. Lesser force on the outer side of the mated rings encourages inflammatory healing. This first-in-human device for anastomosis of intestine is targeted for 18 years and older. For babies and children with congenital gastrointestinal anomalies like esophageal atresia, duodenal atresia and short bowel syndrome, the possibility of making anastomoses minimally invasive without sutures or staples offers many advantages.¹⁵ The device is not available for sale.

Magnamosis First-in-human Study (NCT02043392)¹⁶

Michael R Harrison, MD (U.S., UCSF Medical Center) (member), principal investigator

Size: 10 patients

Non-randomized, prospective, single-center pilot study

This first-in-human, non-randomized, prospective, single-center pilot study will evaluate the feasibility and safety of creating an intestinal anastomosis using the Magnamosis Magnetic Compression Anastomosis (Magnamosis) device. Ten otherwise healthy subjects, ages 18-60 years, with a disease process necessitating open or laparoscopic surgical anastomosis for re-establishment of intestinal continuity that would otherwise be performed using sutures or

stapling devices will be enrolled. Participation in the study requires a time commitment of three months. The total duration of the study is 18 months to ensure three-month follow-up on each subject, with long-term follow-up of each subject at one and two years post operation. The primary outcome measure will be the incidence of anastomotic leaks related to the use of the device within 30 days post operatively leading to a re-interventional procedure. Subject follow-up will be conducted after discharge at two weeks (in person, in clinic), and at one month, three months, one year and two years either in person or via email, telephone, Skype or other non in-person method. No data is currently available.¹⁷

Products in development

LIFEBubble NICU umbilical catheter stabilizer (Novonate)

LIFEBubble is a catheter-stabilization device. The company is focusing on a solution to reduce the rate of infections in babies with an umbilical cord catheter. The device is designed to stabilize the umbilical catheter while preventing bacterial migration and protecting the umbilical stump. The securement device features the ability to keep the insertion site open to permit the natural desiccation of the stump, and accommodating the unique morphology of an umbilical catheter.¹⁸ The device is a small, semi-rigid, open dome that can be secured against the baby's skin.¹⁹ The device is in the development stage. This device is not available for sale in the U.S.

Perf-Fix tympanoplasty gel patch (Tympanogen)

Perf-Fix is a gel patch for nonsurgical eardrum repair. It can be applied in a minimally invasive procedure in an office setting within 10 minutes, without general anesthesia or margin freshening.²⁰ This proprietary gel technology patch encourages regeneration of the entire, three-layered tympanic membrane structure at the same success rates as traditional tympanoplasty.²¹ The gel patch is currently in development in preparation for an upcoming clinical trial scheduled to begin in late 2018. The device is not available for sale in the U.S.

StethAid digital stethoscope (AusculTech DX)

StethAid is a mobile device-based digital stethoscope that aids in the diagnosis of pediatric heart murmurs.²² A small box attaches to a stethoscope and wirelessly communicates with a smartphone. An app records and analyzes the sounds in a patient's chest and determines whether the murmur is benign or abnormal. Through machine learning, the highly accurate computer algorithm is used to discriminate a heart murmur from pathological

murmurs. The algorithm will intimately focus on Still's murmur and allow pediatricians to identify the murmur in the office setting without needing expert consultation. The device may reduce referrals to cardiologists, reduce the financial and emotional cost of testing and provide reassurance to both families and medical personnel.²³ The device is not available for sale.

EOPatch (EOFlow)

The EOPatch is a three-day wearable, adhesive, waterproof insulin pump. The device incorporates a proprietary electroosmotic pumping technology that allows it to be smaller and lighter than other insulin pumps. It comes with a handheld touchscreen-enabled controller, weighs less than an ounce, and measures 49.5 by 12.6 millimeters. A 30-gauge stainless steel needle delivers the drug and the device has sensing technology to detect needle occlusion. The smaller device size can be held by younger diabetes patients. A recent round of funding will be used to conduct a clinical trial for regulatory approval. It is available outside the U.S. but has not received FDA clearance.

Evopump medication system (Cam Med)

The Evopump is a bandage-like, wearable IV pump for subcutaneous delivery of medications targeting Type 1 diabetic patients. Cam Med, which specializes in microfluidic drug-delivery technology, is working on an ultrathin, flexible, bandagelike pump that delivers one or more injectable drugs. The Evopump uses a unique multi-reservoir, electrochemically-actuated design and can be manufactured at a much lower cost than conventional pumps. The comfort and relatively small size of the device makes it especially appealing for pediatric diabetes patients. The pump is still in the development stage. It is not available for sale in the U.S.

neoNAV catheter visualization system

(NAVi Medical Technologies)

The neoNAV device provides accurate, real-time localization of the catheter tip during the umbilical venous catheterization (UVC) procedure used in critically ill newborns to reduce the risk of catheter malposition. The system uses a proprietary algorithm and the patient's own electrical activity from the heart (electrocardiography) to inform and assist catheter tip position navigation and placement. It shows these signals on a display that is similar to a traffic light. The system does not affect the function of the catheter, only how it is being inserted. The device has not been FDA cleared and is not available for sale.

SVS baby box (Prapela)

The SVS is a novel "baby box" that will allow for a nonpharmacological approach to help drug-exposed infants relax and sleep during withdrawal and post-withdrawal care. The box produces gentle, random vibration to stimulate a baby to improve breathing rhythm and relaxation during sleep. The system includes the box, a vibrating platform, a mattress pad and an electronics package. The electronics package stores microprocessors used to control the vibrations. Neonatal abstinence syndrome occurs when a pregnant mother takes opiate drugs like heroin, codeine, oxycodone, methadone or buprenorphine. If the mother continuously uses the drugs, the baby will be born with a dependency, according to the U.S. National Library of Medicine. The product is primarily being targeted for the consumer market with future health care applications. Having a baby sleep in a box isn't as out of the norm as one might think, either. It's been a common practice in Finland since the 1930s.²⁴ The company hopes to commercialize the product in late 2018.

Un-named (Kite Medica)

Kite Medical is in the early development of a novel device for a pain-free, noninvasive means of detecting kidney reflux in children with urinary tract infections. The device is a single-use electrode belt, avoiding the radiation exposure to children under current standard of care.²⁵ Kidney reflux is a common urological disorder in childhood, affecting up to 3 percent of young children. It is most prevalent from 6 months to 5 years of age. The device is not for sale anywhere.

EyeBOX (Oculogica)

EyeBOX is a noninvasive eye tracking device being developed to reliably and objectively diagnose effects of elevated intracranial pressure (ICP) in those with traumatic brain injury (TBI) and concussion. A proprietary algorithm does not require baseline testing. The system analyzes 67 domains of eye movement of neurological function and facilitates objective diagnosis targeted to the individual patient. The system's data collection capability feeds the algorithm that generates an assessment called the BOX SCORE, which indicates the presence of TBI or concussion. The test takes less than four minutes and enables health care providers, parents, coaches and patients to make informed decisions on treatments. The testing is simple, requiring test subjects to rest their chin and forehead comfortably on the device and watch a video for less than four minutes. Accurate results require no literacy, language fluency or even an ability to follow directions.²⁶ The device is investigational and is not cleared for sale by the FDA.

Supplier watch

Spotlight on suppliers in the pediatric market

FUJIFILM Medical Systems, U.S.A., Inc. (XR0386)

Company overview

Fujifilm is a global technology company founded in 1934 as a photographic film maker. Since then, Fujifilm has leveraged its imaging and information technologies to become known for innovation in health care, pharmaceuticals, skincare, graphic arts, optical devices and other high-tech areas.

Pediatric imaging solutions

The company's pediatric imaging solutions ensure gentle dose without sacrificing image quality, eliminate grids to reduce dose and retakes and even improve infection controls with exclusive antibacterial coating on its detectors and mobile system.

Fujifilm innovation: Virtual Grid, Dynamic Visualization and ISS Technology

Virtual Grid This innovative technology intelligently simulates grid use, eliminating scatter effect, to improve contrast and clarity and reduce dose by as much as 50 percent for images acquired without a grid. It is useful in portable exams and simplifies acquisition, positioning, patient comfort, and eliminates artifacts associated with physical grid misalignment and improper source-to-image distance SID. The Virtual Grid can be applied to all body parts (excluding breast imaging) including chest, abdomen, head, spine, pelvis, upper and lower extremities.

Dynamic Visualization Fujifilm's innovative image processing uses artificial intelligence for auto recognition of bone, anatomy patient thickness characteristics and orthopedic hardware. It intelligently adapts image contrast and density to improve uniformity in both dense and thin regions for challenging images, for large anatomy and patients, or for any low-dose or low-penetration exams.

Fujifilm's proprietary **Irradiated Side Sampling (ISS)** technology positions its capture electronics thin film transistors (TFTs) at the irradiation side, in contrast to traditional detectors. This design significantly suppresses scattering and attenuation of X-ray signals, improving efficiency to produce sharper images at up to 20 percent lower doses compared to traditional designs.

FDR D-EVO GL detector

The world's first and only single-exposure, long-length DR detector increases safety and comfort through faster image acquisition and gentle low dose for the youngest and most vulnerable patients.

The FDR D-EVO GL detector includes Fujifilm's innovative technologies: Virtual Grid, Dynamic Visualization and ISS Technology. This long-view single exposure detector ensures consistent, easy patient positioning and image acquisition, reducing exam discomfort and retakes for a better patient experience.

FDR D-EVO GL is 17 by 49 inches, expanding the traditional 14-inch width of CR long length field of view by three full inches to better accommodate a variety of patient sizes and help prevent retakes due to anatomy cut-off. FDR D-EVO GL enhances the workflow of long-view radiography by capturing the entire image in just a few seconds, reducing the chance for patient motion-induced artifacts and reducing the time that the patient must remain still.

FDR AQRO portable

The FDR AQRO is a compact, portable digital X-ray system that combines the high sensitivity of the FDR D-EVO II detectors and Fujifilm's refined image processing advancements to generate high-resolution images with low patient dose.

The FDR AQRO also features Fujifilm's innovative Virtual Grid, Dynamic Visualization II and ISS technologies.

The onboard, full-featured technologist console provides immediate image previews, dose tracking and exposure and deviation index features, in addition to a host of image manipulation and workflow tools. A double-click magnification feature gives technologists the ability to zoom full screen and toggle edge enhancement to better view peripherally inserted central catheter (PICC) lines and detect patient movement.

Pharmaceutical watch

Novel drug approvals, indications and formulations – FDA-approved to treat pediatric patients

New drugs

Burosumab-twza (Crysvita) injection for subcutaneous use (Ultragenyx)

Fibroblast growth factor 23 (FGF23) blocking antibody indicated for the treatment of X-linked hypophosphatemia (XLH) in adult and pediatric patients 1 year of age and older. Burosumab is the first drug approved to treat XLH, which is a rare, inherited form of rickets that affects approximately 3,000 children and 12,000 adults in the United States. Prior

to its approval, common treatment options for XLH were activated vitamin D metabolites and phosphate salts. The approval of burosumab in adults was based on the results of a placebo-controlled trial that demonstrated 94 percent of treated patients achieved normal phosphorus levels compared with 8 percent of those treated with placebo. In a single-arm trial, 94 to 100 percent of children treated with burosumab achieved normal phosphorus levels.

Cannabidiol (Epidiolex) solution for oral use (Greenwich Biosciences)

Indicated for the treatment of seizures associated with Lennox-Gastaut syndrome (LGS) or Dravet syndrome in patients 2 years of age and older. Epidiolex is the first FDA-approved drug that contains highly-purified, plant-derived cannabidiol (CBD). It is also the first drug approved for the treatment of Dravet syndrome. Its phase 3 development program consisted of a single trial in Dravet syndrome and two trials in LGS.²⁷ In all trials, Epidiolex was associated with a significant decrease in monthly seizures compared with placebo. Epidiolex will not be available until the Drug Enforcement Agency reschedules it. Currently, all cannabidiol products are Schedule I products, illegal to sell in the United States.

Epoetin alfa-epbx (Retacrit) injection for intravenous or subcutaneous use (Hospira Inc, a Pfizer company)

Erythropoiesis-stimulating agent (ESA) indicated for treatment of anemia due to chronic kidney disease in patients on dialysis and not on dialysis, zidovudine in patients with HIV-infection and the effects of concomitant myelosuppressive chemotherapy.

Also indicated for reduction of allogeneic red blood cell transfusions in patients undergoing elective, noncardiac, nonvascular surgery. Epoetin alfa-epbx is the first FDA-approved biosimilar of Procrit and Epogen. It was approved for all the same indications as the reference products, but did not receive interchangeable status. As there are no pending patents to prevent biosimilar competition, it is expected that Pfizer will launch epoetin alfa-epbx by the end of 2018.

Moxidectin tablet for oral use (Medicines Development for Global Health)

Anthelmintic indicated for the treatment of onchocerciasis due to *Onchocerca volvulus* in patients aged 12 years and older. Moxidectin is the first new drug treatment approved for onchocerciasis, also known as river blindness, in 20 years. It is estimated that 99 percent of the cases of river blindness occur in sub-Saharan Africa. In the phase 3 trial,²⁸ moxidectin significantly reduced skin microfilariae density at 12 months post-treatment compared with the current standard-of-care treatment, ivermectin.

Ozenoxacin (Xepi) cream for topical use (Medimetriks)

Ozenoxacin is indicated for the topical treatment of impetigo due to *Staphylococcus aureus* or *Streptococcus pyogenes* in adult and pediatric patients 2 months of age and older. Ozenoxacin is the first FDA-approved topical quinolone and is the first new topical treatment approved for impetigo in more than a decade. Mupirocin (Bactroban) and retapamulin (Altabax) are other approved topical treatment options for impetigo.

Pegfilgrastim-jmdb (Fulphila) injection for subcutaneous use (Mylan)

Leukocyte growth factor indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia. Pegfilgrastim-jmdb is the first FDA-approved biosimilar of Amgen's pegfilgrastim (Neulasta). It is approved for all of the same indications as reference pegfilgrastim except for the hematopoietic subsyndrome of acute radiation syndrome indication, which is protected by orphan-drug exclusivity until November 2022.

Tecovirimat (Tpoxx) capsule for oral use (Siga Technologies)

Inhibitor of the orthopoxvirus VP37 envelope-wrapping protein indicated for the treatment of human smallpox disease in adults and pediatric patients weighing at least 13 kg. Tecovirimat is the first FDA-approved drug for the treatment of smallpox. While smallpox was eradicated in 1980, there is fear that smallpox could be used as a future bioweapon. The effectiveness of tecovirimat was based on demonstration of significant reductions in mortality and viral load compared with placebo in animal studies.

Tezacaftor/ivacaftor and ivacaftor (Symdeko) tablets for oral use (Vertex Pharmaceuticals)

A combination product indicated for the treatment of patients with cystic fibrosis (CF) age 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 or clinical evidence. Symdeko is Vertex's third FDA-approved disease-modifying CF therapy. Vertex's other therapies include the combination of lumacaftor/ivacaftor (Orkambi) and ivacaftor (Kalydeco).

Voretigene neparvovec-rzyl (Luxturna) intraocular suspension for subretinal injection (Spark Therapeutics)

Adeno-associated virus vector-based gene therapy indicated for the treatment of patients with confirmed biallelic RPE65 mutation-associated retinal dystrophy. Patients must have viable retinal cells as determined by the treating physician or physicians. Voretigene neparvovec is the first FDA-approved gene therapy for a genetic disease.²⁹ It is approved for the indication, biallelic RPE65 mutation-associated retinal dystrophy. Thirteen (65 percent) patients assigned to voretigene demonstrated maximum possible improvement versus no control participants. Spark Therapeutics announced that voretigene will cost \$850,000.

New indications

Blinatumomab (Blincyto) for injection for intravenous use (Amgen)

Bispecific CD19-directed CD3 T-cell engager indicated for the treatment of adults and children with B-cell precursor acute lymphoblastic leukemia (ALL) in first or second complete remission with minimal residual disease (MRD) greater than or equal to 0.1 percent. Blinatumomab is the first FDA-approved treatment for patients with MRD-positive ALL. MRD is a strong prognostic factor for relapse in patients with ALL. Accelerated approval for blinatumomab for MRD-positive ALL was based on the results of the phase 2 BLAST trial.³⁰ In the BLAST trial, 88 of 113 patients (78 percent; 95 percent CI, 69-85percent) achieved a complete MRD response after one cycle of treatment. Further study will be required to confirm that blinatumomab improves disease-free survival.

Fingolimod (Gilenya) capsule for oral use (Novartis Pharmaceuticals Corporation)

Sphingosine 1-phosphate receptor modulator indicated for the treatment of relapsing forms of multiple sclerosis (MS) in patients 10 years of age and older. This approval represents the first FDA approval of a drug to treat MS in pediatric patients. It is estimated that approximately 8,000 to 10,000 pediatric patients in the United States have MS. The approval of fingolimod was supported by PARADIGMS, a double-blind, randomized, phase 3 comparative trial. In the trial, the annualized relapse rate was significantly

lower in pediatrics treated with fingolimod (0.122 percent) than in patients who received interferon beta-1a (0.675 percent). The annualized rate of the number of new or newly enlarged T2 lesions was also significantly lower with fingolimod treatment.

Influenza vaccine (Fluarix Quadrivalent) suspension for intramuscular use (GlaxoSmithKline)

Vaccine indicated for active immunization in persons age 6 months and older for the prevention of disease caused by influenza A subtype viruses and type B viruses contained in the vaccine. This approval expands the indication of Fluarix to include use in patients aged 6 months and older. Previously, the vaccine was only approved in patients 3 years of age and older. With this approval, there are now three vaccines approved for use in patients aged 6 to 35 months: Fluarix, Fluzone Pediatric and FluLaval.

Nilotinib (Tasigna) capsule for oral use (Novartis Pharmaceuticals)

Kinase inhibitor indicated for the treatment of pediatric patients greater than or equal to 1 year of age with newly diagnosed Philadelphia chromosome positive chronic myeloid leukemia (Ph+ CML) in chronic phase (CP) and with Ph+ CML-CP resistant or intolerant to prior tyrosine-kinase inhibitor therapy. Nilotinib is the third kinase inhibitor that is approved as first-line treatment for children with CML. Imatinib (Gleevec) and dasatinib (Sprycel) are also FDA approved for first-line treatment.

New formulations/combinations

Efavirenz, lamivudine and tenofovir disoproxil fumarate (Symfi) tablet for oral use (Mylan)

Three-drug combination indicated as a complete regimen for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adult and pediatric patients weighing at least 40 kg. Mylan has made a commitment to launch lower-cost antiretrovirals. To this end, Mylan has recently received FDA approval for Symfi Lo, Symfi and Cimduo. Symfi Lo, which was launched in March, and Symfi contain the same triple combination of ingredients; however, Symfi Lo has a reduced dose of efavirenz.

Hydroxyurea (Siklos) tablet for oral use (Medunik USA)

An antimetabolite indicated to reduce the frequency of painful crises and to reduce the need for blood transfusions in pediatric patients, 2 years of age and older, with sickle cell anemia with recurrent moderate to severe painful crises. This is the first product that has received FDA approval for the reduction of the frequency of painful sickle cell crises in pediatric patients. Approval was based on an open-label, single-arm trial that demonstrated a decreased percent of patients after 12 months of treatment having at least one vaso-occlusive episode, one episode of acute chest syndrome, one hospitalization due to sickle cell disease or one blood transfusion.

Insulin lispro (Admelog) injection for subcutaneous or intravenous use (Sanofi-Aventis)

Rapid-acting insulin analog indicated to improve glycemic control in adults and pediatric patients 3 years and older with type 1 diabetes mellitus and adults with type 2 diabetes mellitus. Insulin lispro is the first short-acting insulin approved as a follow-on biologic through the 505(b)(2) pathway. Its approval relied, in part, on the FDA's findings of safety and efficacy for insulin lispro (Humalog) and on two Admelog-specific phase 3 trials (SORELLA 1³¹ and 2³²).

Valsartan (Prexartan) oral solution (Carmel Biosciences)

An angiotensin II receptor blocker indicated for hypertension in adults and children 6 years and older, heart failure and stable left ventricular failure or dysfunction following myocardial infarction. This is the first and only commercially-available FDA approved oral liquid dosage form of an angiotensin receptor blocker.

Black box warning – fetal toxicity. The most common adverse reactions are headache, dizziness, fatigue, abdominal pain, diarrhea, arthralgia, back pain, hyperkalemia, hypotension, cough and increased creatinine.

Vancomycin hydrochloride (Firvanq) powder for oral solution (CutisPharma)

Glycopeptide antibacterial indicated in adults and pediatric patients less than 18 years of age for the treatment of Clostridium difficile-associated diarrhea (CDAD) and for the treatment of enterocolitis caused by Staphylococcus aureus (including methicillin-resistant strains). Firvanq is the only FDA-approved vancomycin oral liquid.

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