

Emerging pediatric technologies

Pediatric Technology Watch | 2019 Volume 3



Table of contents

Introduction	3
Market watch.....	3
The Food and Drug Administration and pediatric medical devices	4
Economic watch	4
Technology watch	6
Innovative medical devices in the pediatric pipeline	6
Currently available products	7
Products in development	7
Supplier watch	10
Procter & Gamble	10
Alcresta Therapeutics	10
Pharmaceutical watch	11
Novel drug approvals, indications and formulations, and in clinical trials....	11
New drug approvals	11
New indications.....	13
New formulations	13
In clinical trials.....	14
References.....	15

Disclaimer: Vizient® staff attend clinical sessions at important scientific meetings throughout the year. The staff meet with suppliers, review new technologies and monitor 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. 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. It also features Vizient pricing projections for both products and pharmaceuticals.

Market watch

National health spending is projected to grow 0.8 percentage points faster than gross domestic product (GDP) per year over the 2018-2027 period; as a result, the health share of GDP, which was 17.9% in 2017, is expected to rise to 19.4% by 2027.¹ In addition, prices for health care goods and services are projected to grow 2.5% per year, on average, for 2018-2027—faster than the average price growth experienced over the last decade—and to account for nearly half of projected personal health care spending growth.¹

The global pediatric clinical trials market is expected to exhibit a compound annual growth rate of 8.8% over the forecast period, owing to a robust product pipeline and increasing approvals of new pediatric drugs.² Among clinical trial phases, the preclinical segment held a dominant position in the pediatric clinical trials market in 2018, owing to safety and efficacy concerns

regarding new molecules or drugs, as the former must go through preclinical study.² Among study design type, the randomized trial segment held a dominant position in the pediatric clinical trials market in 2018, as this type of design eliminates the chance of bias in clinical trials and is considered the most favorable.² Among medical conditions, the neuropsychiatric conditions segment held a dominant position in the pediatric clinical trials market in 2018, owing to an increasing number of mental disorders in children and adolescents aged 14 and under.² Key players operating in the global pediatric clinical trials market include Syneos Health Inc.; Iqvia Holdings, Inc.; Charles River Laboratories International Inc.; Covance Inc.; Icon PLC; Pharmaceutical Product Development, LLC; Genentech (F. Hoffmann-La Roche AG); Pfizer, Inc.; Bristol-Myers Squibb; GlaxoSmithKline PLC; Sanofi S.A.; Novartis AG; Johnson & Johnson; Merck & Co., Inc.; Shire PLC; and Vertex Pharmaceuticals Inc.²

The Food and Drug Administration and pediatric medical devices

Each year, far fewer medical devices are approved by the U.S. Food and Drug Administration (FDA) for children than adults. This means pediatricians don't always have the most up-to-date tools available to address medical challenges in infants and children. In 2007, with the enactment of the Pediatric Medical Device Safety and Improvement Act, the FDA was required to provide annual reports to congressional committees that included a report on pediatric indications for use in premarket approvals (PMAs) and Humanitarian Device Exemptions (HDEs).³ The most recent information collected in fiscal year 2017 for devices approved through the Center for Devices and Radiological Health indicates that out of 66 PMA and HDE devices, 62 (94%) had a pediatric subpopulation that suffered from the disease or condition that the device was intended to treat, diagnose or cure.³ Out of those 62 devices, only 18 had an indication for use in the pediatric population.³ Moreover, only 11 out of those 18 devices were indicated for use in children under the age of 18.³ Over the last 10 years there have been more innovative technologies entering the market. Overall, there's been an upward trajectory in the total number of PMAs and HDEs approved per year; however, adult approvals have increased at a rate of 3.8 per year compared with the number of devices with pediatric indications, which increased at a rate of only one device per year.³ However, the FDA remains committed to supporting the development and availability of safe and effective pediatric medical devices.

Current initiatives include³:

- Increasing the number of medical devices with labeling for pediatric patients by incorporating known information about device effects in other populations to support pediatric indications.
- Recruiting pediatric experts for FDA advisory panels whenever there is a reasonable likelihood that the device under discussion will be used for children.
- Protecting children who participate in clinical trials.
- Collaborating with the Institute of Medicine on the effectiveness of postmarket surveillance of pediatric medical devices.
- Collecting data on the unmet needs for pediatric medical devices and the barriers to the development of new pediatric devices.

Economic watch

Price projections affecting the pediatric market

Prescription drug spending grew just 0.4% in 2017, while 2018 saw a 3.3% increase.⁴ This acceleration was due to a faster than anticipated utilization growth partially driven by an increase in new drug introductions. Prescription drug spending growth is projected to reach 4.6% in 2019, due to faster utilization growth from both existing and new drugs, as well as a modest increase in drug price growth.⁴ For 2020-2027, prescription drug spending is projected to grow by 6.1% per year on average, or 1.5 percentage points more rapidly than in 2019, influenced by the potentially increased use of new drugs and efforts by employers and

insurers to encourage patients with chronic conditions to consistently treat their diseases.⁴

Vizient expects overall market prices for supplies to increase 1.4% in 2019 (Table 1). Table 2 shows projected changes in drug prices over the next 18 months.

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

Product category	National price inflation projection (%)
Cardiology	1.5
Cardiac rhythm management	-0.5
Drug-eluting stents	-1.1
Orthopedic overall	-0.7
Neurosurgical	1.7
Orthopedic supplies	0.5
Joint implant	-2.1
Spinal	-0.1
Trauma	1.0
IV solutions	3.0
Medical/surgical supplies	0.5
Medical equipment	1.2
Imaging equipment	-1.3
Laboratory equipment	0.3
Laboratory consumables	0.5
Medical gases	3.1
IT hardware	-2.3
IT software	-1.3
Purchased services	1.9
IT services	1.0
Commercial printing	0.3
Office supplies	2.1
Furniture	3.3
Water	3.6
Electricity	1.9
Natural gas	2.1
Telephone	-1.5
Internet	0.5
Food overall	2.2
Overall projected price change	1.4

Source: Vizient Budget Impact Projections Report, Q1 2019.
Abbreviations: IT = information technology; IV = intravenous.

Table 2. Projected drug price changes

Product group	Estimated price change weighted by Vizient purchases (%)
Contract purchases	+1.12
Noncontract purchases	-3.16
Total weighted average drug price inflation estimate	-4.28

Source: Vizient Drug Price Forecast, January 2019. The January 2019 Drug Price Forecast is our best estimate of the change in the cost of pharmaceuticals that participants in the Vizient Pharmacy Program will be purchasing between July 1, 2019, and June 30, 2020. The forecast focuses on pharmaceutical products used across multiple health system settings, including inpatient and non-acute environments, and provides a year-over-year estimate of the expected price change. 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

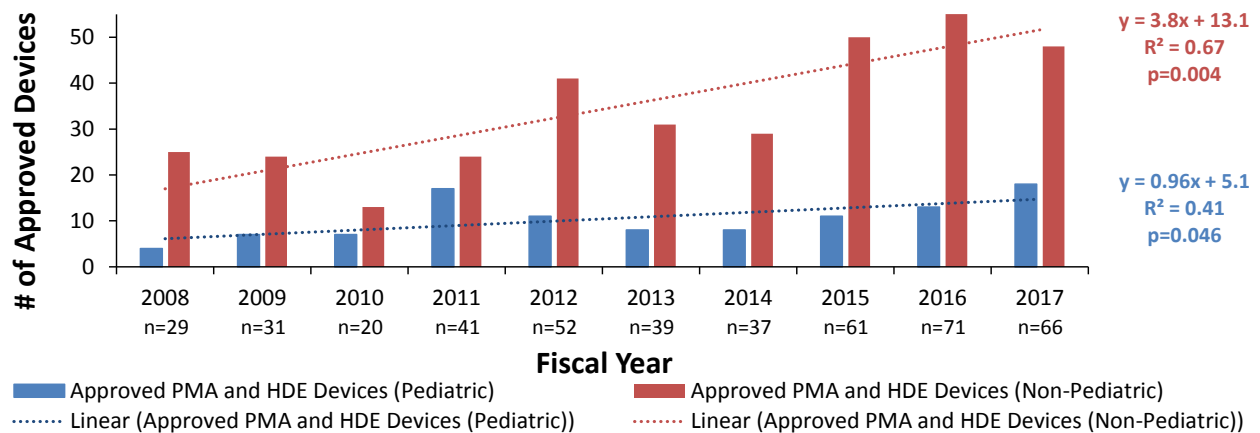
Innovative medical devices in the pediatric pipeline

Although a need for pediatric medical devices has existed for many years, product development has lagged. However, innovation in the pediatric market is increasing. 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. Innovation will help health care providers improve their care of pediatric patients.

Prior editions of this publication discussed the increase in pediatric product development. A recently published paper dramatically demonstrates this increase over the past four years. According to McCorry,⁵ a significantly greater number of new pediatric devices were FDA approved and cleared in 2011. In addition, the average number of pediatric device approvals has doubled over the past five years and is up 50% over prior years⁵ (Figure 1).

This is an exciting trend for pediatric health care. These new devices are not simply revisions of adult medical devices, but are designed to meet the unique needs of children.

Figure 1. Rate of approved adult devices compared to approved pediatric devices



Source: McCorry MC. FDA numbers and facts on pediatric medical devices. Presented at: Pediatric Medical Device Development Public Meeting; August 13-14, 2018; Silver Spring, MD. <https://www.fda.gov/downloads/MedicalDevices/NewsEvents/WorkshopsConferences/UCM618909.pdf>. Accessed April 8, 2019.

Currently available products

Amplatzer Piccolo Occluder (Abbott Vascular)

The Amplatzer Piccolo Occluder is a percutaneous, transcatheter occlusion device intended for the nonsurgical closure of a patent ductus arteriosus. The self-expanding, wire mesh medical device is inserted through a small incision in the leg and guided through vessels to the heart. The device can be implanted in tiny babies weighing as little as two pounds, and is intended for babies who need corrective treatment but who may be nonresponsive to medical management and are considered too high risk to undergo corrective surgery. Because the device is deployed in a minimally invasive procedure, many of the babies are able to be weaned from artificial respirator support soon after the procedure. The device is contraindicated in infants weighing < 700 grams, or who are younger than 3 days old at time of the procedure. The device received a PMA from the FDA in January 2019.

Cast21 arm exoskeleton (Cast21, Inc.)

The Cast21 exoskeleton cast has been developed as an alternative to traditional plaster casting to help treat orthopedic fractures. The device is constructed of a malleable material that can be easily applied to the patient's arm. Once in proper position, a proprietary material is injected into the lattice structure, forming a rigid and anatomical contoured support. The combination of waterproof and biocompatible materials in the latticed design of the exoskeleton may provide a more comfortable and hygienic solution for patients. The product has been FDA 510K-approved.

Sherpak Cardiac Transport System (Paragonix Technologies)

The Sherpak Cardiac Transport System is a pediatric donor insulated heart transport system designed for small and pediatric hearts. The single-use system is designed to maintain a safe preservation temperature evenly across the donor organ—between 4 and 8 degrees Celsius—compared to uncontrolled ice chests and coolers. The storage temperature has been validated for more than 12 hours in various environments. The system includes connectors covering most aorta sizes, allowing both adult and pediatric hearts to be carried in its proprietary suspension system. The system was cleared for organ transport for up to four hours. The company's donor lung transport system and active heart preservation system, which provides oxygenated perfusion, are not yet available in the U.S. The cardiac transport system was FDA 510k cleared for sale and use in the U.S. in January 2019.

Snoo Smart Sleeper (Happiest Baby)

The Snoo baby sleeper is a responsive bassinet that improves sleep for babies by imitating the womb. It is indicated for use in infants up to 6 months or until baby can get up on hands and knees. The sleeper is constructed of breathable mesh walls to allow airflow. The core technology uses three specially engineered, white noise sounds to calm crying and enhance sleep. The sleeper has three built-in microphones and an algorithm that distinguishes cries from room noise, automatically responding by rocking babies gently to the same white noise sounds and even mimicking womb motion. The company offers the product directly to the consumer, and it can be either purchased or rented. The product is available for use in the U.S.

Products in development

Arteriovenous Fistula Eligibility System (Flow Forward Medical)

The Arteriovenous Fistula Eligibility (AFE) System is a small, temporary, external blood pump designed to stimulate flow-mediated dilation to increase patient eligibility for an arteriovenous fistula (AVF) and improve success rates after surgery. The system is indicated for hemodialysis vascular access in children with end-stage kidney disease.

In a proof of concept computational fluid dynamics study supporting the development of the device, data showed the AFE System can dilate veins 20 times faster than a traditional AVF, with a dramatic reduction in the formation

of internal hyperplasia (vascular scarring). Ovine cephalic veins were treated for six days with the system. On average, maximum vein diameter increased 89%, from 5.5 mm to 10.4 mm with treatment. After six weeks, both inflow arteries and outflow veins were larger in AFE System-assisted AVFs than in control AVFs, suggesting improved AVF maturation. An independent analysis of outflow veins of the AVFs created using the pretreated veins demonstrated an average blood flow rate that was 398% higher than AVFs created using untreated veins (1,712 mL/min vs. 344 mL/min) after six weeks of maturation. An independent histology review of these AVFs at six weeks

indicated the average cross-sectional area of AVF inflow arteries and outflow veins was 10.6 mm² and 200 mm², respectively, for pretreated AVFs, and 5.3 mm² and 86 mm², respectively, for control AVFs. These results are powering additional clinical trials. The system is investigational and is not currently available for use or sale.

Bioscrub central line cleaning system (Hub Hygiene)

Bioscrub is a low-cost, single-use cleaning technology that helps prevent central line-associated bloodstream infections. The system consists of a sugar cube-sized, open-cell, micro-abrasive foam saturated with isopropyl alcohol. The foam and alcohol help remove and absorb infection-causing agents. The sponge-like foam enables it to reach between luer lock threads to clean the septum. Capillary forces draw the removed infectious agents into the open-cell foam for disposal. The device is in the early clinical investigation phase. It is not available for use or sale within the U.S.

Boppli blood pressure monitor (PyrAmes, Inc.)

The Boppli blood pressure monitor is a lightweight wireless device that continuously and noninvasively monitors neonates' blood pressure in real time. The device uses a paper-thin, flexible sensor in compact wristwatch form as an alternative to arterial lines and inflatable cuff-based blood pressure monitoring systems. The device is in the early stages of development and is not currently available for use or sale.

exGraft expandable cardiac conduit (PECA Labs)

The exGraft is an expandable cardiovascular conduit that uses a minimally-invasive balloon catheter to allow for pediatric growth, thereby reducing surgeries. The device uses expanded polytetrafluoroethylene, with the addition of a radiopaque design and twist indicator to create a synthetic vascular graft. The design enhances visualization during surgery and follow-up. The product is available in 6- to 16-mm diameters and 15- to 35-mm lengths. The device has received Conformité Européenne (CE) Mark approval and 510(k) clearance from the FDA is being pursued.

Flowatch pulmonary artery banding (EspeRare Foundation)

The FloWatch pulmonary artery banding device has been medically proven to protect the hearts and lungs of newborn babies with severe cardiac defects while they wait to undergo open-heart surgery. The device has been used outside the U.S. in children in Europe and Asia from 2002 until 2012. The technology uses a micro-motor inspired by Swiss watchmakers, and has a telemetry flow control technology platform for remote adjustment and precise control of pulmonary artery blood flow and blood pressure in congenital heart diseases. The device comprises an active implant coupled with an external control unit, which allows blood pressure to be remotely controlled and regulated post-implantation without having to physically access the device, resulting in shorter intensive care stays and bypassing the need for revision surgery. The enhanced system is investigational and awaiting CE Mark approval, and is not for sale in the U.S.

Labready home diagnostic system (Vax-Immune)

Labready is a home-use proprietary diagnostic device that allows parents to collect their own child's culture, and know the results within minutes without leaving their home. The device uses a handheld processor that collects, protects, processes, transports and enriches a child's sample at the bedside. The device makes diagnosing infection faster, simpler, easier and less expensive. The device transmits the results to parents and the health care provider. The device is in development and is not currently available for sale or use.

Leap Heart Valve (Draper)

The Leap Heart Valve is a pediatric valve designed for children from birth to age 6 that passively expands to a twofold diameter to accommodate child growth. The initial goal is to serve the most critical unmet population—very young children who require heart valve diameters of less than 15 mm, as opposed to the 18 to 30 mm needed for adults. The design goal of the valve is to reduce the number of surgeries, as in some cases young children may need to undergo three to five major surgeries before adulthood to replace valves that fail or that are outgrown. The first-generation prototypes are currently in animal trials. This device is investigational and is not currently available for use or sale.

Neonav accurate catheter locator (NAVi Medical Technologies)

The Neonav, an electrocardiograph tip location system designed specifically for critically ill babies and infants, provides accurate information about the localization of an umbilical venous catheter to help reduce the risk of catheter malposition. The ability of clinical staff to confirm the central line location leads to reduced patient X-ray exposure, faster drug delivery and improved workflow. According to the manufacturer, current techniques result in 40% of lines being misplaced during the procedure due to lack of real-time feedback. A misplaced catheter can often cause severe harm to a patient. The device is not available for sale in the U.S.

NuPulseCV intravascular ventricular assist system (NuPulseCV, Inc.)

The NupulseCV intravascular ventricular assist system (iVAS) is a minimally invasive, long-term mechanical circulatory support device for pediatric patients with cardiac dysfunction. It works by using counterpulsation through a balloon-type device placed in the descending aorta. The device is intended to reduce pressure that the heart must work against, making it easier for the heart to pump blood to the body. The pump is powered by a small, battery-powered console contained in a satchel that can be worn over the shoulder. The implantation of the iVAS device is minimally invasive and requires only a small incision near the left or right clavicle, the placement of electrodes under the skin and a skin interface device, which enables communication between the implanted components and the external console. The company implanted its first device in its FDA clinical trial in February 2018. The system is not yet available for sale in the U.S.

Pediatric pulmonary valve (PolyVascular)

This pediatric pulmonary valve replacement is intended for young children with congenital heart disease. The minimally invasive, stent-mounted valve can be crimped to a very low profile to pass through children's small vessel sizes. It uses a proprietary polymer that enables reliable production and offers significant improvements in biocompatibility and durability compared with previous polymeric options. According to the company's website, the valve can accommodate children's growth and reduce the need for open-heart surgeries. The device is in early stage development, and is not currently available for use or sale.

Unnamed (Noninvasix, Inc.)

Noninvasix is developing a monitoring system for hypoxia-induced cerebral palsy. The system uses optoacoustic monitoring of cerebral venous oxygenation, and pulsing laser light directly measures the amount of oxygen the infant is receiving in real time. Prompt recognition of low cerebral venous oxygenation can be used to guide therapeutic interventions and reduce adverse outcomes. A sensitive, wide-band head strap is placed around the baby's head and pulsing frequencies of near-infrared light are sent into the brain's superior sagittal sinus vein. Hemoglobin in the blood absorbs the light at different frequencies depending on whether or not it is carrying oxygen. Absorption causes rapid thermal expansion of the hemoglobin, resulting in a measurable acoustic wave. The system is in development and is not currently available for sale or use.

Ureteral stent (Stent-X)

Ureteral stents are often used in children after surgery to repair an obstruction between the ureter and the kidney. These stents are temporary and must be removed via a cystoscopy procedure, which requires children to receive additional general anesthesia and a trip to the operating room. The Stent-X device simplifies stent removal by using a small magnetic bead and a precisely designed magnet to gently slide the stent out of a child's body. The device is investigational and if proven effective, this new innovation could avoid the risks associated with early overexposure of children to general anesthesia. The company received a National Institutes of Health award to support early-stage development and testing, which is currently underway. The device is not available for sale in the U.S.

VentriFlo extracorporeal blood pump (Design Mentor)

The VentriFlo True Pulse Pump is an extracorporeal blood pump for short-term cardiopulmonary support of pediatric open-heart surgery patients who require full or partial cardiopulmonary bypass. The pump delivers complete stroke volume, natural cadence and physiologic rest, just like the human heart. It is single-use and scalable with a flexible membrane, plastic housing and valves. Its pump driver is a linear electromagnetic motor that couples directly to the membrane driving the biomimetic waveform. Its small, electronic control console directs the pump driver based upon predefined waveform algorithms and user input. The pump is investigational and is not currently available for use or sale in the U.S.

Supplier watch

Procter & Gamble

Company overview

For more than 50 years, parents have trusted Pampers products while caring for their babies. Pampers are manufactured by Procter & Gamble, and are the No. 1-selling diaper worldwide. Every day, more than 25 million babies in 100 countries around the world wear Pampers. Pampers products include a complete range of diapers, wipes and training pants designed to provide protection and comfort for every stage of baby's development.

Swaddlers Pure Protection diapers

Swaddlers Pure Protection diapers combine Pampers trusted protection with thoughtfully selected materials.

This Innovative Technology-designated product approved by the Vizient Pediatric Council is clinically proven to be hypoallergenic, and provides trusted leakage protection and softness. Its premium mesh topsheet, stretchy sides, breathable materials and wetness indicator mean no performance compromises. Swaddlers Pure Protection also has urine color detection technology and an umbilical cord notch for neonatal patients. The innovative Absorb Away Liner is optimized with DualLayer Technology. The first hydrophobic layer touches infants' skin and helps keep it dry. The second hydrophilic layer draws urine and stool into the diaper. The product is made with sustainable sourced pulp and guaranteed Cotton Leads cotton.

Alcresta Therapeutics

Company overview

Alcresta Therapeutics is dedicated to developing and commercializing novel, enzyme-based products designed to address challenges faced by people living with gastrointestinal disorders and rare diseases. The company uses its proprietary technology platform to support a broad pipeline of products, with an initial focus on pancreatic insufficiency and fat malabsorption, which results in malabsorption common in cystic fibrosis (CF), digestive cancers, preterm birth and other serious diseases.

Relizorb digestive enzyme cartridge

As the first-of-its-kind digestive enzyme cartridge, Relizorb was selected to be a part of the Vizient Preferred Pediatric Program effective April 15, 2019, and was also awarded an Innovative Technology designation.

Fat malabsorption is a significant issue for patients with CF, short bowel syndrome, digestive cancers, pancreatitis and other diseases affected by exocrine pancreatic insufficiency (EPI), and these patients are also at higher risk of malnutrition. In addition, malnourished patients have been shown to have up to a 300% increase in hospital costs, as well as an increase in hospital length of stay and 30-day readmissions. Finally, enteral feeding intolerance due to EPI results in nutrient deficiency, prolonged intensive care unit/hospital length of stay and increased cost of care.

Current treatment options do not adequately address fat malabsorption in enterally fed patients. As a result, health care providers resort to switching from low-priced enteral formulas that are high in calories and long-chain triglycerides to more expensive semi-elemental formulas, which are lower in calories. However, feeding intolerance in EPI patients with fat malabsorption remains uncontrolled, causing patients to resort to the addition of oral pancreatic enzyme replacement therapy (PERT). PERT is not indicated in this patient population, nor has it been proven to be safe and effective when used with enteral tube feedings. In addition, PERT activity only lasts for an hour or less, which is a major disadvantage for overnight or continuous feeding.

Alcresta's lead product, Relizorb, is designed to reliably and efficiently deliver the optimal nutritional and caloric benefit from existing enteral feeding formulas by improving the breakdown and absorption of fats, in particular long-chain polyunsaturated fatty acids such as omega-3 (including docosahexaenoic acid [DHA] and eicosapentaenoic acid [EPA]) in patients aged 5 and above. Relizorb is the only FDA-approved product indicated to hydrolyze fats in enteral formula by mimicking the pancreatic lipase. By hydrolyzing more than 90% of the available fats in enteral formulas, Relizorb increases absorbable calories and normalizes fat absorption while improving tube feeding tolerance. Studies have shown that Relizorb increases

plasma levels of omega-3 fatty acids, including DHA and EPA; increases fat-soluble vitamin levels; and improves protein absorption.

Two prospective human clinical trials and a number of real-world reports support the safety and efficacy of

Relizorb. It can potentially reduce health care utilization by improving weight outcomes, decreasing gastrointestinal (GI) intolerance to tube feeding and normalizing absorption of fatty acids level. Moreover, its cost will be offset by the reduction in use of pancreatic enzymes and more expensive semi-elemental formulas.

Pharmaceutical watch

Novel drug approvals, indications and formulations, and in clinical trials

Antimicrobial resistance has been increasing globally and has reached a point that the World Health Organization (WHO) identifies it as a major threat to humanity.⁶ The WHO released a list of 12 bacteria that pose the greatest risk, with *Pseudomonas aeruginosa*, *Acinetobacter baumannii* and *Enterobacteriaceae* species being the three most critical highly resistant gram-negative organisms.⁶ In the U.S., data from the Centers for Disease Control and Prevention suggest that more than 2 million infections each year are caused by resistant organisms, while antimicrobial resistance is blamed for 23,000 deaths annually.⁶

The growing threat of antimicrobial resistance has been coupled with a decline in the research and discovery of

new and effective antibiotic agents.⁶ As a way to combat this, the FDA has created the qualified infectious disease product designation to grant priority review and give the pharmaceutical industry incentives in this field.⁶ Although newer antimicrobials have been brought to market over the past few years, a need for more potent antimicrobials still exists.⁶

When it comes to the innovative development of new drugs, therapies and treatments, the pharmaceutical industry tackles the science used to create new products, testing and manufacturing procedures, as well as the diseases and conditions that new products are designed to treat. Keeping up with new pediatric innovations and discoveries in drugs and formularies down the pipeline is critical.

New drug approvals

Baloxavir (Xofluza) tablet for oral use (Genentech)

Baloxavir is a polymerase acidic endonuclease inhibitor indicated for the treatment of acute uncomplicated influenza in patients 12 years of age and older who have been symptomatic for no more than 48 hours. It is the first new antiviral flu treatment with a novel mechanism of action approved by the FDA in almost 20 years.

In one trial, baloxavir was associated with a shorter time to alleviation of symptoms compared with placebo in adolescents (median difference: 38.6 hours) and in adults (median difference: 25.6 hours).

Calaspargase pegol-mknl (Asparlas) injection for intravenous use (Servier Pharmaceuticals LLC)

Calaspargase pegol-mknl is an asparagine-specific enzyme indicated as a component of a multiagent chemotherapeutic regimen for the treatment of acute lymphoblastic leukemia (ALL) in pediatric and young adult patients aged 1 month to 21 years. It is a novel formulation designed to extend the dosing interval compared with other available pegaspargase products, such as Oncaspar.

Fish oil triglycerides (Omegaven) injectable emulsion for intravenous use (Fresenius Kabi USA LLC)

Omegaven is an intravenous lipid emulsion that provides calories and fatty acids for pediatric patients with parenteral nutrition-associated cholestasis. Omegaven is the first and only FDA-approved fish oil lipid emulsion for this condition.

Jivi PEGylated-aucl antihemophilic factor (recombinant), lyophilized powder for solution for intravenous use (Bayer)

Jivi is a recombinant deoxyribonucleic acid-derived, factor VIII concentrate indicated for use in previously treated adults and adolescents aged 12 years and older with hemophilia A. It provides on-demand treatment and control of bleeding episodes, perioperative management of bleeding and routine prophylaxis to reduce the frequency of bleeding episodes. Jivi enters a crowded hemophilia A market; according to Bayer, however, its dosing flexibility is a differentiator. While Jivi must initially be dosed twice weekly, its frequency can be adjusted based on a patient's clinical response.

Lanadelumab-flyo (Takhzyro) injection for subcutaneous use (Dyax Corporation)

Lanadelumab is a plasma kallikrein inhibitor indicated to prevent attacks of hereditary angioedema (HAE) in patients 12 years of age and older. Lanadelumab is the first FDA-approved monoclonal antibody that provides targeted inhibition of plasma kallikrein. Cinryze and Haegarda, C1 esterase inhibitors, are also approved for prophylaxis of HAE attacks; however, lanadelumab is dosed less frequently.

Lobenguane I 131 (Azedra) injection for intravenous use (Progenics Pharmaceuticals Inc.)

Lobenguane I 131 is the first and only FDA-approved treatment for locally advanced or metastatic pheochromocytoma or paraganglioma. In trial results, 25% of patients experienced at least a 50% reduction in the use of all antihypertensive medications for at least six months. An overall tumor response was achieved in 22% of patients.

Lumacaftor/ivacaftor (Orkambi) tablet and granule for oral use (Vertex Pharmaceuticals Inc.)

Lumacaftor/ivacaftor is a cystic fibrosis transmembrane conductance regulator (CFTR) potentiator indicated for the treatment of CF in patients age 2 years and older who are homozygous for the F508del mutation in the CFTR gene.

Pegfilgrastim-cbqv (Udenyca) injection for subcutaneous use (Coherus Biosciences)

Pegfilgrastim-cbqv is a leukocyte growth factor indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anticancer drugs associated with a clinically significant incidence of febrile neutropenia.

Pembrolizumab (Keytruda) injection for intravenous use (Merck Sharp & Dohme)

Pembrolizumab, a programmed death receptor-1 (PD-1)-blocking antibody, is indicated for:

- Treatment of adult and pediatric patients with refractory primary mediastinal large B-cell lymphoma
- Treatment of patients with recurrent or metastatic cervical cancer who have disease progression on or after chemotherapy, and whose tumors express PD-L1 (combined positive score ≥ 1) as determined by an FDA-approved test

Sarecycline (Seysara) tablet for oral use (Almirall)

Sarecycline is a tetracycline class drug indicated for the treatment of inflammatory lesions of moderate to severe acne vulgaris in patients 9 years of age and older. Unlike other tetracycline antibiotics, sarecycline has a narrow spectrum with limited activity against enteric gram-negative bacteria, thereby limiting side effects.

Stiripentol (Diacomit) capsule and powder for oral suspension for oral use (Biocodex)

Stiripentol is indicated for the treatment of seizures associated with Dravet syndrome in patients 2 years of age and older taking clobazam. Stiripentol is the second FDA-approved drug labeled for the treatment of Dravet syndrome. The first, cannabidiol (Epidiolex), was approved in June 2018.

Tagraxofusp-erzs (Elzonris) injection for intravenous use (Stemline Therapeutics Inc.)

Tagraxofusp-erzs is a CD123-directed cytotoxin for the treatment of plastic plasmacytoid dendritic cell neoplasm (BPDCN) in adults and in pediatric patients 2 years and older. It is the first and only biologic approved for the treatment of BPDCN. Prior to approval, the standard of care for the treatment of BPDCN was intensive chemotherapy followed by bone marrow transplantation.

New indications

C1 esterase inhibitor (human) (Cinryze) for intravenous use (Shire)

C1 esterase inhibitor is indicated for routine prophylaxis against angioedema attacks in pediatric patients 6 years of age and older with hereditary angioedema. Cinryze is the first FDA-approved therapy to prevent angioedema attacks in pediatric patients as young as 6. Haegarda is also approved for routine prophylaxis, but has only been evaluated in pediatric patients aged 12 years and older. Approval for the label expansion was based on the results from a single-blind, phase 3 study that enrolled 12 patients aged 7 to 11 years.

Dasatinib (Sprycel) tablet for oral use (Bristol-Myers Squibb)

This new approval expands the indication of dasatinib to include the treatment of pediatric patients with newly diagnosed Ph+ ALL and marks its second pediatric leukemia indication. Dasatinib joins imatinib (Gleevec) as the second kinase inhibitor approved for this indication. Philadelphia-positive ALL is rare in pediatric patients, with an estimated occurrence in 2% to 4% of cases.

Dupilumab (Dupixent) injection for subcutaneous use (Regeneron)

This new approval expands the use of dupilumab as an add-on therapy for the treatment of moderate to severe asthma. Dupilumab was approved in 2017 for the treatment of atopic dermatitis. Uniquely, dupilumab's new approval also includes patients with oral corticosteroid-dependent asthma.

Emicizumab-kxwh (Hemlibra) injection for subcutaneous use (Genentech)

This new approval expands the use of emicizumab to treat patients with hemophilia A without factor VIII inhibitors. It also provides new dosing options of every two or four weeks. With this new approval, emicizumab is indicated for

routine prophylaxis in all hemophilia A patients and has a much larger market potential. Compared with competitors, it has a convenience advantage – namely, it can be administered subcutaneously and at a frequency of every one, two or four weeks.

Epinephrine (Symjepi) injection for intramuscular or subcutaneous use (Adams Pharmaceuticals Corporation)

This approval of a lower dose of Symjepi expands its use for the treatment of allergic reactions in children that weigh 15 to 30 kilograms. In July, Sandoz purchased U.S. rights to Symjepi and plans to commercialize the pen as soon as possible. With continued EpiPen shortages, another addition to the epinephrine market is welcome. In addition to EpiPen, other alternatives include an authorized Mylan generic; a recently approved, but not yet launched, Teva generic; Auvi-Q; and an authorized generic of Adrenaclick.

Human papilloma virus valent vaccine, recombinant (Gardasil 9) suspension for intramuscular injection (Merck Sharp & Dohme)

This approval expands the use of the human papilloma virus (HPV) valent vaccine to women and men aged 27 through 45 years. The expanded approval was based on data from a phase 3 trial conducted in women aged 24 to 45 years who received three doses of Gardasil 9's predecessor, the quadrivalent HPV vaccine (Gardasil). Over a median of four years of follow-up, vaccine efficacy against the incidence of persistent infection, cervical intraepithelial neoplasia and external genital lesions related to the four HPV strains contained in the vaccine was 88%.

Tbo-filgrastim (Granix) injection for subcutaneous use (Teva Pharmaceuticals USA Inc.)

This new approval expands the indication of tbo-filgrastim for use in pediatric patients. With this new indication, the FDA also approved a new presentation of the drug in 300-mcg/1-mL and 480-mcg/1.6-mL single-dose vials.

New formulations

Clobazam (Sympazan) film for oral use (Acquisitive Therapeutics)

Clobazam is a benzodiazepine indicated for adjunctive treatment of seizures associated with Lennox-Gastaut Syndrome in patients 2 years of age or older. Sympazan is the first and only FDA-approved oral film formulation

of clobazam. Results of multiple pharmacokinetic studies demonstrate that clobazam oral film is bioequivalent to clobazam tablets.

Glycopyrronium (Qbrexza) cloth for topical use (Dermira)

Glycopyrronium is an anticholinergic indicated for topical treatment of primary axillary hyperhidrosis in adults and pediatric patients 9 years of age and older. Glycopyrronium cloth for topical use is the third FDA-approved treatment for primary axillary hyperhidrosis (i.e., excessive sweating). Other approved treatments include aluminum chloride and botulinum toxin A (Botox).

Meloxicam (Qmiiz ODT) disintegrating tablet for oral use (TerSera Therapeutics LLC)

Meloxicam is a nonsteroidal anti-inflammatory drug indicated for osteoarthritis (OA) in adults, rheumatoid arthritis (RA) in adults and juvenile rheumatoid arthritis (JRA) with pauciarticular or polyarticular onset in pediatric patients who weigh greater than or equal to 60 kilograms. In addition to approval of this new oral disintegrating formulation, meloxicam is also available as a generic oral tablet (7.5 mg and 15 mg), oral suspension (7.5 mg/mL) and as a branded capsule (Vivlodex; 5 mg and 10 mg). The disintegrating oral tablet, oral tablet and oral suspension are approved for the same indications; the capsule is only approved for the treatment of OA pain. The launch plans for Qmiiz ODT are pending.

Methylphenidate hydrochloride (Jornay PM) extended-release capsule for oral use (Ironshore Pharmaceuticals Inc.)

Methylphenidate hydrochloride is a central nervous system stimulant indicated for the treatment of attention deficit hyperactivity disorder (ADHD) in patients 6 years of age and older. Jornay PM is the first stimulant medication that is approved for administration in the evening. The drug delivery system is designed to delay the initial release of the drug for up to 10 hours; thus, it is delivered in the morning when parents have indicated that ADHD symptoms are at their worst. In addition to traditional outcomes, the pivotal phase 3 trials also assessed Jornay PM's efficacy in the early morning period.

In clinical trials

AR101 (Aimmune)

AR101 is an investigational oral biologic drug designed to help protect patients from severe allergic reactions in case they are accidentally exposed to peanut. Patients would receive gradually increasing doses of AR101 to desensitize them to peanut over a period of about six months. Afterward, patients would continue to take maintenance doses of AR101 to maintain desensitization. Phase 3 clinical trials are currently being conducted for patients aged 4-17.

AVXS-101 (Novartis)

AVXS-101, a gene therapy for the treatment of spinal muscular atrophy, is intended to be an intravenous alternative to intrathecal nusinersen. STRIVE, an open-label, single-arm, single-dose, multicenter trial, is being conducted to evaluate the efficacy and safety of a one-time intravenous infusion of AVXS-101. Novartis announced that it believes a \$4 million to \$5 million price tag for a one-time treatment of AVXS-101 would be cost-effective; this cost could be a record price for a drug.

Bronchitol inhaled mannitol (Pharmaxis)

Bronchitol is indicated for the treatment of certain patients with CF to help them clear mucus from their lungs. Bronchitol, a dry powder mannitol that is inhaled twice daily using a small handheld device, works by rehydrating the airway, lung surface or both, and promoting a productive cough. Clinical trials have shown that it helps to increase mucus clearance, and improve the lung function and quality of life of people living with CF. Bronchitol is currently in phase 3 clinical trials for pediatric use.

Imipenem/relebactam (Merck)

Infections caused by gram-negative bacteria continue to be a major problem for hospitalized patients. The prevalence of carbapenem-resistant pathogens is increasing globally, highlighting the need for effective new antibacterial agents with gram-negative coverage. Imipenem/relebactam is in a phase 3 study targeting highly resistant gram-negative organisms.

NKTR-181 (Nektar)

NKTR-181, a selective mu-opioid agonist for pain relief, promises to be an opioid with a lower risk of dependence. According to Nektar, this is because it does not produce the same high levels of euphoria present with other opioids. It has a low permeability across the blood/brain barrier. Unlike many other addiction-resistant opioids—which are most often different formulations of existing drugs, with a tamper-evident mechanism added or a long-acting formulation—NKTR-181 is a new molecular entity, a first-in-class opioid.

Spravato esketamine nasal spray (Janssen)

Esketamine is a fast-acting nasal spray approved on March 5, 2019, for use in conjunction with an oral antidepressant in adults with treatment-resistant depression. This is the first new mechanism of action in three decades to treat major depressive disorder. This product would supplement therapy for patients on selective serotonin reuptake inhibitors and serotonin and norepinephrine reuptake inhibitor antidepressants. A trial is currently underway for adolescents aged 12–18 who are at risk for suicide.

Viaskin Peanut patch (DBV Technologies)

The Viaskin Peanut immunotherapy patch is indicated for the treatment of peanut hypersensitivity in children. Two phase III long-term studies in children aged 4–11 are ongoing, as well as a phase III trial in patients 1–3 years of age.

References

- 1 Sisko AM, Keehan SP, Poisal JA, et al. National health expenditure projections, 2018–27: Economic and demographic trends drive spending and enrollment growth. *Health Aff.* 2019;38(3):491–501. <https://www.healthaffairs.org/doi/pdf/10.1377/hlthaff.2018.05499>. Accessed April 8, 2019.
- 2 Pediatric clinical trials market to surpass US\$21,047.5 million by 2026. Coherent Market Insights website. <https://www.coherentmarketinsights.com/press-release/pediatric-clinical-trials-market-to-surpass-us-210475-million-by-2026-1274>. Accessed April 8, 2019.
- 3 FDA's efforts to optimize medical device innovation for pediatrics. U.S. Food and Drug Administration website. <https://www.fda.gov/downloads/MedicalDevices/NewsEvents/WorkshopsConferences/UCM616155.pdf>. Accessed April 8, 2019.
- 4 National health expenditure projections 2018–2027. Centers for Medicare & Medicaid Services website. <https://www.cms.gov/research-statistics-data-and-systems/statistics-trends-and-reports/nationalhealthexpenddata/downloads/forecastsummary.pdf>. Accessed April 8, 2019.
- 5 McCorry MC. FDA numbers and facts on pediatric medical devices. Presented at: Pediatric Medical Device Development Public Meeting; August 13–14, 2018; Silver Spring, MD. <https://www.fda.gov/downloads/MedicalDevices/NewsEvents/WorkshopsConferences/UCM618909.pdf>. Accessed April 8, 2019.
- 6 Kish T. New antibiotics in development target highly resistant gram-negative organisms. P&T Community website. <https://www.ptcommunity.com/journal/article/full/2018/2/116/new-antibiotics-development-target-highly-resistant-gram-negative>. Accessed April 9, 2019.

Notes

Notes

Notes

vizient[®]

290 E. John Carpenter Freeway
Irving, TX 75062
(972) 830-0000
www.vizientinc.com



For more information, contact us at (800) 842-5146
or vizient.support@vizientinc.com.

As the nation's largest member-driven health care performance improvement company, Vizient provides network-powered insights in the critical areas of clinical, operational, and supply chain performance and empowers members to deliver exceptional, cost-effective care.