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August 2023

New FDA Approvals and Market Updates

Recent US Food and Drug Administration (FDA) approvals and market updates of interest to Medicaid are highlighted in the following pharmacy FLASH. Topics covered include the following:

- **Gene therapy for Duchenne muscular dystrophy (DMD) approved June 22, 2023:** Elevidys (delandistrogene moxeparvovec) received accelerated approval for pediatric patients four years through five years of age with DMD
- **Gene therapy for hemophilia A approved July 6, 2023:** Roctavian (valoctocogene roxaparvovec) received approval for the treatment of adults with severe hemophilia A
- **Antibody treatment for Alzheimer's granted full approval on July 6, 2023:** The FDA converted the accelerated approval for Leqembi (lecanemab) to a traditional approval for the treatment of adult patients with early Alzheimer's disease (AD)
- **Respiratory syncytial virus (RSV) prevention approved July 17, 2023:** Beyfortus (nirsevimab) received approval for the prevention of RSV in neonates and infants born during or entering their first RSV season, and in children up to 24 months of age who remain vulnerable to severe RSV through their second RSV season. On August 3, 2023 the CDC Advisory Committee unanimously voted to include Beyfortus in the Vaccines for Children (VFC) program to support equitable access for all eligible infants. Beyfortus will be available ahead of the 2023-2024 RSV season.
- **First over-the-counter (OTC) birth control pill approved July 13, 2023:** Opill (norgestrel) oral tablet is the first daily oral contraceptive approved in the United States (US) for use without a prescription

Considerations for State Medicaid Programs

State Medicaid programs should evaluate how to best manage each drug in the fee-for-service and managed care environments. In particular, states should consider:

- Site of service and claims payment: Intravenous (IV) administered drugs can be billed through the medical or pharmacy claim systems. States should establish policy to ensure consistency and efficiency in payment and administration
- Prior authorization and medical necessity criteria development, as appropriate
- Managed care capitation rate impact potential, in select populations
- Risk mitigation arrangements such as risk pools, risk corridors, and/or individually carved out drugs, as appropriate

Additional drug-specific considerations are outlined in the drug summaries below.

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Drug Summary:

Elevidys (delandistrogene moxeparvovec)

Approved June 22, 2023

Gene therapy for Duchenne muscular dystrophy (DMD): Received accelerated approval for pediatric patients four years through five years of age with DMD

Indication	Elevidys is approved for the treatment of ambulatory pediatric patients four years through five years of age with DMD, with a confirmed mutation in the DMD gene. This indication is approved under accelerated approval based on the surrogate marker of expression of microdystrophin in skeletal muscle observed in patients treated with Elevidys.
Dosing	Elevidys is an adeno-associated virus-based gene therapy that is administered as a one-time, single IV dose
Cost	$3.2 million for one-time treatment
Market Landscape	DMD is a progressive neuromuscular disease caused by a dystrophin gene mutation, resulting in muscle weakness and significantly reduced life expectancy Patients are typically diagnosed by three years of age DMD prevalence in the US is approximately 10,000 to 15,000 males Elevidys is the first gene therapy approved for DMD; there are others in the pipeline, including Pfizer's fordadistrogene movaparvovec Current treatment consists of standard of care glucocorticoids (e.g., Emflaza, costing ~$115,000 to $230,000 annually) and antisense oligionucleotides (e.g., Exondys 51, Vyondys 53, Viltepso, and Amondys 45, costing ~$700,000 to $750,000 annually). Antisense oligonucleotides increase dystrophin expression, but have limited data on realized clinical benefit and only address a minority of the gene mutations.
Clinical Studies	Clinical efficacy evaluated in a placebo-controlled trial of 41 patients aged four years to seven years with mutation between exons 18 to 58. Results found a change in dystrophin levels, which is a surrogate endpoint considered to be reasonably likely to produce a clinical benefit. However, the trial failed to demonstrate statistically significant improvements in performance on a functional test called North Star Ambulatory Assessment (NSAA). Additional subgroup analyses of NSAA performance showed a numerical advantage for Elevidys in the four year to five year age group.
Important Clinical Considerations	Elevidys was approved in a more narrow population than the age range of patients studied in clinical trials; if the drug receives traditional approval rather than the current accelerated approval, the age range may be widened. The manufacturer is expected to share additional data with the FDA, later in 2023, for patients aged six years to seven years. Elevidys is contradicted in patients with deletion in exon 8 or exon 9 in DMD gene due to the observed immune-mediated myositis in clinical trials following Elevidys infusion in patients with the aforementioned deletions Baseline testing for the presence of anti-AAVrh74 is required as preexisting anti-AAV antibodies may limit the effectiveness of the therapy. Additional safety warnings include liver monitoring, myocarditis, and immune-mediated myositis.
Next Steps for State Medicaid Programs	Aforementioned considerations for State Medicaid programs (see pg. 1) States should monitor for durability of response as patients may require additional therapy following Elevidys treatment Additional market changes may include: • Traditional approval and additional data related to an established clinical benefit • Potential for an expanded patient population of six years to seven years of age • Additional gene therapy approvals for the DMD patient population

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Drug Summary:

Roctavian (valoctocogene roxaparvovec)

Approved July 6, 2023

Gene therapy for hemophilia A: Received approval for the treatment of adults with severe hemophilia A

Indication	Treatment of adults with severe hemophilia A without preexisting AAV5 antibodies
Dosing	One-time IV infusion
Cost	$2.9 million for one-time treatment
Market Landscape	Estimated 30,000 to 33,000 people in the US with hemophilia, with the majority having hemophilia A. Approximately 48% of hemophilia patients are expected to have the severe form of the disease. Approximately 30% of patients with severe hemophilia A develop antibodies to factor VIII, known as inhibitors. Patients are not eligible to receive Roctavian if they have inhibitors. The manufacturer estimates 2,500 patients are eligible to receive Roctavian Patients currently use high-cost prophylactic factor VIII or Hemlibra (emicizumab) to reduce the frequency of bleeding episodes; estimated annual costs of prophylactic therapies in Roctavian-eligible patients is ~$700,000+ Roctavian is the first gene therapy approved for hemophilia A; additional gene therapies for hemophilia A are under development, including Pfizer's giroctocogene fitelparvovec
Clinical Studies	In the clinical trial of 112 patients with baseline annualized bleed rate (ABR) data, patients experienced a mean ABR reduction of 52% through the end of follow-up (median of three years). Patients were able to reduce factor VIII by 98.6%. Long-term durability remains in question; five-year follow-up date from the manufacturer indicates durability of effect was maintained with patients able to continue to discontinue factor VIII prophylaxis.
Important Clinical Considerations	Baseline antibodies to adeno-associated virus serotype 5 (AAV5) testing is required, and Roctavian should not be administered to patients with a positive test for antibodies to AAV5 Baseline testing for antibodies to factor VIII (inhibitors) is required. Patients are not eligible to receive Roctavian if they have inhibitors. Baseline liver testing and follow-up is required A majority of patients treated with Roctavian received immunosuppressive medications, including steroids, to control elevations in liver enzymes and to prevent loss of transgene expression
Next Steps for State Medicaid Programs	Aforementioned considerations for State Medicaid programs (see pg. 1) States should review manufacturer warranty contracts. Roctavian could lead to decreased use of inhibitor products and Hemlibra; long-term durability could result in overall cost-effective treatment: • The manufacturer, BioMarin, announced that it will provide a four-year warranty to payers to address risk related to Roctavian's initial response and durability. The warranty will reimburse payers up to 100% drug cost if the patient does not respond to Roctavian or if the patient loses response in the first four years after dosing.

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Drug Summary:

Leqembi (lecanemab)

Approved July 6, 2023

Antibody treatment for Alzheimer's: The FDA converted the accelerated approval for Leqembi (lecanemab) to a traditional approval for the treatment of adult patients with early Alzheimer's disease (AD)

Indication	AD in patients with mild cognitive impairment (MCI) or mild dementia stage of disease
Dosing	10 mg/kg administered via IV every two weeks
Cost	$26,500 per year, based on an average patient weight of 75 kg The institute for Clinical and Economic Review's cost-effective annual list price range for Leqembi is $8,500 to $20,600
Market Landscape	Leqembi was initially approved in January under the Accelerated Approval pathway based on a surrogate endpoint of reducing amyloid plaques in the brain; reduction of amyloid plaques is a surrogate marker considered reasonably likely to predict a clinical benefit. The FDA required the manufacturer of Leqembi to conduct a confirmatory trial to verify the anticipated clinical benefit. The June approval is a full traditional approval following an FDA determination that the confirmatory trial verified clinical benefit. Leqembi is the first amyloid beta-directed antibody to be converted from an accelerated approval to a traditional approval for the treatment of AD. Leqembi is the second FDA-approved anti-amyloid monoclonal antibody for AD following Aduhelm (aducanumab) in 2021; initial uptake of therapies was limited by Centers for Medicare & Medicaid Services (CMS) national coverage determination requiring patients receiving anti-amyloid therapies approved under the accelerated approval pathway to be enrolled in a clinical trial. CMS has indicated that Medicare will cover anti-amyloid AD drugs that receive traditional approval in appropriate settings that also support the collection of real-world data in a registry Approximately five million Americans 65 years of age and older have mild cognitive impairment due to AD Another anti-amyloid therapy, donanemab, is pursing traditional FDA approval following a complete response letter in January regarding the accelerated approval submission of donanemab
Clinical Studies	In clinical trials of approximately 1,800 patients with early-stage AD, Leqembi slowed clinical decline by 27% compared with placebo after 18 months. Leqembi reduced beta-amyloid plaques in the brain and slowed the decline of three other validated measures of memory and function. Some experts have called efficacy "modest" but caveat the "modest" effect given the limited number of treatment options for AD with proven efficacy.
Important Clinical Considerations	Treatment with Leqembi is only recommended in patients with MCI or mild dementia stages of AD Patients should have confirmed presence of amyloid plaques prior to starting treatment A boxed warning is included in the prescribing information to alert patients and caregivers to the potential risks associated with amyloid-related imaging abnormalities (ARIA) : • Patients who are homozygous for the ApoE ε4 allele have a higher incidence of ARIA; ApoE ε4 status should be assessed before starting treatment to inform the risk of developing ARIA Use of anticoagulant medication was associated with an increased number of intracerebral hemorrhages in patients taking Leqembi compared to placebo
Next Steps for State Medicaid Programs	Aforementioned considerations for State Medicaid programs (see pg. 1) States should consider current Medicare coverage policies related to these therapies. Medicare is likely to be the primary payer for most patients receiving Leqembi. CMS coverage of anti-amyloid therapies for AD with traditional FDA approval requires prescribers to participate in a new CMS-facilitated registry or in other registries that CMS will identify. Prescribers participating in the registry will be required to submit baseline data, and then every six months, for up to two years. Potential impact to managed care capitation rates in select populations as utilization accelerates, particularly in light of the CMS coverage change for traditionally approved anti-amyloid therapies Additional market changes may include the traditional approval of donanemab, which is expected to compete with Leqembi

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Drug Summary:

Beyfortus (nirsevimab)

Approved July 17, 2023

Respiratory syncytial virus (RSV) prevention: Received approval for the prevention of RSV in neonates and infants born during or entering their first RSV season, and in children up to 24 months of age who remain vulnerable to severe RSV through their second RSV season. On August 3, 2023 the CDC Advisory Committee unanimously voted to include Beyfortus in the Vaccines for Children (VFC) program to support equitable access for all eligible infants. Beyfortus will be available ahead of the 2023-2024 RSV season.

Indication	The prevention of RSV lower respiratory tract disease in neonates and infants born during or entering their first RSV season, and in children up to 24 months of age, who remain vulnerable to severe RSV disease through their second RSV season
Dosing	Single intramuscular injection prior to or during RSV season
Cost	Although pricing information for Beyfortus is not yet available, Sanofi has previously indicated that the cost of Beyfortus will be closer to that of a pediatric vaccine series. The cost of some newer pediatric vaccines is approximately $1,000 per vaccination series.
Market Landscape	The American Academy of Pediatrics estimates 1% to 3% of children younger than 12 months of age are hospitalized each year due to RSV in the US. The manufacturer estimates 590,000 RSV disease cases in infants under one year require medical care. Premature infants, and children and infants with lung or heart disease, are at highest risk for severe RSV requiring medical intervention. Beyfortus is a long-acting monoclonal antibody administered as a single intramuscular injection prior to or during the RSV season. Beyfortus has a broad indication that includes healthy term infants, in addition to those at high risk of severe RSV. Prior to approval of Beyfortus, Synagis (palivizumab) was the only FDA-approved product for prevention of RSV in infants and young children. With a cost of approximately $5,000 to $10,000 per treatment course over five monthly doses per season, Synagis is recommended by the American Academy of Pediatrics only in infants at high risk for serious RSV. Beyfortus is expected to be available for the upcoming 2023–2024 RSV season The Centers for Disease Control and Prevention's (CDC's) Advisory Committee on Immunization Practices met on August 3, 2023, and unanimously voted to include Beyfortus in the CDC's Vaccines for Children (VFC) program. If included in the VFC, the cost of Beyfortus treatment would be federally funded for medically underserved infants and children, including Medicaid recipients Another potential competitor for Beyfortus is an RSV vaccine, Abrysvo, which is currently under FDA review for use in pregnant individuals for the prevention of RSV lower respiratory tract illness (LRTI) in infants from birth up to six months of age, with an FDA review date in August 2023. Abrysvo was previously approved in May 2023 for the prevention of RSV LRTI in older adults.
Clinical Studies	Phase 3 MELODY trial found a statistically significant reduction in the incidence of medically attended LRTI in the Beyfortus group (1.2%) compared to the placebo group (5.0%) in healthy late, preterm, and term infants (35 weeks or more) during their first RSV season. The manufacturer also evaluated Beyfortus for RSV prevention during the second RSV season for high-risk infants, with data supporting the approval of Beyfortus for high-risk children up to 24 months of age.
Important Clinical Considerations	Approval of Beyfortus was in a broader patient population, including healthy term infants, than currently approved therapies (e.g., Synagis) No data is yet available to determine whether a pregnant individual receives Abrysvo for the prevention of RSV LRTI in infants, that the infant should then still receive Beyfortus in the first six months of life
Next Steps for State Medicaid Programs	Aforementioned considerations for State Medicaid programs (see pg. 1) Monitor final CDC decision regarding VFC inclusion in August 2023. Potential impact to managed care capitation rates in pediatric populations as utilization accelerates, if not included in VFC. Additional market changes may include the approval of Abrysvo, which is expected to compete with Beyfortus States should track guideline recommendations regarding use of Beyfortus in infants, following Abrysvo administration to pregnant individuals

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Drug Summary:

Opill (norgestrel)

Approved July 13, 2023

First over-the-counter (OTC) birth control pill: The first daily oral contraceptive approved in the United States for use without a prescription

Indication	Approved as the first non-prescription daily oral contraceptive to prevent pregnancy
Dosing	One tablet by mouth daily
Cost	Anticipated price is not yet available; cost could decline as additional OTC products enter the market
Market Landscape	Progestin-only oral contraceptive pill provides an option to purchase oral contraceptive medication without a prescription The manufacturer anticipates Opill to be available in early 2024. Other approved formulations and dosages of other oral contraceptives will remain available by prescription only, unless they also pursue similar FDA approval.
Next Steps for State Medicaid Programs	OTC claims for Medicaid payment will need a prescription to process, and states should check whether a standing order is issued that pharmacists can use for dispensing the OTC contraceptives States should also review the following in assessment of OTC oral contraceptive coverage: • State plan/MCO contract language regarding OTC coverage. CMS asked states to remove mention of specific OTC drugs/drug classes from their state plans and replace it with language that points to their provider manual. This limits the need for state plan amendments to update the list of covered OTCs. ◦ A provider manual update may be required if state plan language or MCO contract language defers to a coverage list in the provider manual • Preferred drug list placement and utilization management, where appropriate • Logistics for documentation of diagnosis to claim enhanced federal match when used for contraception

For questions:

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