Elivaldogene autotemcel (Skysona®, Eli-cel)

April 20, 2023

DURB Meeting

NEW YORK STATE | Department of Health | Office of Health Insurance Programs
SUNY The State University of New York

Purpose

- The aim of the DURB review is to provide recommendations for the management of elivaldogene autotemcel (Skysona®, eli-cel) in the New York State Medicaid program.

Background

- X-linked adrenoleukodystrophy (X-ALD) is a genetic condition caused by mutations in the *ABCD1* gene on the X chromosome
- A defect in the *ABCD*1 gene results in increased levels of very long-chain fatty acids (VLCFAs) in plasma and tissues. The buildup of VLCFA leads to progressive destruction of myelin
- The phenotypes of X-linked ALD can be classified into asymptomatic, cerebral ALD (CALD), adrenomyeloneuropathy, and Addison-only ALD
- The estimated prevalence of X-linked ALD is 1 in 10,000 individuals to 1 in 17,000 in the general population
- All newborns in New York State are required to be screened for ALD unless the parents confirm in writing that they have a religious objection

Engelen M, et al. *Orphanet J Rare Dis*. 2012;7:51.
X-Linked Adrenoleukodystrophy. Rare Disease Database. National Organization for Rare Disorders. Accessed Apr 6, 2023. https://rarediseases.org/rare-diseases/adrenoleukodystrophy/

Newborn Screening Program. Screened Disorders. Department of Health, Wadsworth Center. Accessed Apr 6, 2023. Available at https://www.wadsworth.org/programs/newborn/screening/screened-disorders

Background (continued)

- Major functional disabilities (MFD) associated with CALD: loss of communication, cortical blindness, tube feeding, total incontinence, wheelchair dependence, and complete loss of voluntary movement
- CALD-specific Neurologic Function Scale (NFS) is a clinical scoring system that assesses 15 disabilities across multiple domains with scores ranging from 0 (no clinically evident dysfunction) to 25 (most severe deficits)
- Loes score is a scoring system that utilizes brain magnetic resonance imaging (MRI) to assess the burden of cerebral disease and determine the extent of lesion involvement and atrophy
  - Loes scores range from 0 to 34 points; a score of ≤0.5 is considered normal
  - A stable Loes score has been defined as an increase from a baseline of <6 points or a score ≤9
- The onset of CALD before age of 3 years is rare. The American Academy of Neurology (AAN) recommends screening for CALD in all males with ALD, regardless of symptoms, with a baseline MRI at 2 years of age, followed by semi-annual MRIs for males between 2 and 12 years of age and annual MRIs for males >12 years of age

Eichler F, et al. *N Engl J Med.* 2017;377(17):1630-1638.
Engelen M, van Ballegoij WJC, Mallack EJ, et al. *Neurology*. 2022;99(21):940-951.

FDA-approved indication for eli-cel (Skysona®)

Indication	• Slow the progression of neurologic dysfunction in males 4-17 years of age with early, active CALD.
	• Early, active CALD refers to asymptomatic or mildly symptomatic males with:
	  ○ NFS score ≤1
	  ○ Gadolinium enhancement on brain MRI
	  ○ Loes scores of 0.5-9
	• FDA granted accelerated approval based on 24-month MFD-free survival.

FDA-approval date	September 16, 2022
Limitations of use	• Eli-cel does not treat or prevent adrenal insufficiency. • An immune response to eli-cel may cause rapid loss of efficacy of eli-cel in patients with full deletions of the human *ABCD1* gene. • Eli-cel has not been studied in CALD secondary to head trauma. • Given the risk of hematologic malignancy, unclear long-term durability, and human ALDP expression, careful consideration should be given to the timing of eli-cel for each patient. Clinical manifestations do not usually occur until adulthood in boys with isolated pyramidal tract disease.

ABCD1 gene=adenosine triphosphate binding cassette, sub family D, member 1 gene, ALDP=adrenoleukodystrophy protein, CALD=cerebral adrenoleukodystrophy, eli-cel=elivaldogene autotemcel, MFD=major functional disability, MRI=magnetic resonance imaging, NFS=Neurologic Function Scale

Skysona® [package insert]. Bluebird bio Inc. Somerville. Massachusetts. Sep 2022.

Manufacturer-recommended dosage and administration and mechanism of action

Dosing regimen	• Eli-cel is a single dose infusion. • The dose is calculated based on the patient's weight prior to first apheresis. • The minimum recommended dose is 5.0×10^6 CD34+ cells/kg.
Administration	• Eli-cel is an IV infusion administered by a healthcare practitioner. • Patients must undergo HSC mobilization and apheresis to obtain CD34+ cells for eli-cel manufacturing.
Mechanism of action	• Eli-cel adds functional copies of the *ABCD1* cDNA into patients' HSCs through transduction of autologous CD34+ cells with the Lenti-D LVV. • Functional ALDP participates in the degradation of VLCFAs. Following infusion of eli-cel, transduced CD34+ HSCs engraft in the bone marrow and differentiate into various cell types, including monocytes (CD14+) capable of producing functional ALDP.

ABCD1 gene=adenosine triphosphate binding cassette, sub family D, member 1 gene, ALDP=adrenoleukodystrophy protein, CD34=cluster of differentiation 34, cDNA=complementary deoxyribonucleic acid, eli-cel=elivaldogene autotemcel, HSC=hematopoietic stem cell, IV=intravenous, Lenti-D LVV=elivaldogene tavalentivec lentiviral vector, VLCFA=very long chain fatty acid

Skysona® [package insert]. Bluebird bio Inc. Somerville. Massachusetts. Sep 2022.

Warnings and precautions

- Risk of hematologic malignancy (boxed warning): myelodysplastic syndrome had been diagnosed in 3 patients after administration of eli-cel at the time of initial approval
  - Monitor patients lifelong for hematologic malignancy. For the first 15 years after treatment, monitor via CBC with differential at least twice per year and via integration site analysis or other testing for evidence of clonal expansion and predominance at least twice in the first year and then annually
- Serious infections
- Prolonged cytopenia
- Delayed platelet engraftment
- Risk of neutrophil engraftment failure
- Hypersensitivity reactions
- Laboratory test interference: eli-cel affects polymerase chain reaction (PCR) assays for human immunodeficiency virus (HIV) due to lentiviral vector provirus insertion. A PCR-based assay should not be used to screen for HIV infection in patients treated with eli-cel as a false-positive result is likely

Skysona® [package insert]. Bluebird bio Inc. Somerville. Massachusetts. Sep 2022.

Drug interactions

- Anti-retroviral drugs: anti-retroviral medications should not be taken for at least 1 month prior to initiation of medications for stem cell mobilization and for the expected duration for the elimination of the medications, and until all cycles of apheresis are completed
  - If a patient requires anti-retroviral drugs for HIV pre-exposure prophylaxis, mobilization and apheresis of CD34+ cells should be delayed until HIV infection is adequately ruled out
- Vaccination is not recommended during the 6 weeks preceding the start of myeloablative conditioning and until hematological recovery after administering eli-cel
  - When possible, administer childhood vaccinations prior to myeloablative conditioning

Skysona® [package insert]. Bluebird bio Inc. Somerville. Massachusetts. Sep 2022.

Use in specific populations

Pregnancy and lactation	• No available data on utilizing eli-cel in pregnancy; no information regarding the presence of eli-cel in human milk and the effects on breastfed infants and on milk production.
Reproductive potential	• Insufficient data to provide a precise recommendation on the duration of contraception following treatment with eli-cel. • Males and their female partners of reproductive potential are advised to use an effective method of contraception from the start of mobilization through at least 6 months after administration of eli-cel.
Age <4 years	• Safety and effectiveness have not been established.
Full *ABCD1* gene deletion	• In the only patient with a full *ABCD1* deletion, CALD progressed after treatment with eli-cel. The patient experienced radiologic disease progression in the setting of declining peripheral blood vector copy number, which is indicative of loss of product efficacy. The patient subsequently received allo-HSCT.
Renal or hepatic impairment	• No studies were conducted in patients with renal or hepatic impairment.
HIV or HTLV	• No studies were conducted in patients with HIV-1, HIV-2, HTLV-1, or HTLV-2. A negative serology test for HIV is required to ensure acceptance of apheresis material for eli-cel manufacturing.

ABCD1 gene=adenosine triphosphate binding cassette, sub family D, member 1 gene, CALD= cerebral adrenoleukodystrophy, eli-cel=elivaldogene autotemcel, HIV=human immunodeficiency virus, allo-HSCT=allogeneic hematopoietic stem cell transplantation , HTLV=human T-lymphotropic virus

Skysona® [package insert]. Bluebird bio Inc. Somerville. Massachusetts. Sep 2022.

AAN recommendations

- The AAN recommends allogeneic hematopoietic stem cell transplantation (allo-HSCT) as a standard treatment for CALD that can halt disease progression, but the AAN notes that outcomes are poor in advanced disease.
  - The AAN recommends determination of eligibility by an ALD transplantation expert.
  - Eligibility criteria are not exclusive, but generally include the following:
    - Boys with demyelination with gadolinium enhancement (Loes score ≤9) and NFS of 0 or 1, and
    - Adult males with demyelinating lesions with gadolinium enhancement and no or few neurocognitive impairments
- The AAN states that genetically transduced autologous stem cell transplantation (i.e., gene therapy) should be considered, if available, in boys for whom allo-HSCT donor options are poor.

Engelen M, et al. International *Neurology*. 2022;99(21):940-951.

STARBEAM (ALD-102, NCT01896102) study design

- STARBEAM was a phase 2/3 study designed to assess the efficacy and safety of eli-cel for the treatment of early, active CALD in males ≤17 years of age:
  - NFS score of 0 or 1
  - Have gadolinium enhancement on MRI of demyelinating lesions in the brain
  - A Loes score of 0.5 to 9.0
- Key exclusion criteria: receipts of allo-HSCT or gene therapy and patients with the availability of a willing 10/10 human leukocyte antigen (HLA)-matched sibling donor; patients with HIV, human T lymphotropic virus 1 (HTLV), hepatitis B, or hepatitis C infection
- Primary outcomes were patients who were alive and did not have any of the 6 MFDs at month 24 and no allo-HSCT or rescue cell administration; proportion of patients who had experienced graft-versus-host disease (GVHD)
- Key secondary outcomes were lesion regression measured with Loes score, gadolinium enhancement on MRI, and proportion of patients undergoing allo-HSCT by month 24

Eichler F, et al. *N Engl J Med.* 2017;377(17):1630-1638.
A Study of the Efficacy and Safety of Hematopoietic Stem Cells Transduced With Lenti-D Lentiviral Vector for the Treatment of Cerebral Adrenoleukodystrophy (CALD). Last update posted April 25, 2022. Accessed Apr 6, 2023. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT01896102?cond=CALD&intr=elivaldogene&draw=2&rank=2.

STARBEAM (ALD-102, NCT01896102) results

- Patients baseline characteristics: median 6 years of age (4-13); median Loes score of 2 (1.0-7.5); NFS score of 0
- Primary outcomes (at the time of the interim analysis at month 24):
  - 15 of the 17 patients (88%) were alive and free of MFD. Patients free of MFD maintained a score on the NFS of 0 or 1
  - No episode of GVHD was reported
  - 2 patients had neurologic disease progression
    - Patient 2016 was withdrawn from the study by month 12 to receive allo-HSCT and later died from transplantation-related causes
    - Patient 2018: neurologic function deteriorated rapidly after treatment and developed total incontinence by month 9. The patient died from a viral infection complication approximately 22 months after the infusion
- Secondary outcomes (at the time of the interim analysis at month 24):
  - Lesion progression measured with the Loes score had stabilized in 12 of the 17 patients (71%)
  - Gadolinium enhancement had resolved by month 6 in the 16 patients who could be evaluated

Eichler F, et al. *N Engl J Med.* 2017;377(17):1630-1638.

ALD-102, NCT01896102 results

- Since the publication of interim results of STARBEAM study, the study was completed, and additional data have been posted on ClinicalTrials.gov
- Primary outcomes (at month 24):
  - 90.6% of 32 patients were alive and free of MFD and without allo-HSCT or rescue cell administration
  - No episodes of graft failure or GVHD were reported
- Secondary outcomes (at month 24):
  - 86.7% of 30 patients who could be evaluated demonstrated resolution of gadolinium enhancement
  - 6.5% of 31 patients underwent a subsequent allo-HSCT
- Adverse events:
  - No transplantation-related deaths by 12 months post-infusion
  - 65.6% of 32 patients experienced at least 1 serious adverse event. Febrile neutropenia was the most common serious adverse event
  - 9.4% of 32 patients experienced at least 1 eli-cel related adverse event. 3.1% patients experienced at least 1 serious eli-cel related adverse event

A Study of the Efficacy and Safety of Hematopoietic Stem Cells Transduced With Lenti-D Lentiviral Vector for the Treatment of Cerebral Adrenoleukodystrophy (CALD). Last update posted April 25, 2022. Accessed Apr 6, 2023. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT01896102?cond=CALD&intr=elivaldogene&draw=2&rank=2.

Summary

- Elivaldogene autotemcel (Skysona®, Eli-cel) is the first cell-based gene therapy approved by the FDA to slow the progression of neurologic dysfunction in males 4 to 17 years of age with early, active CALD (asymptomatic or mildly symptomatic [NFS score ≤1] disease with gadolinium enhancement on brain MRI and Loes score of 0.5 to 9)
- The AAN recommends allo-HSCT as a standard treatment for CALD that can halt disease progression. The AAN states that genetically transduced autologous stem cell transplantation (i.e., gene therapy) should be considered, if available, in boys for whom allo-HSCT donor options are poor

Skysona® [package insert]. Bluebird bio Inc. Somerville. Massachusetts. Sep 2022.
Engelen M, et al. International *Neurology*. 2022;99(21):940-951.

Summary (continued)

- In a phase 2/3 clinical trial STARBEAM (ALD-102, NCT01896102),15 of the 17 patients (88%) were alive and free of MFD at month 24; Patients free of MFD maintained a score on the NFS of 0 or 1
  - 1 patient underwent a subsequent allo-HSCT by month 12 and later died from transplantation-related causes
- Unpublished results of ALD-102, NCT01896102 posted on ClinicalTrials.gov:
  - 90.6% of 32 patients were alive and free of MFD and without allo-HSCT or rescue cell administration
  - 6.5% of 31 patients underwent a subsequent allo-HSCT
- ALD-104 (NCT03852498) is an ongoing phase 3 trial evaluating the efficacy and safety of eli-cel
  - All patients who completed ALD-102 and patients who will complete ALD-104 have been or will be asked to participate in LTF-304 (NCT02698579)
  - After completing a 2-year-parent clinical study, an estimate of 60 eligible participants will be followed for an additional 13 years

Eichler F, et al. *N Engl J Med.* 2017;377(17):1630-1638.
A Study of the Efficacy and Safety of Hematopoietic Stem Cells Transduced With Lenti-D Lentiviral Vector for the Treatment of Cerebral Adrenoleukodystrophy (CALD). Last update posted April 25, 2022. Accessed Apr 6, 2023.
ClinicalTrials.gov.
https://clinicaltrials.gov/ct2/show/NCT01896102?cond=CALD&intr=elivaldogene&draw=2&rank=2.

Long-term Follow-up of Participants With Cerebral Adrenoleukodystrophy Who Were Treated With Lenti-D Drug Product. ClinicalTrials.gov. Last update posted Mar 30, 2023. Apr 6, 2023.
https://clinicaltrials.gov/ct2/show/NCT02698579?cond=CALD&intr=elivaldogene&draw=2&rank=3.

Recommendations for eli-cel clinical coverage policy

1. The patient is male 4-17 years of age with active, early CALD due to an *ABCD1* genetic mutation
   - Active, early CALD is defined as asymptomatic or mildly symptomatic males with a NFS score ≤1 and who have gadolinium enhancement on brain MRI and Loes score of 0.5 to 9
2. The patient does not have early CALD due to full deletion of the *ABCD1* gene or CALD secondary to head trauma
3. The patient is eligible to undergo an allo-HSCT, but an HLA-matched donor is not available
4. The patient is not receiving antiretroviral drugs 1 month prior to initiating medications for stem cell mobilization and until all cycles of apheresis are completed
5. The patient does not have HIV or HTLV infection
6. The practitioner agrees to monitor the patient for hematologic malignancy
   - For the first 15 years after treatment with eli-cel, monitor CBC with differential at least twice per year and via integration site analysis or other testing for evidence of clonal expansion and predominance at least twice in the first year and then annually

References

- Engelen M, Kemp S, de Visser M, et al. X-linked adrenoleukodystrophy (X-ALD): clinical presentation and guidelines for diagnosis, follow-up and management. Orphanet J Rare Dis. 2012;7:51. Published 2012 Aug 13. doi:10.1186/1750-1172-7-51
- X-Linked Adrenoleukodystrophy. Rare Disease Database. National Organization for Rare Disorders. Accessed Apr 6, 2023. https://rarediseases.org/rare-diseases/adrenoleukodystrophy/
- Newborn Screening Program. Screened Disorders. Department of Health, Wadsworth Center. Accessed Apr 6, 2023. Available at https://www.wadsworth.org/programs/newborn/screening/screened-disorders
- Eichler F, Duncan C, Musolino PL, et al. Hematopoietic Stem-Cell Gene Therapy for Cerebral Adrenoleukodystrophy. N Engl J Med. 2017;377(17):1630-1638. doi:10.1056/NEJMoa1700554.
- Engelen M, van Ballegoij WJC, Mallack EJ, et al. International Recommendations for the Diagnosis and Management of Patients With Adrenoleukodystrophy. A Consensus-Based Approach. Neurology. 2022;99(21):940-951. doi:10.1212/wnl.0000000000201374

References

- Skysona® [package insert]. Bluebird bio Inc. Somerville. Massachusetts. Sep 2022.
- A Study of the Efficacy and Safety of Hematopoietic Stem Cells Transduced With Lenti-D Lentiviral Vector for the Treatment of Cerebral Adrenoleukodystrophy (CALD). Last update posted April 25, 2022. Accessed Apr 6, 2023. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT01896102?cond=CALD&intr=elivaldogene&draw=2&rank=2.
- Long-term Follow-up of Participants With Cerebral Adrenoleukodystrophy Who Were Treated With Lenti-D Drug Product. ClinicalTrials.gov. Last update posted Mar 30, 2023. Apr 6, 2023. https://clinicaltrials.gov/ct2/show/NCT02698579?cond=CALD&intr=elivaldogene&draw=2&rank=3.

Drug Utilization Review: Etranacogene dezaparvovec-drlb (Hemgenix®)

April 20, 2023
DURB Meeting

Background

- The aim of this review is to examine etranacogene dezaparvovec-drlb and its potential utilization across the entire New York State (NYS) Medicaid population
- Recommendations will be provided based on a review of the literature and results from utilization data analyses

Hemophilia

- Bleeding disorder characterized by an inability to form clots due to a deficiency in clotting factors
- Deficiencies result from mutations in the *F8* and *F9* genes
- X-linked; may be diagnosed in females but incidence is much lower than in males
- Congenital or acquired

DiPiro: Pharmacotherapy A Pathophysiologic Approach. 12th ed. McGraw Hill; 2021.
Centers for Disease Control and Prevention. Hemophilia. https://www.cdc.gov/ncbddd/hemophilia/facts.html.
National Hemophilia Foundation. Hemophilia B. https://www.hemophilia.org/bleeding-disorders-a-z/types/hemophilia-b.
Srivastava A et al. WFH guidelines for the management of hemophilia, 3rd edition. *Haemophilia*. 2020:26(Suppl 6):1-158.

Types of Hemophilia

Characteristics	Hemophilia A	Hemophilia B
Other names	Classic hemophilia	Christmas disease
Clotting factor deficiency	FVIII	FIX
Prevalence	17.1 per 100,000	3.8 per 100,000
Genetic variants*	*F8* gene; inhibitors are most commonly directed at FVIII	*F9* gene; acquired disease is extremely rare

FVIII=Factor VIII; FIX=Factor IX

*Variants lead to immune-mediated depletion or inhibition of a coagulation factor

DiPiro: Pharmacotherapy A Pathophysiologic Approach. 12th ed. McGraw Hill; 2021.
Centers for Disease Control and Prevention. Hemophilia. https://www.cdc.gov/ncbddd/hemophilia/facts.html.
National Hemophilia Foundation. Hemophilia B. https://www.hemophilia.org/bleeding-disorders-a-z/types/hemophilia-b.
Srivastava A et al. WFH guidelines for the management of hemophilia, 3rd edition. *Haemophilia*. 2020:26(Suppl 6):1-158.

Presentation and Diagnosis

- Signs/symptoms:
  - Palpable ecchymoses, hemarthroses, spontaneous bleeding, excessive bleeding following surgery or trauma
- Diagnosis based on:
  - Clinical presentation
  - Screening tests (e.g., prothrombin time [PT], activated partial thromboplastin time [aPTT], platelet function tests)
  - Confirmation with factor assays
    - Chromogenic, fluorogenic
    - One-stage (based on aPTT)

DiPiro: Pharmacotherapy A Pathophysiologic Approach. 12th ed. McGraw Hill; 2021.
Srivastava A et al. WFH guidelines for the management of hemophilia, 3rd edition. *Haemophilia*. 2020:26(Suppl 6):1-158.

Severity

Severity	Units/mL of FVIII or FIX (% activity)*	Symptoms
Normal (non-hemophilic)	0.5 to 1.5 (50% to 150%)	--
Mild hemophilia	0.05 to 0.4 (5% to 40%)**	Relatively absent
Moderate hemophilia	0.01 to 0.05 (1% to 5%)	Excessive bleeding after mild trauma
Severe hemophilia	<0.01 (<1%)	Frequent, spontaneous hemorrhages

FVIII=Factor VIII; FIX=Factor IX

*1 unit/mL represents 100% of the factor found in 1 mL of normal plasma

**6% to 49% per the National Hemophilia Foundation

DiPiro: Pharmacotherapy A Pathophysiologic Approach. 12th ed. McGraw Hill; 2021.
Srivastava A et al. WFH guidelines for the management of hemophilia, 3rd edition. *Haemophilia*. 2020:26(Suppl 6):1-158.
National Hemophilia Foundation. Hemophilia B. https://www.hemophilia.org/bleeding-disorders-a-z/types/hemophilia-b.

Management of Hemophilia

- Primary aim: prevention and control of bleeding and complications
- Hemostatic agents:
  - Clotting factor concentrates (CFCs – FVIII and FIX)
  - Bypassing agents (recombinant activated factor VIIa [rFVIIa], activated prothrombin complex concentrate [aPCC])
  - Other plasma products (fresh frozen plasma [FFP], cryoprecipitate)
  - Medications (desmopressin, tranexamic acid, epsilon aminocaproic acid)
  - Non-factor replacement therapies (emicizumab)

DiPiro: Pharmacotherapy A Pathophysiologic Approach. 12th ed. McGraw Hill; 2021.
Srivastava A et al. WFH guidelines for the management of hemophilia, 3rd edition. *Haemophilia*. 2020:26(Suppl 6):1-158.

Gene Therapies

- Valoctocogene roxaparvovec (Roctavian™)
  - Investigational therapy for treatment of adults with severe **hemophilia A**
  - Food and Drug Administration (FDA) decision anticipated in June 2023
  - Approved by the European Commission in August 2022
- Etranacogene dezaparvovec-drlb (Hemgenix®)
  - FDA-approved in November 2022 for treatment of adults with **hemophilia B** who:
    - are on prophylactic therapy with FIX CFCs;
    - have current or historical life-threatening hemorrhage; or
    - have repeated, serious spontaneous bleeding episodes

BioMarin. BioMarin provides update on FDA review of ROCTAVIAN™ (valoctocogene roxaparvovec) gene therapy for adults with severe hemophilia A. https://investors.biomarin.com/2023-03-06-BioMarin-Provides-Update-on-FDA-Review-of-ROCTAVIAN-TM-Valoctocogene-Roxaparvovec-Gene-Therapy-for-Adults-with-Severe-Hemophilia-A.
Hemgenix® (etranacogene dezaparvovec-drlb) [package insert]. Kankakee, IL: CSL Behring LLC; 2022.

Overview of Etranacogene Dezaparvovec

Characteristics	Description
Trade name (manufacturer)	• Hemgenix® (CSL Behring LLC)
Mechanism of action	• AAV5-based gene therapy intended to deliver a copy of the gene encoding the Padua variant of human FIX. Following administration in patients with hemophilia B, transduction and increases in circulating FIX have been observed
Dosing regimen	• Single-use infusion at dose of 2 x 10^{13} GC/kg (2 mL/kg)
Administration	• IV infusion through peripheral venous catheter at 500 mL/h • Prior to administration, dose must be diluted with normal saline • Administration rate should be reduced or stopped if infusion reaction occurs
Availability and storage	• Supplied as a kit containing 10 to 48 vials with dosage units corresponding to patient weight • Nominal concentration is 1 x 10^{13} GC/mL; each vial has a volume of 10 mL
WAC	• $3.5 million per kit, as of November 28, 2022

AAV5=adeno-associated virus type 5; FIX=factor IX; GC=genome copies; IV=intravenous; WAC=wholesale acquisition cost

Hemgenix® (etranacogene dezaparvovec-drlb) [package insert]. Kankakee, IL: CSL Behring LLC; 2022.

Overview, Continued

Characteristics	Description
Contraindications	• None
Warnings and precautions	• Infusion reactions • Hepatotoxicity and hepatocellular carcinogenicity • Immune-mediated neutralization of AAV5 vector capsid • Monitoring post-administration: FIX activity, using same assay and reagents each time, and development of FIX inhibitors
Adverse events	• Reactions occurring in ≥5% of subjects in a clinical trial: ALT elevations, AST elevations, CK elevations, infusion-related reactions, headache, flu-like symptoms, fatigue, malaise, nausea
Specific populations	• Hemgenix® only intended for administration in men • Safety and efficacy not established in pediatric patients • No dose adjustments are recommended in geriatric patients • Safety and efficacy not established in patients with advanced hepatic impairment, including cirrhosis or uncontrolled hepatitis B and C • Safety and efficacy not established in patients with severe renal impairment or end-stage renal disease

AAV5=adeno-associated virus type 5; ALT=alanine transaminase; AST=aspartate transaminase; CK=creatine kinase; FIX=factor IX; GC=genome copies; IV=intravenous

Hemgenix® (etranacogene dezaparvovec-drlb) [package insert]. Kankakee, IL: CSL Behring LLC; 2022.

Guidelines and Consensus Statements

Characteristics	World Federation of Hemophilia, 2020	International working group (Hart et al.), 2022
Scope	Principles of care in hemophilia	Management of hemophilia B
Recommended treatment	• CFCs – choice should be based on multiple factors* • Hemophilia B: products containing FIX only (pure concentrates) are recommended rather than PCCs • Hemophilia B and inhibitors or history of severe allergy to FIX CFCs: rFVIIa	• CFCs containing FIX – choice should be based on multiple factors* • Prophylaxis and early initiation of FIX recommended in severe hemophilia B • Hemophilia B and inhibitors or history of severe allergy to FIX CFCs: rFVIIa
Gene therapy	• No recommendations; acknowledged as a treatment option but evaluation through long-term follow-up in clinical trials and registries deemed necessary • Notes potential for discrepancies in results of chromogenic and one-stage assays for factor activity following gene therapy	• Should be considered a future treatment option due to limited clinical data and experience • Attainable FIX levels and duration of expression are unpredictable • Pre-existing liver morbidities may preclude use • If administered, long-term monitoring of safety and efficacy needed

CFCs=clotting factor concentrates; FIX=Factor IX; PCCs=prothrombin complex concentrates; rFVIIa=recombinant Factor VIIa
*World Federation of Hemophilia: availability, cost, and patient preferences; Hart et al.: venous access, bleeding phenotype, lifestyle, patient preference, pharmacokinetic characteristics

Srivastava A et al. WFH guidelines for the management of hemophilia, 3rd edition. *Haemophilia*. 2020:26(Suppl 6):1-158.
Hart DP et al. International consensus recommendations on the management of people with haemophilia B. *Ther Adv Hematol*. 2022;13:20406207221085202.

Clinical Trials

- The biologics license application for etranacogene dezaparvovec received Priority Review, Orphan, and Breakthrough Therapy designations from the FDA
- Primary evidence of safety and effectiveness:
  - Completed Phase 2b trial with 3-year follow-up
  - Ongoing Phase 3 trial (HOPE-B)

Von Drygalski A et al. Etranacogene dezaparvovec (AMT-061 phase 2b): normal/near normal FIX activity and bleed cessation in hemophilia B. *Blood Adv*. 2019;3(21):3241-3247.
Von Drygalski A et al. Stable and durable factor IX levels in hemophilia B patients over 3 years post etranacogene dezaparvovec gene therapy *Blood Adv*. 2022;bloodadvances.2022008886.
Pipe SW et al. Gene therapy with etranacogene dezaparvovec for hemophilia B. *N Engl J Med*. 2023;388(8):706-718.

Phase **2b** Trial: Design and Methodology

Reference	Design, duration of follow-up	Population, selection criteria	Intervention	Primary endpoint
Phase 2b	Open-label, multicenter 52 weeks in initial study; 3 years in extension	**n=3** Inclusion: • Male • age ≥18 years • FIX activity ≤2%, • Continuous routine prophylaxis with FIX or on-demand treatment with ≥4 bleeding episodes per year, or chronic hemophilic arthropathy • >20 previous exposure days of treatment with FIX Exclusion: • History of FIX inhibitors or positive FIX inhibitor test at screening • Thrombocytopenia • Other coagulation disorder • Uncontrolled infection • Liver function tests >2 x ULN	**Etranacogene dezaparvovec**: single 500 mL IV infusion of 2 x 10^{13} GC/kg over 1 hour **Short-acting FIX**: single dose of 40 IU/kg administered at baseline; repeat administration at 3 days allowed at investigator discretion, and subsequently if FIX <2% in ≥2 consecutive measurements	Achievement of FIX ≥5% at 6 weeks after administration of gene therapy FIX activity measured using one-stage assay at central laboratory

FIX=Factor IX; GC=genome copies; IV=intravenous; ULN=upper limit of normal

Von Drygalski A et al. *Blood Adv*. 2019;3(21):3241-3247. Von Drygalski A et al. *Blood Adv*. 2022;bloodadvances.2022008886.

Phase **3** Trial: Design and Methodology

Reference	Design, duration of follow-up	Population, selection criteria	Intervention	Primary endpoint
Phase 3 (HOPE-B)	Open-label, multicenter Interim: 18 months (Planned: 5 years)	**n=54 (53 received full-dose)** Inclusion: • Male • age ≥18 years • FIX activity ≤2%, • Continuous routine prophylaxis with FIX • >150 previous exposure days of treatment with FIX Exclusion: same as phase 2b criteria	Lead-in period of ≥6 months: continuous routine prophylaxis with **FIX** **Etranacogene dezaparvovec**: single IV infusion of 2 x 10^{13} GC/kg	Annualized bleeding rate during the 52 weeks after stable FIX expression (months 7 through 18 after gene therapy) FIX activity measured using one-stage assay and chromogenic assay

FIX=Factor IX; GC=genome copies; IV=intravenous

Pipe SW et al. Gene therapy with etranacogene dezaparvovec for hemophilia B. *N Engl J Med*. 2023;388(8):706-718.

Phase 2b and Phase 3 Trials: Results

Reference	Baseline characteristics	Primary Outcomes	Other Results
Phase 2b	• Age: mean 46.7 years (43 to 50) • Moderately severe to severe hemophilia B (all had FIX activity ≤1%) • All participants required continuous routine prophylaxis with FIX • All had pre-existing neutralizing antibodies to AAV5	• Significant increases in FIX activity observed: mean 31% at 6 weeks (range 23.9% to 37.8%) • At 3 years: mean FIX activity was 36.9% (range: 32.3% to 41.5%)	• In 52-week follow-up, none of participants required FIX following gene therapy • In 3-year follow-up, FIX use: 714.6 IU/year (compared to 306,205 IU/year prior to gene therapy) • No joint bleeds reported
Phase 3 (HOPE-B)	• Age: mean 41.5 years (19 to 75) • 81% had severe hemophilia B; (FIX activity 1%); remainder had moderately severe hemophilia B (FIX activity 1 to 2%) • All participants required continuous routine prophylaxis with FIX	• Annualized bleeding rate decreased from 4.19 in lead-in phase to 1.51 in post-treatment phase (ratio: 0.36, 95% Wald CI 0.20 to 0.64)	• No bleeding episodes reported in 26% in lead-in phase vs. 63% in post-treatment phase • LS mean increases in FIX activity at 6, 12, and 18 months: 36.2%, 38.8%, 34.3% by one-stage assay; 16.5%, 17.9%, 19.7% by chromogenic assay • 2 participants continued FIX prophylaxis from day 21 through 18 months*

CI=confidence interval; FIX=Factor IX; LS=least-squares

*One had received partial dose of gene therapy; other had highest levels of anti-AAV5 antibodies on day of treatment

Von Drygalski A et al. *Blood Adv*. 2019;3(21):3241-3247. Von Drygalski A et al. *Blood Adv*. 2022;bloodadvances.2022008886. Pipe SW et al. *N Engl J Med*. 2023;388(8):706-718.

NYS Medicaid FFS Coverage

- Etranacogene dezaparvovec is not currently covered
- In NYS, there are 9 hemophilia treatment centers registered with the Centers for Disease Control and Prevention (CDC)

New York State Department of Health. List of Medicaid reimbursable drugs. https://www.emedny.org/info/fullform.pdf.
Centers for Disease Control and Prevention. Division of Blood Disorders Gateway. Hemophilia treatment center (HTC) directory. https://dbdgateway.cdc.gov/HTCDirSearch.aspx.

Comparator State Medicaid Coverage

- 9 comparator state Medicaid programs
  - California, Colorado, Florida, Illinois, Massachusetts, Michigan, Pennsylvania, Texas, Washington
- Etranacogene dezaparvovec covered by 2 programs
  - Florida: minimum age (18 years)
  - Washington: prior authorization

Drug Utilization Data: Overview of Analyses

- Pharmacy claims and claims with procedure codes indicating utilization of FIX CFCs were identified to evaluate potential utilization of etranacogene dezaparvovec
- Data source: Medicaid Data Warehouse (MDW)
- Analysis period: January 1, 2020 – December 31, 2022

Overview of Analyses, Continued

- Medicaid Confidential Data Cell Size Policy (OHIP-0001)
  - Requires that no cell containing a value of 1 to 30 be reported; such values must be reported as ≤30 in all public-facing documents
- The following limitations should also be considered:
  - While time periods analyzed take into account inherent delays in claim/encounter submissions, data may not be fully complete
  - Due to the small sample size, reporting the raw numbers or the percentages of patients would violate the Medicaid Confidential Data Cell Size Policy

Members

Characteristic	Number (%) of members by calendar year			Total number (%) of members* n=379
	2020 n=154	2021 n=148	2022 n=185	
Gender				
Male	66.9%	70.9%	68.1%	60.9%
Female	33.1%	29.1%	31.9%	39.1%
Age				
<18 years	21.4%	23.6%	21.1%	13.5%
≥18 years	78.6%	76.4%	78.9%	86.5%

*Total of 2,135 claims for FIX products

- In the overall analysis period:
  - 60.9% of members utilizing FIX products were identified as male
  - 86.5% of members utilizing FIX products were ≥18 years of age
- Note: clinical trials of etranacogene dezaparvovec included only male subjects, ≥18 years of age

Data source: MDW, January 1, 2020 – December 31, 2022

Von Drygalski A et al. *Blood Adv*. 2019;3(21):3241-3247. Von Drygalski A et al. *Blood Adv*. 2022;bloodadvances.2022008886. Pipe SW et al. *N Engl J Med*. 2023;388(8):706-718.

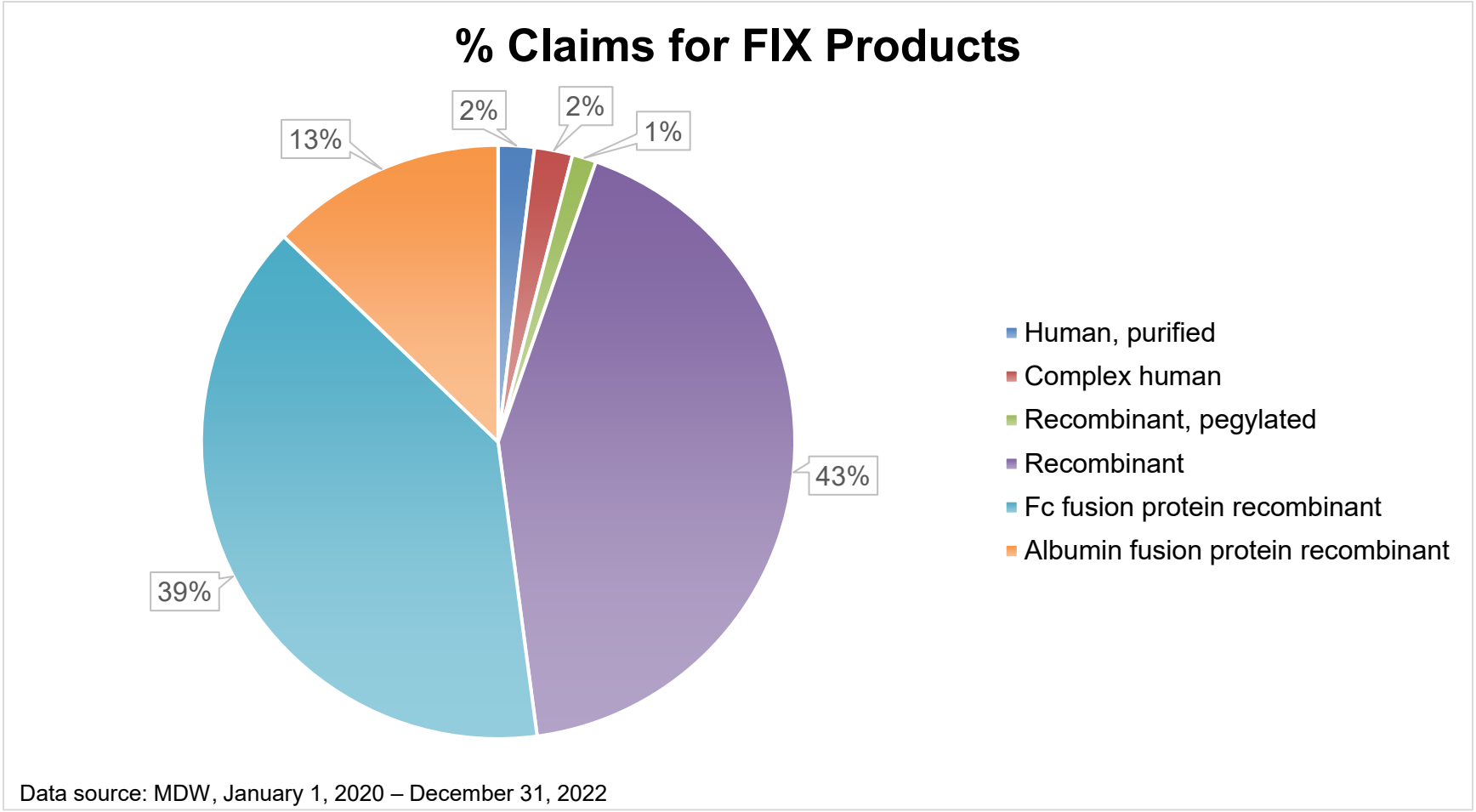
Congenital Hemophilia B in the Overall Population

- Documentation of the diagnosis code for hereditary FIX deficiency was assessed among members in NYS Medicaid without regard to use of FIX
- A total of 309 members had a diagnosis during the analysis period
  - 30.1% (n=93) had ≥1 claim for FIX
  - ≤10% (n≤30) had ≥1 claim for rFVIIa, but no claims for FIX
    - Utilization of rFVIIa but no FIX suggests presence of inhibitors or allergic reactions to FIX
    - Clinical trials of etranacogene dezaparvovec excluded patients with history of FIX inhibitors or with a positive FIX inhibitor test at screening

Data source: MDW, January 1, 2020 – December 31, 2022

Von Drygalski A et al. *Blood Adv*. 2019;3(21):3241-3247. Von Drygalski A et al. *Blood Adv*. 2022;bloodadvances.2022008886. Pipe SW et al. *N Engl J Med*. 2023;388(8):706-718.

FIX Products Utilized by Members with Hereditary FIX Deficiency



Data source: MDW, January 1, 2020 – December 31, 2022

Continuous Utilization of FIX

- An analysis was performed to identify members who had continuous utilization of FIX for ≥6 months.
  - Defined as a minimum of 12 claims during a 6-month period
- In total, ≤30 members had continuous utilization of FIX for ≥6 months during the analysis period.

Data source: MDW, January 1, 2020 – December 31, 2022

Conclusions

- Hemophilia is a bleeding disorder characterized by an inability to form clots, due to a deficiency in clotting factors
  - Hemophilia A is caused by a deficiency of FVIII and hemophilia B is caused by a deficiency of FIX
- The primary aim of care is prevention and control of bleeding and complications
- Etranacogene dezaparvovec-drlb (Hemgenix®) is an AAV5 vector-based gene therapy approved for treatment of adults with hemophilia B who are on prophylactic therapy with FIX CFC, have current or historical life-threatening hemorrhage, or have repeated, serious spontaneous bleeding episodes

DiPiro: Pharmacotherapy A Pathophysiologic Approach. 12th ed. McGraw Hill; 2021.
Srivastava A et al. WFH guidelines for the management of hemophilia, 3rd edition. *Haemophilia*. 2020:26(Suppl 6):1-158.
Hemgenix® (etranacogene dezaparvovec-drlb) [package insert]. Kankakee, IL: CSL Behring LLC; 2022.

Conclusions, Continued

- The role of etranacogene dezaparvovec in the treatment of hemophilia B is unclear; current guidelines/guidance recognize this therapy as an option for adults with moderately severe or severe hemophilia B but also highlight the limited amount of clinical data and experience with this therapy
- Available studies of etranacogene dezaparvovec are limited to 2 trials: one phase 2b and one phase 3
- Both studies demonstrated reductions in bleeding rates, increases in FIX activity, and resolution in need for prophylactic FIX CFC therapy during the follow-up period (3 years and 18 months, respectively)

Srivastava A et al. WFH guidelines for the management of hemophilia, 3rd edition. *Haemophilia*. 2020:26(Suppl 6):1-158.
Hart DP et al. International consensus recommendations on the management of people with haemophilia B. *Ther Adv Hematol*. 2022;13:20406207221085202.
Von Drygalski A et al. *Blood Adv*. 2019;3(21):3241-3247. Von Drygalski A et al. *Blood Adv*. 2022;bloodadvances.2022008886. Pipe SW et al. *N Engl J Med*. 2023;388(8):706-718.

Conclusions, Continued

- A retrospective analysis of claims for FIX CFCs was conducted to evaluate potential utilization of etranacogene dezaparvovec
- During the analysis period of January 1, 2020 – December 31, 2022, a total of 379 members had 2,135 claims for FIX products
- Approximately 60.9% were identified as male and 86.5% were ≥18 years of age
- Approximately 24.5% had a diagnosis of hereditary FIX deficiency
- In a separate analysis, without regard to use of FIX, a total of 309 members in NYS Medicaid were identified as having a diagnosis of hereditary FIX deficiency
  - 30.1% had ≥1 claim for FIX, while ≤10% had ≥1 claim for rFVIIa but no claims for FIX
- ≤10% had continuous utilization of FIX for ≥6 months during the analysis period

Data source: MDW, January 1, 2020 – December 31, 2022

UB Recommendations

- The following should be considered:
  - Etranacogene dezaparvovec should be prescribed and administered at a registered hemophilia treatment center
  - Clinical criteria:
    - Confirmation of a diagnosis of hemophilia B
    - Confirmation of moderately severe or severe hemophilia, defined as FIX activity of 1 to 2% of normal or <1% of normal, respectively
    - Use of FIX concentrates either as continuous routine prophylaxis, defined as the intent of treating with an a priori defined frequency of infusions, or as on-demand replacement therapy in patients with ≥4 bleeding episodes in the past 12 months or chronic hemophilia arthropathy in ≥1 joint(s)
    - Absence of history of FIX inhibitors and absence of positive FIX inhibitor test
    - Laboratory measurements of liver function, including alanine transaminase, aspartate transaminase, total bilirubin, alkaline phosphatase, and creatinine, <2 times the upper limit of normal

NEW YORK STATE | Department of Health

Drug Utilization Review (DUR) Board Meeting
April 20, 2023

Procedures for DUR Board Member Videoconferencing

Procedures for Member Videoconferencing

On April 9, 2022, Governor Hochul signed Chapter 56 of the Laws of 2022 relating to the New York State budget for the 2022-2023 state fiscal year.

Included in the bill is an amendment to the Open Meetings Law (OML) §103-a that expands the use of videoconferencing by public bodies to conduct open meetings, under extraordinary circumstances, regardless of a declaration of emergency. The provision is set to expire July 1, 2024.

Procedures for Member Videoconferencing

The DUR Board may pass a resolution and adopt procedures to satisfy the requirement of Public Offers Law (POL) §103-a(2)(b), which permits members of a public body to participate in meetings by videoconferencing from a non-public location under extraordinary circumstances.

- Open Meetings Law (OML)
  - §103-a. Videoconferencing by public bodies
    - Model Resolution and Model Procedures for member videoconferencing pursuant to Public Officers Law §103-a Chapter 56 of the Laws of 2022 Guidance Document

Procedures for Member Videoconferencing

Open Meetings Law (OML)

The Open Meetings Law applies to "public bodies." That term is defined to include entities consisting of two or more people who conduct public business and perform a governmental function for New York State, for an agency of the state or for public corporations, such as cities, counties, towns, villages and school districts including committees and subcommittees of these entities. Consequently, city councils, town boards, village boards of trustees, school boards, commissions, legislative bodies, and committees and subcommittees consisting of members of those groups fall within the coverage of the Law.

Open Meetings Law | Open Government (ny.gov)

Open Meetings Law FAQs

Procedures for Member Videoconferencing

Open Meetings Law (OML)

§103-a. Videoconferencing by public bodies

2. A public body may, in its discretion, use videoconferencing to conduct its meetings pursuant to the requirements of this article provided that a minimum number of members are present to fulfill the public body's quorum requirement in the same physical location or locations where the public can attend, and the following criteria are met:

(a) the governing board of a county, city, town or village has adopted a local law, or a public body has adopted a resolution, or the senate and assembly have adopted a joint resolution, following a public hearing, authorizing the use of videoconferencing: (i) for itself and its committees or subcommittees; or, (ii) specifying that each committee or subcommittee may make its own determination; (iii) provided however, each community board in a city with a population of one million or more shall make its own determination;

Model resolution for Member videoconferencing pursuant to Public Officers Law § 103-a Chapter 56 of the Laws of 2022 Guidance Document

Procedures for Member Videoconferencing

Open Meetings Law (OML)

§103-a. Videoconferencing by public bodies

(b) the public body has established written procedures governing member and public attendance consistent with this section, and such written procedures shall be conspicuously posted on the public website of the public body;

(c) members of the public body shall be physically present at any such meeting unless such member is unable to be physically present at any such meeting location due to extraordinary circumstances, as set forth in the resolution and written procedures adopted pursuant to paragraphs (a) and (b) of this subdivision, including disability, illness, caregiving responsibilities, or any other significant or unexpected factor or event which precludes the member's physical attendance at such meeting;

Model procedures for Member videoconferencing pursuant to Public Officers Law § 103-a Chapter 56 of the Laws of 2022 Guidance Document

Procedures for Member Videoconferencing

Open Meetings Law (OML)

§103-a. Videoconferencing by public bodies

(d) except in the case of executive sessions… the public body shall ensure that members of the public body can be heard, seen, and identified, while the meeting is being conducted, including but not limited to any motions, proposals, resolutions, and any other matter formally discussed or voted upon;

(e) the minutes of the meeting involving videoconferencing shall include, which, if any, members participated remotely and shall be available to the public…;

(f) if videoconferencing is used to conduct a meeting, the public notice for the meeting shall inform the public that videoconferencing will be used, where the public can view and/or participate in such meeting, where required documents and records will be posted or available, and identify the physical location for the meeting where the public can attend;

Procedures for Member Videoconferencing

Open Meetings Law (OML)

§103-a. Videoconferencing by public bodies

(g) the public body shall provide that each meeting conducted using videoconferencing shall be recorded and such recordings posted or linked on the public website of the public body within five business days following the meeting and shall remain so available for a minimum of five years thereafter. Such recording shall be transcribed upon request;

(h) If videoconferencing is used to conduct a meeting, the public body shall provide the opportunity for members of the public to view such meeting via video, and to participate in proceeding via videoconference in real time where public comment or participation is authorize and shall ensure that videoconferencing authorizes the same public participation or testimony as in person participation or testimony; and

(i) a local public body electing to utilize videoconferencing to conduct its meetings must maintain an official website.

Procedures for Member Videoconferencing

Open Meetings Law (OML)

§103-a. Videoconferencing by public bodies

3. The in person participation requirements… shall not apply during a state disaster emergency declared by the governor… or a local state of emergency proclaimed by the chief executive of the of a county, city, village or town…if the public body determines that the circumstances necessitating the emergency declaration would affect or impair the ability of the public body to hold an in person meeting.

4. No later than January 1, 2024 the Committee on Open Government,… shall issue a report to the Governor and Legislature concerning the application and implementation of such law and any further recommendations governing the use of videoconferencing by public bodies to conduct meetings… Please note that the current provisions are repealed July 1, 2024.

5. Open meetings of any public body that are broadcast or that use videoconferencing shall utilize technology to permit access by members of the public with disabilities consistent with the 1990 Americans with Disabilities Act (ADA), as amended, and corresponding guidelines.

Procedures for Member Videoconferencing Model Resolution

Chapter 56 of the Laws of 2022 Guidance Document

Resolution No. _____
[PUBLIC BODY]

WHEREAS, by passing Chapter 56 of the Laws of 2022 ("Chapter 56"), the New York State Legislature amended Section 103 of the Open Meetings Law; and

WHEREAS, Chapter 56 adds Section 103-a of the Open Meetings Law, permitting the [PUBLIC BODY] to authorize its members to attend meetings by videoconferencing under extraordinary circumstances; and

WHEREAS, Section 103-a(2)(a) requires the [PUBLIC BODY] to adopt a resolution following a public hearing authorizing the limited use of videoconferencing under such circumstances; and

WHEREAS, Section 103-a(2) allows for hybrid meetings by requiring "that a minimum number of members are present to fulfill the public body's quorum requirement in the same physical location or locations where the public can attend"; and

WHEREAS, Section 103-a(2)(c) requires that members be physically present at any such meeting "unless such member is unable to be physically present at any such meeting location due to extraordinary circumstances . . . including disability, illness, caregiving responsibilities, or any other significant or unexpected factor or event which precludes the member's physical attendance at such meeting"; and

WHEREAS, in accordance with Section 103-a(2)(d), any members attending by videoconference must, excerpt during executive session, be "heard, seen and identified, while the meeting is being conducted, including but not limited to any motions, proposals, resolutions, and any other matter formally discussed or voted upon"; and

WHEREAS, Section 103-a(2)(g) requires that any meeting where a member attends by videoconference be recorded, posted to the [PUBLIC BODY] webpage within five business days, and transcribed upon request; and

WHEREAS, Section 103-a(2)(h) requires that members of the public be permitted to attend and participate, if authorized, in any meeting by videoconference when a member attends by videoconference.

BE IT RESOLVED, that the [PUBLIC BODY] authorizes its members who experience an extraordinary circumstance, as described above and further defined by any rules or written procedures later adopted, to attend meetings by videoconference: (i) as long as a quorum of the members attend in-person at one or more locations open to the public; (ii) as long as the member can be seen, heard, and identified while the open portion of the meeting is being conducted; and (iii) as otherwise permitted under Chapter 56 of the Laws of 2022; and be it further

RESOLVED, that the [PUBLIC BODY] shall create written procedures further governing its use of videoconferencing by its members in compliance with Chapter 56 of the Laws of 2022.

Model Procedures for Member Videoconferencing Pursuant to Public Officers Law §103-a

Chapter 56 of the Laws of 2022 Guidance Document

In compliance with Public Officers Law (POL) § 103-a(2)(a), the [PUBLIC BODY], following a public hearing, authorized by resolution on [insert date] the use of videoconferencing as described in POL § 103-a.

The following procedures are hereby established to satisfy the requirement of POL § 103-a(2)(b) that any public body which in its discretion wishes to permit its members to participate in meetings by videoconferencing from private locations – under extraordinary circumstances – must establish written procedures governing member and public attendance.

1. [PUBLIC BODY] members shall be physically present at any meeting of the [PUBLIC BODY] unless such member is unable to be physically present at one of the designated public meeting locations due to extraordinary circumstances.

2. For purposes of these procedures, the term “extraordinary circumstances” includes disability, illness, caregiving responsibilities, or any other significant or unexpected factor or event which precludes the member’s physical attendance at such meeting.

3. If a member is unable to be physically present at one of the designated public meeting locations and wishes to participate by videoconferencing from a private location due to extraordinary circumstances, the member must notify [REPRESENTATIVE OR CHAIR OF PUBLIC BODY] no later than four business days prior to the scheduled meeting in order for proper notice to the public to be given. If extraordinary circumstances present themselves on an emergent basis within four days of a meeting, the [PUBLIC BODY] shall update its notice as soon as practicable to include that information. If it is not practicable for the [PUBLIC BODY] to update its notice, the [PUBLIC BODY] may reschedule its meeting.

4. If there is a quorum of members participating at a physical location(s) open to the public, the [PUBLIC BODY] may properly convene a meeting. A member who is participating from a remote location that is not open to in-person physical attendance by the public shall not count toward a quorum of the [PUBLIC BODY] but may participate and vote if there is a quorum of members at a physical location(s) open to the public.

5. Except in the case of executive sessions conducted pursuant to POL § 105, the [PUBLIC BODY] shall ensure that its members can be heard, seen, and identified while the meeting is being conducted, including but not limited to any motions, proposals, resolutions, and any other matter formally discussed or voted upon. This shall include the use of first and last name placards physically placed in front of the members or, for members participating by videoconferencing from private locations due to extraordinary circumstances, such members must ensure that their full first and last name appears on their videoconferencing screen.

Model Procedures for Member Videoconferencing Pursuant to Public Officers Law §103-a

Chapter 56 of the Laws of 2022 Guidance Document

6. The minutes of the meetings involving videoconferencing based on extraordinary circumstances pursuant to POL § 103-a shall include which, if any, members participated by videoconferencing from a private location due to such extraordinary circumstances.

7. The public notice for the meeting shall inform the public: (i) that extraordinary circumstances videoconferencing will (or may) be used, (ii) where the public can view and/or participate in such meeting, (iii) where required documents and records will be posted or available, and (iv) the physical location(s) for the meeting where the public can attend.

8. The [PUBLIC BODY] shall provide that each open portion of any meeting conducted using extraordinary circumstances videoconferencing shall be recorded and such recordings posted or linked on the [PUBLIC BODY] website within five business days following the meeting, and shall remain so available for a minimum of five years thereafter. Such recordings shall be transcribed upon request.

9. If members of the [PUBLIC BODY] are authorized to participate by videoconferencing from a private location due to extraordinary circumstances, the [PUBLIC BODY] shall provide the opportunity for members of the public to view such meeting by video, and to participate in proceedings by videoconference in real time where public comment or participation is authorized. The [PUBLIC BODY] shall ensure that where extraordinary circumstances videoconferencing is used, it authorizes the same public participation or testimony as in person participation or testimony.

10. Open meetings of the [STATE PUBLIC BODY OR AUTHORITY] conducted using extraordinary circumstances videoconferencing pursuant to the provisions of POL § 103-a shall be broadcast pursuant to the requirements of POL § 103(f) and shall utilize technology to permit access by members of the public with disabilities consistent with the 1990 Americans with Disabilities Act (ADA), as amended, and corresponding guidelines. For the purposes of this guideline, “disability” shall have the meaning defined in Executive Law § 292.

11. The in-person participation requirements of POL § 103-a(2)(c) shall not apply during a [state disaster emergency declared by the governor pursuant to Executive Law § 28 or a local state of emergency proclaimed by the chief executive of a county, city, village or town pursuant to § 24 of the Executive Law] if the [PUBLIC BODY] determines that the circumstances necessitating the emergency declaration would affect or impair the ability of the [PUBLIC BODY] to hold an inperson meeting.

12. These procedures shall be conspicuously posted on the [PUBLIC BODY] website

Procedures for Member Videoconferencing

Open Meetings Law (OML) –Resources

Member videoconferencing pursuant to Public Officers Law § 103-a
Chapter 56 of the Laws of 2022 Guidance Document

The Guidance Document contains Questions and Answers, a Model Resolution, and a Model Procedure.

Open Meetings Law | Open Government (ny.gov)

The website for the Committee on Open Government -Open Meetings contains the Law Text, Advisory Opinions, Case Law Summaries, Model Rules for Public Bodies, Publications and Frequently Asked Questions.

Procedures for Member Videoconferencing

Questions

Open Meetings Law (OML)?

§103-a. Videoconferencing by public bodies?

Open Meetings Law Text

Model Resolution or Model Procedures for member videoconferencing pursuant to Public Officers Law § 103-a?

Chapter 56 of the Laws of 2022 Guidance Document

Discussion

Retrospective Drug Utilization Review Program Update

New York State

Drug Utilization Review Board Meeting

April 20, 2023

NEW YORK STATE | Department of Health | Office of Health Insurance Programs
SUNY The State University of New York

Objectives

1. Introduce new RetroDUR reviewers
2. Provide overview of Retrospective Drug Utilization Review (RetroDUR) program
3. Detail program updates

RetroDUR Program Updates

Personnel Changes at University at Buffalo,
School of Pharmacy and Pharmaceutical Sciences (UB SPPS)

- New RetroDUR reviewers
  - Clinical pharmacists

RetroDUR Overview

- Case Review
  - UB SPPS
    - Clinical pharmacists
  - Review New York State Medicaid fee-for-service (FFS) claims monthly
- Program goals
  - Educate providers
  - Improve medication therapy

RetroDUR Overview

- Program flow
  - Data processed
  - Therapeutic areas of focus selected
  - Cases reviewed
  - Interventions
    - Educational letters
      - Sent to prescribers and pharmacies
  - Feedback

RetroDUR Program Updates

- Transition to new electronic platform
  - Launched April 2021

RetroDUR Program Updates

- Platform transition evaluation
  - Time to complete an individual review
    - Unchanged
  - Increased number of cases reviewed to 850 per month
    - July 2022

RetroDUR Program Updates

- Platform transition evaluation
  - Assign cases to specific reviewers
    - Allow for therapeutic focus
  - Enhanced reporting
    - Outcomes

RetroDUR Program Updates

- Quarterly Reports
  - Pharmacist reviewer-generated
    - Letters sent
    - Survey responses
    - Evaluation of criteria
  - Example report topics
    - SUPPORT Act medications
    - Anti-retrovirals with drug-drug interactions
    - Skeletal muscle relaxants

- Quarterly Report Example – Quetiapine
  - Background
    - Per quetiapine product monograph, for schizophrenia and bipolar disorder, the safety of doses above 800 mg/day have not been evaluated. Clinical trials have indicated that usually the treatment dose range is 300-600 mg/day
  - Criterion number and language
    - 1571- Quetiapine (Seroquel/Seroquel XR) may be over-utilized. The safety of doses above 800 mg/day has not been evaluated in clinical trials.

- Quarterly Report Example – Quetiapine
  - Letters sent

Members Reviewed	To Prescriber	To Pharmacy	Total Letters
42	44	42	86

- Quarterly Report Example – Quetiapine
  - Survey responses

Total Letters	Total Responses	Modification in therapy	Patient counseled	No further action
86	11	4	5	2

RetroDUR Program Updates

- Continue monthly case reviews
- Continue quarterly reports
- Possible increase in number of case reviews each month

Questions

Use of Antipsychotic Medication by Children as Related to the Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment (SUPPORT) for Patients and Communities Act

April 20, 2023

New York State Medicaid

Drug Utilization Review Board

NEW YORK STATE Department of Health Office of Health Insurance Programs
SUNY The State University of New York

SUPPORT Act

- Enacted October 24, 2018
- Law designed to address the overprescribing and abuse of opioids in the United States
- Consists of 8 titles:
  - Title I: Medicaid Provisions to Address the Opioid Crisis
  - Title II: Medicare Provisions to Address the Opioid Crisis
  - Title III: FDA and Controlled Substance Provisions
  - Title IV: Offsets
  - Title V: Other Medicaid Provisions
  - Title VI: Other Medicare Provisions
  - Title VII: Public Health Provisions
  - Title VIII: Miscellaneous

The SUPPORT for Patients and Communities Act (P.L.115-271): Medicare Provisions (congress.gov)

SUPPORT Act
Section 1004 Medicaid Drug Review and Utilization

- Standards added to the SUPPORT Act included:
  - Requirements for refilling opioid prescriptions;
  - Prescription monitoring for opioids and other drugs when prescribed at the same time, such as benzodiazepines;
  - **Antipsychotic prescription monitoring for children**; and
  - Fraud and abuse detection.

- States were required to implement the requirements by October 1, 2019, and to submit an amendment to their State plan no later than December 31, 2019.

Centers for Medicare and Medicaid. Available at CMS Announces New Standards for Medicaid DUR Programs to Combat Opioid Misuse and Abuse | CMS Accessed March 2023.
Center for Medicaid and CHIP Services. Available at Support 1004 DUR CIB (medicaid.gov). Accessed March 2023.

SUPPORT Act
Program to Monitor Antipsychotic Medications by Children

- Public Health Law 115-271 Section 1004:
  - *PROGRAM TO MONITOR ANTIPSYCHOTIC MEDICATIONS BY CHILDREN.—The State has in place a program (as designed and implemented by the State) to monitor and manage the appropriate use of antipsychotic medications by children enrolled under the State plan (or under a waiver of the State plan) and submits annually to the Secretary such information as the Secretary may require on activities carried out under such program for individuals not more than the age of 18 years generally and children in foster care specifically.*

- *In New York State, pediatrics and adolescents may remain in foster care until 21 years of age.*

Section 1902(oo)(1)(B) of the Act, as added by section 1004 of the SUPPORT for Patients and Communities Act

Background: Previous Drug Utilization Review Board (DURB) Reports

- December 2013: Second-Generation Antipsychotics (SGA) in Pediatric Members
- March 2014: Combined use of Antipsychotic and Stimulant Medications in Children and Adolescents
- February 2017: SGA– Duplicate Therapy in Adults
- June 2019: Use of Antipsychotics in Adolescents and Pediatric Members
  - First report presented to the DURB that focused on the SUPPORT Act

Current Clinical Criteria for Oral Antipsychotics-Second Generation

- Automated at the point-of-service (POS) for members receiving oral SGA medications:
  1. Age edits, for each individual agent, based on the Food and Drug Administration (FDA)-approved product information and Compendia-support indications.

  2. Prior authorization is required for patients <21 years of age when there is the concurrent use of ≥2 different oral antipsychotics for >90 days.

  3. Confirmation of an FDA-approved or Compendia-supported indication is required.

NYS Medicaid Fee-For-Service Preferred Drug List. Available at NYRx, the Medicaid Pharmacy Program | Preferred Drug Program (fhsc.com) . Accessed March 2023.

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Current Clinical Criteria for Oral Antipsychotics- Second Generation *Continued*

4. Confirmation of diagnoses that support concurrent use of central nervous system (CNS) stimulants and oral SGA for members <18 years of age.

5. For all oral SGAs used in treating major depressive disorder (MDD) in the absence of other psychiatric comorbidities, a trial with ≥ 2 different antidepressants is required before an SGA is used.

6. A trial of risperidone prior to paliperidone therapy is required.

7. Frequency/ quantity/ duration (F/Q/D) clinical criteria for some of the SGAs.

NYS Medicaid Fee-For-Service Preferred Drug List. Accessed at https://newyork.fhsc.com/downloads/providers/NYRx_PDP_PDL.pdf. August 2019.

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Objectives

1. Determine the total number of members in the New York State (NYS) Medicaid program <21 years of age, receiving an antipsychotic medication for ≥91 consecutive days.

2. For those members <21 years of age receiving antipsychotic medication for ≥91 consecutive days, evaluate the following parameters:
   a. Utilization of ≥2 different antipsychotic medications for ≥91 consecutive days;
   b. Completed metabolic testing (e.g., one diabetes screening and one cholesterol screening test);
   c. Had an FDA-approved or Compendia-supported indication to support the use of their antipsychotic therapy; and
   d. Utilization of other psychotropic agents (e.g., stimulants, antidepressants, sedatives/hypnotics, and/or mood stabilizers) concomitantly.

Methods

- A retrospective analysis of antipsychotic medications in members <21 years of age was conducted for the following timeframes:
  - State Fiscal Year (SFY) 2017: April 1, 2016 – March 31, 2017
  - SFY 2018: April 1, 2017 – March 31, 2018
  - SFY 2019: April 1, 2018 – March 31, 2019
  - SFY 2020: April 1, 2019 – March 31, 2020
  - SFY 2021: April 1, 2020 – March 31, 2021
  - SFY 2022: April 1, 2021 – March 31, 2022

- Data Source:
  - Medicaid Data Warehouse (MDW)

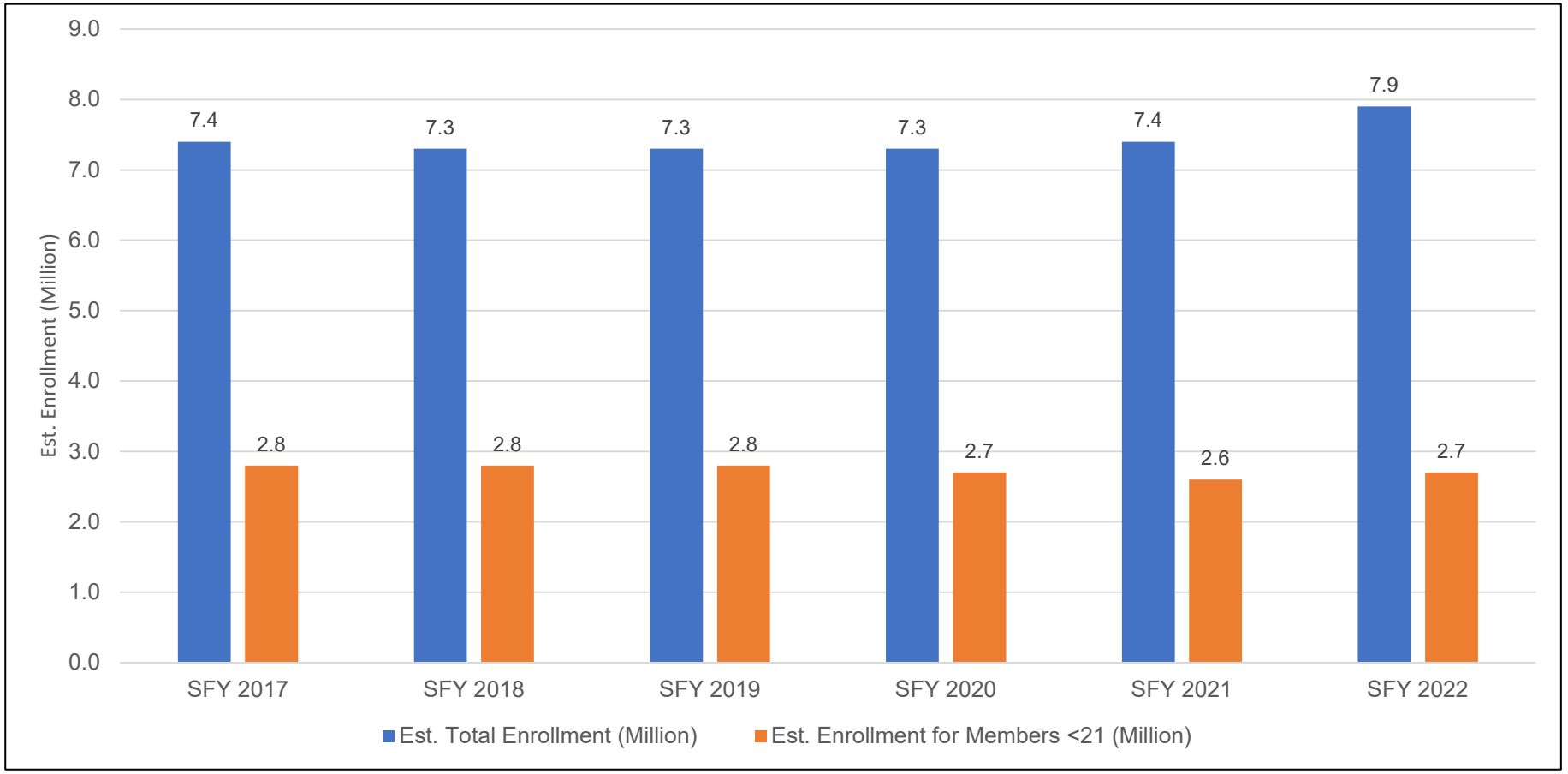
Limitations

- The member's eligibility was not evaluated. A member's eligibility may have changed during the analysis timeframe, which could result in the member's claim history being incomplete.

- Only pharmacy claims were included.
  - Injectable antipsychotics can be billed via both the pharmacy and medical systems; this analysis only included claims processed at the pharmacy.

- The Medicaid Confidential Data Cell Size Policy (OHIP-0001) requires that no cell containing a value of 1 to 30 be reported. The cell size value must be reported as ≤30 in all public-facing documents. Additionally, no cell can be reported that allows a value of 1 to 30 to be derived from other reported cells or information. Due to the small sample size, reporting the raw numbers or the percentages of patients would violate the Medicaid Confidential Data Cell Size Policy.

Estimated NYS Medicaid Program Enrollment by SFY (FFS+MC)



Mean Total Enrollment= 7.44 Million

Mean Enrollment for Members <21 Years of Age= 2.73 Million

Source= MDW

Extract date= 12/2022

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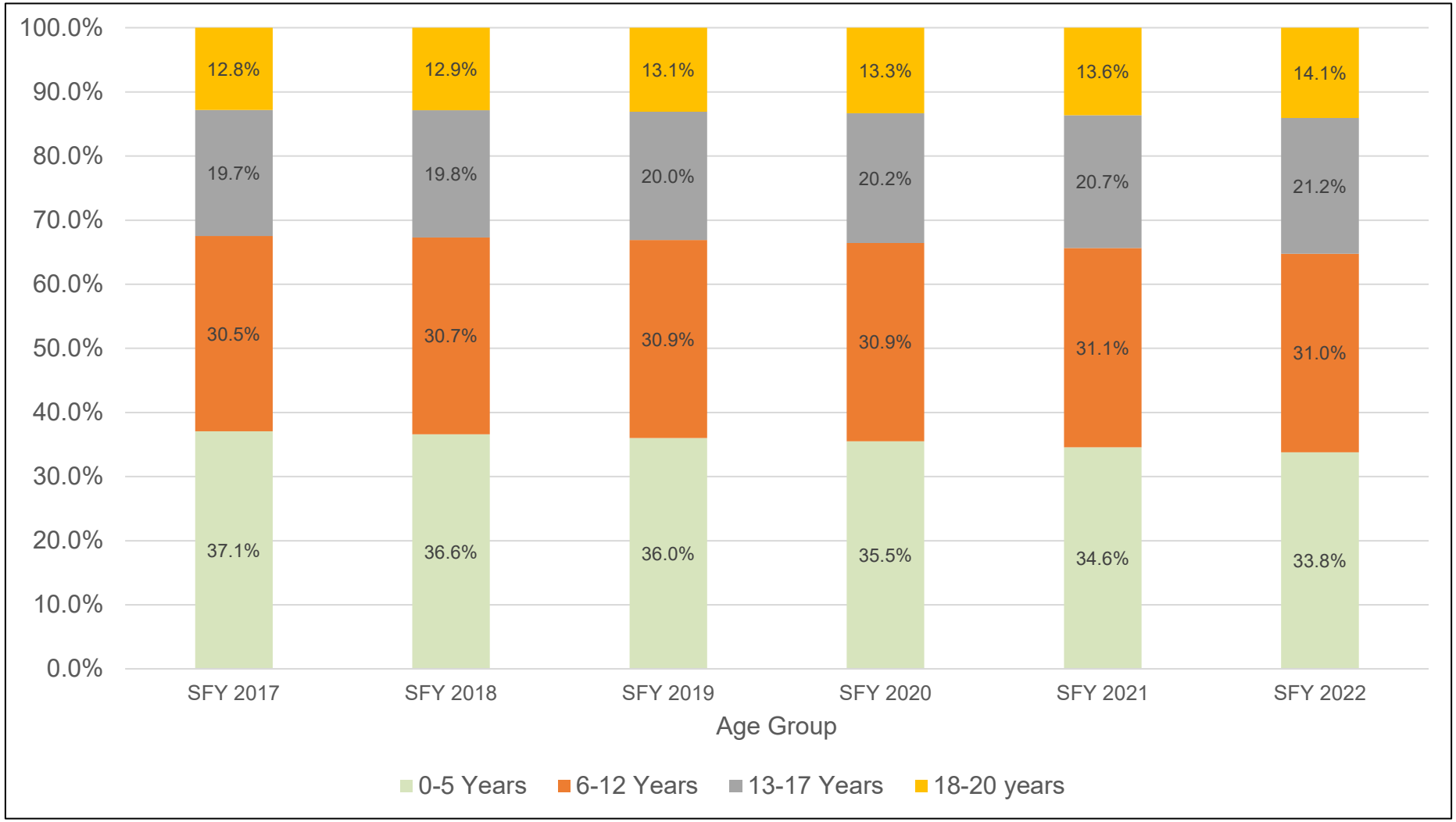
Enrollment by Age Group for Members <21 Years of Age (FFS+MC)



Source= MDW
Extract Date= 12/ 2022

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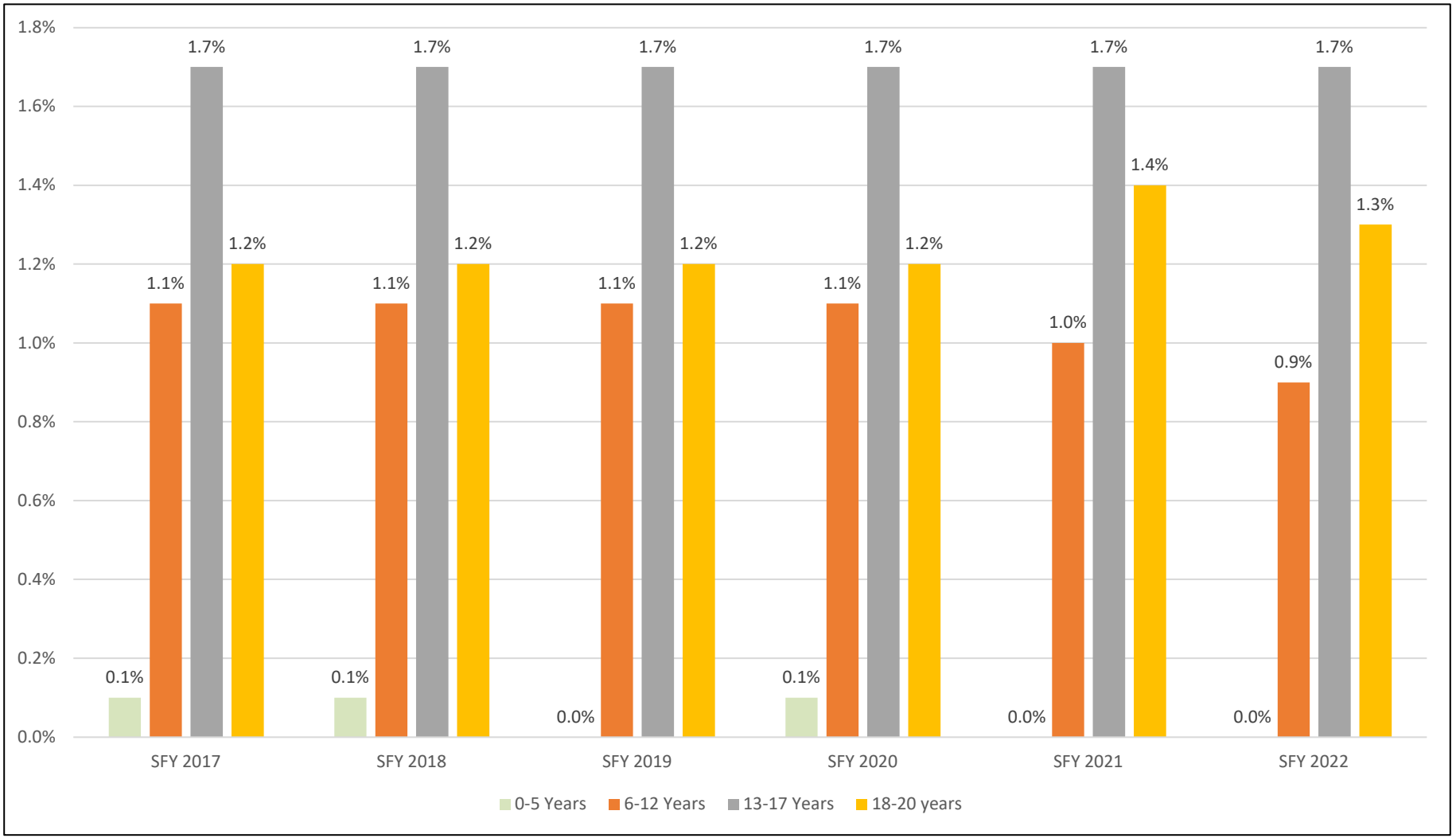
Members <21 Years of Age Utilizing ≥91 Days of Antipsychotic Therapy (FFS+MC)



Source= MDW
Extract Date= 12/2022

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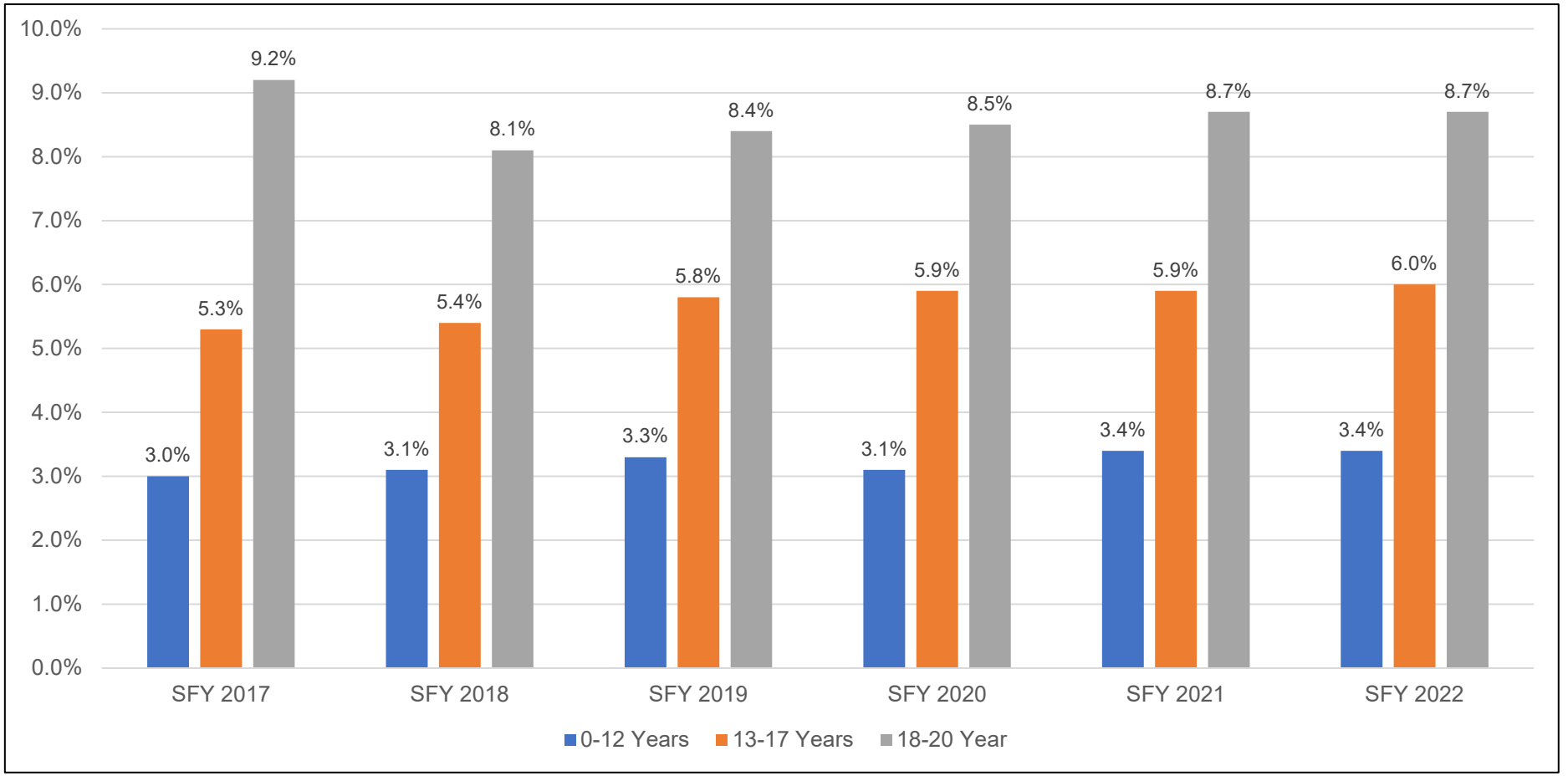
Members <21 Years of Age Utilizing ≥2 Different Antipsychotic Agents Concomitantly for ≥91 Days (FFS+MC)



Source= MDW
Extract Date= 12/2022

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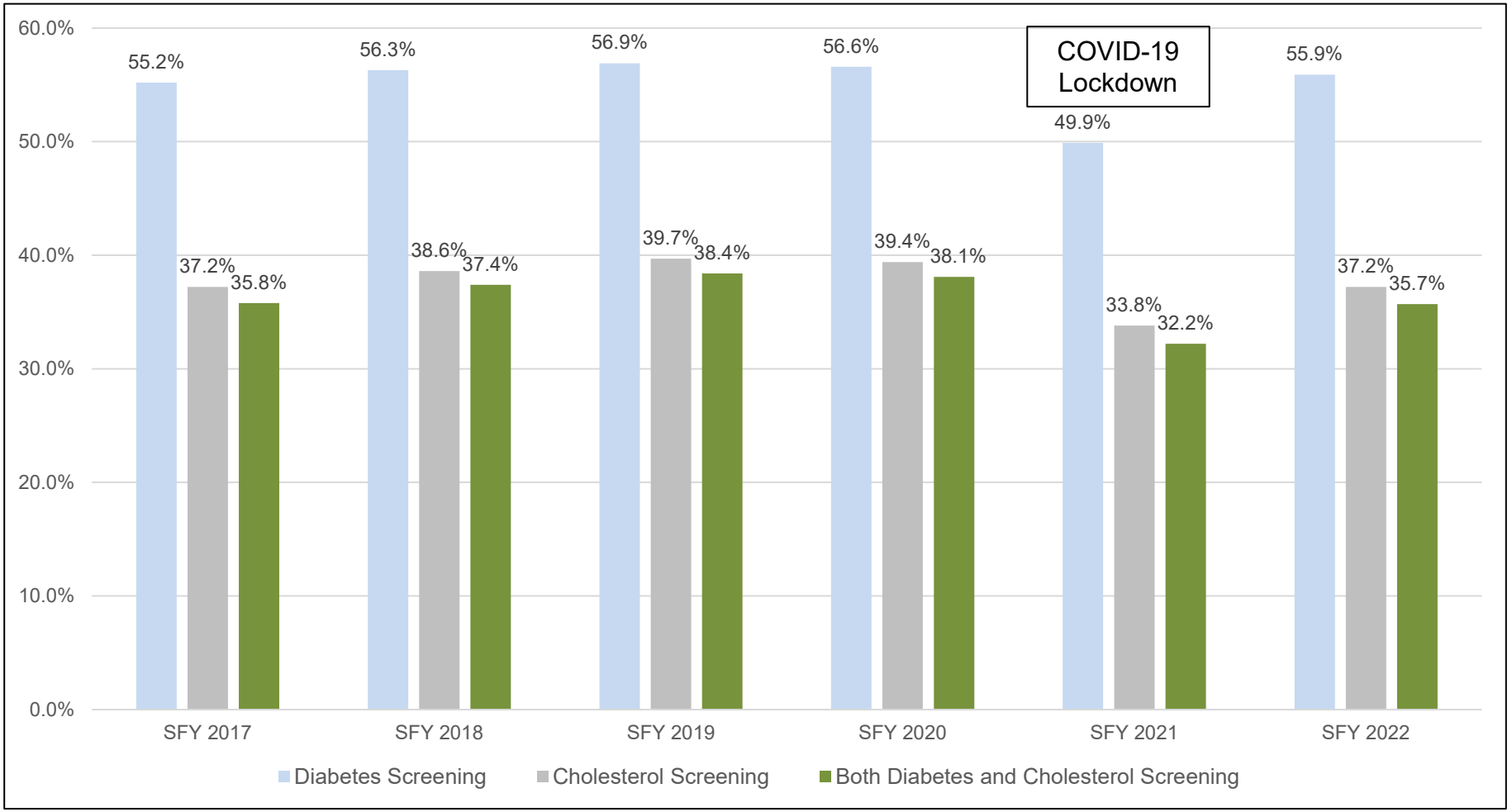
Diabetes and Cholesterol Screenings in Members <21 Years of Age Utilizing ≥91 Days of Antipsychotic Therapy (FFS+MC)



Source= MDW
Extract date= 12/2022

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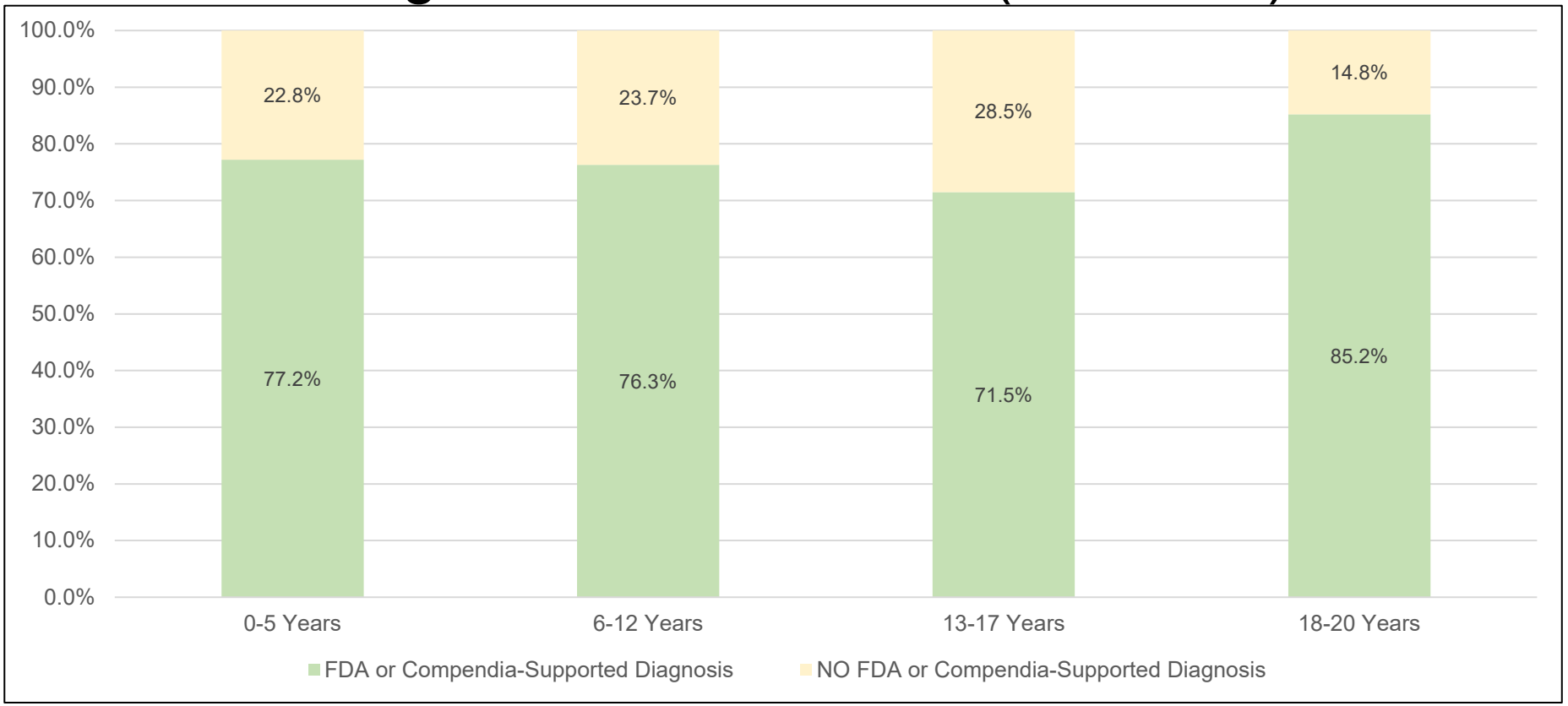
Percent of Members Utilizing ≥91 Days of Antipsychotic Therapy with an FDA or Compendia-Supported Diagnosis for SFY 2022 (FFS+MC)



76.3% of members <21 years of age utilizing an antipsychotic agent for ≥91 days consecutively had an FDA and/or Compendia-supported indication.

The Centers for Medicare and Medicaid Services drug compendium authorized sources are the American Hospital Formulary Service- Drug Information, Clinical Pharmacology, Micromedex DrugDex, and Lexi-Drug.

Source= MDW
Extract date= 12/2022

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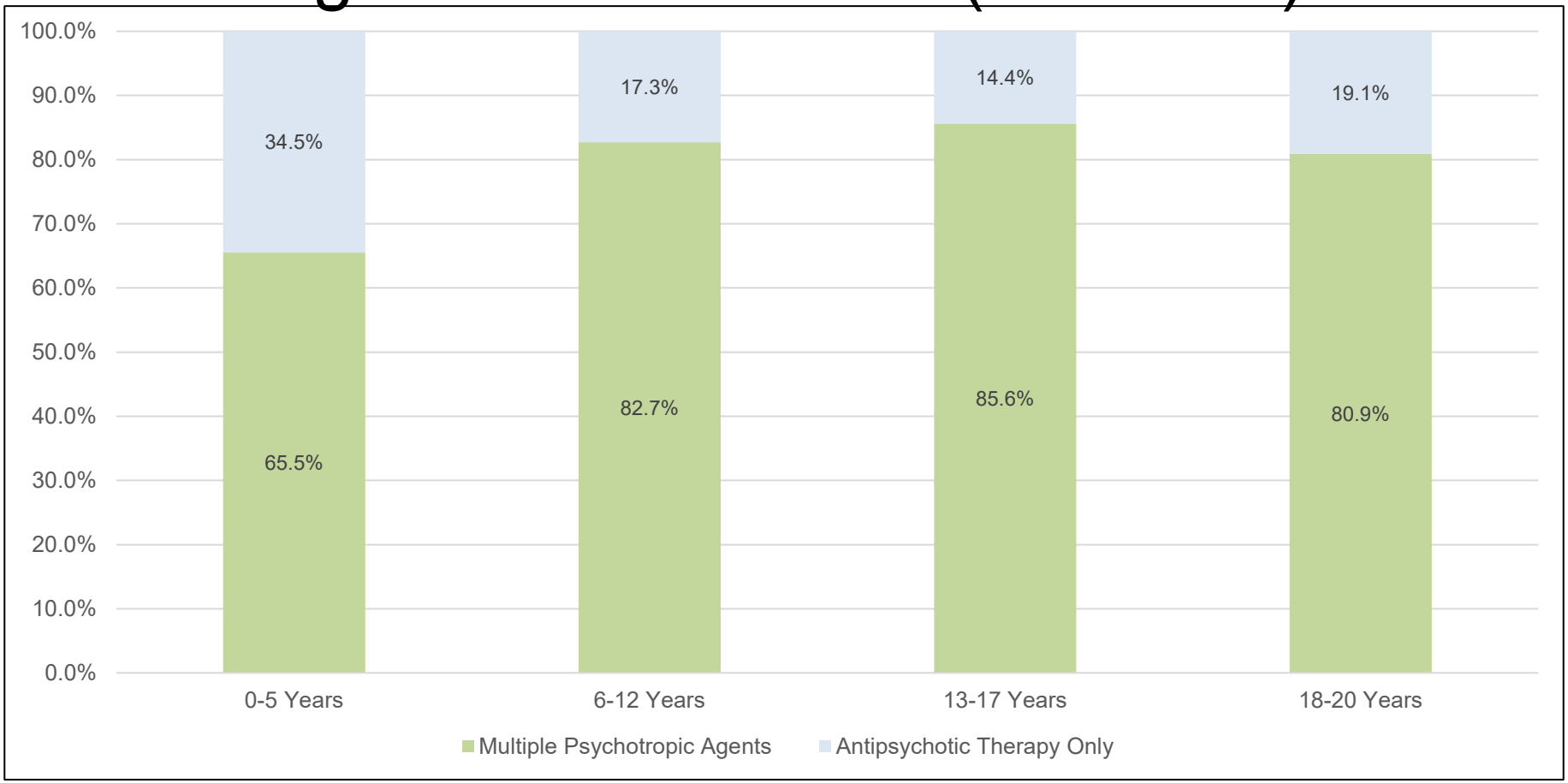
Medicare Benefit Policy Manual (cms.gov)

Percent of Members Utilizing ≥91 Days of Antipsychotic Therapy with other Psychotropic Agents for SFY 2022 (FFS+MC)



Psychotropic agents included in the analysis were stimulants, anxiolytics, hypnotics, mood stabilizers, and antidepressants.

Source=MDW
Extract Date: 12/2022

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Summary

- Use of an antipsychotic agent for ≥91 consecutive days in members <21 years of age has remained stable between SFY 2017 and SFY 2022.
- The fee-for-service program has established clinical criteria to require prior authorization for members <21 years of age utilizing ≥2 antipsychotic agents concomitant for >90 days.
- Metabolic screening rates have remained relatively low.
- Most members used an antipsychotic agent for an FDA or Compendia-supported indication.
- Most members were receiving psychotropic medications from other therapeutic categories concurrently.

Recommendations

- Continue to monitor the use of antipsychotic medications in children and report results to the DURB. The following measures should be evaluated:
  - The number of members receiving antipsychotic medication for ≥91 days;
  - The number of members receiving >1 different antipsychotic medication for ≥91 days concomitantly;
  - The number of members receiving metabolic monitoring (e.g., diabetes and cholesterol screening tests);
  - The number of members utilizing concurrent psychotropic medications; and
  - The number of members with an FDA or Compendia-supported indication.

- Develop educational materials to encourage metabolic monitoring for members receiving antipsychotic therapy.