[W2] Gene Therapy in Sickle Cell Disease – Breakthroughs in Treatment and Coverage

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Learning Objectives

1. Explain the differences between newly-approved gene therapies and the standard of care in the SCD space.
2. Identify risk mitigation options for gene therapies that are utilized by commercial and Medicaid programs.
3. Describe CMS Cell and Gene Therapy Access Model and the impact to Medicaid.

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Faculty/Reviewer/Planner	Reported Relevant Financial Relationships
Kevin Niehoff, PharmD, BCMAS *Faculty*	Disclosed no relevant financial relationships.
Janine Statt, PharmD *Faculty*	Disclosed no relevant financial relationships.
Michelle Aslami, PharmD *Reviewer*	Disclosed no relevant financial relationships.
Brittany V. Henry, PharmD, MBA *Planner*	Disclosed no relevant financial relationships.

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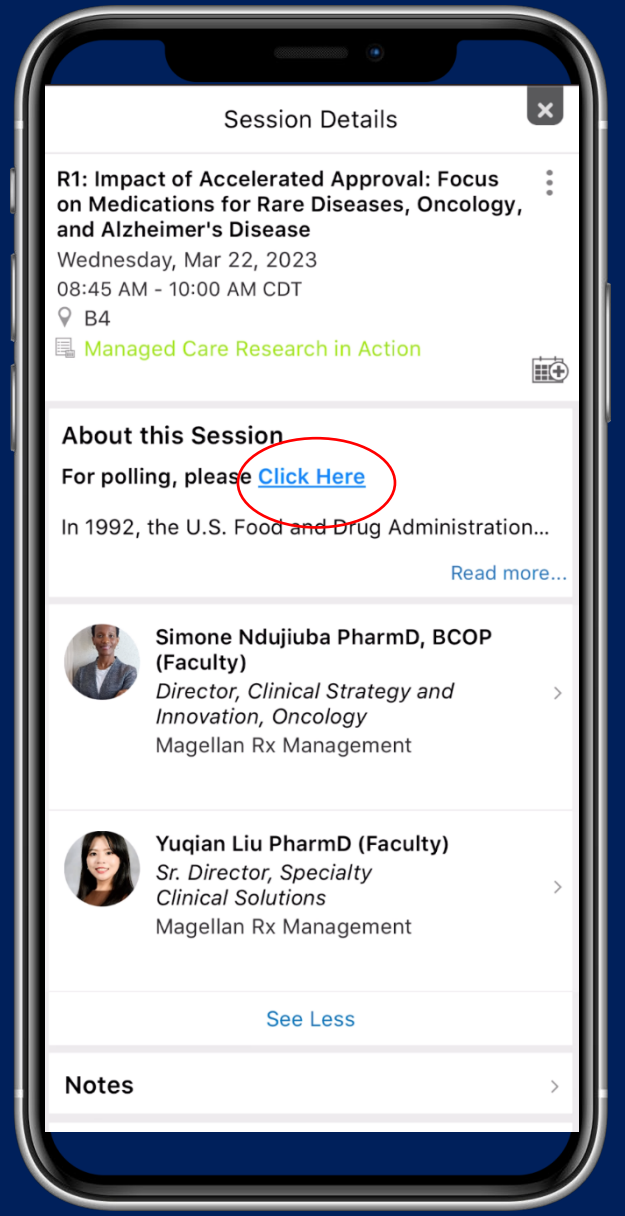

Faculty

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Pre-Test

Polling Question

LQ1: Which of the following is true of gene therapies relative to traditional sickle cell disease treatments?

a) Low cost
b) Limited distribution and access
c) Minimal administration burden
d) Minimal utilization management applied

Polling Question

LQ2: Which is not a potential coverage solution for high-cost therapies?

a) Subscription model
b) Lottery model
c) Outcomes-based model
d) Mortgage model

Polling Question

LQ3: Which of the following is NOT a risk mitigation option utilized by state Medicaid programs?

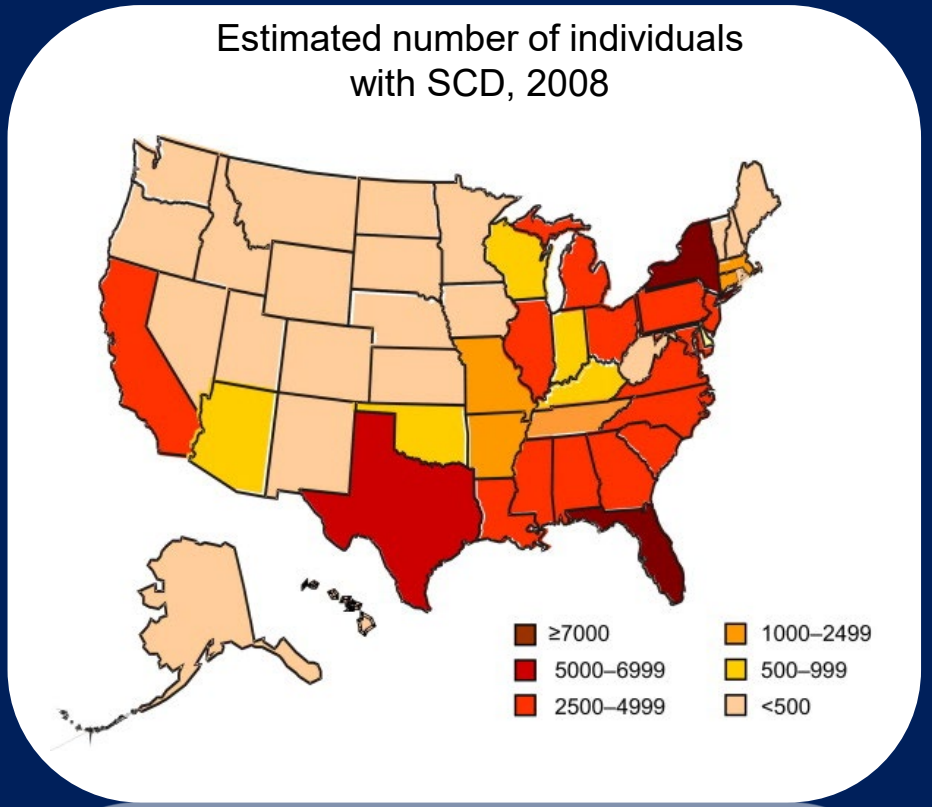
a) Risk Corridor
b) Risk Pool
c) Coverage Exclusion
d) Kick Payment

Sickle Cell Disease (SCD)

- What makes sickle cell disease unique?

- Ethnic and geographic concentration
  - Majority of patients affected are of African descent
  - Disproportionate burden on some health systems

- Adherence challenges
  - Access to care
  - Limitations of treatment options
  - Adverse effects



Pokhrel A, Olaymea A, Ogbonda S et al. Racial and ethnic differences in sickle cell disease within the United States: From demographics to outcomes. *Eur J Haematol.* 2023;110(5):554-563.
Hassel KL. Population estimates of sickle cell disease in the U.S. *Am J Prev Med.* 2010;38(4 Suppl):S512-S521.

SCD Treatment Options

Hydroxyurea (Siklos)

- Mainstay of SCD therapy
- Monitoring and myelosuppression
- Incompatible with pregnancy; concerns with fertility and live vaccines

L-glutamine (Endari)

- Over-the-counter L-glutamine therapy available
- Recently genericized
- Approved for 5yo and up
- Oral powder formulation

Siklos [package insert]. Bryn Mawr, PA: Medunik USA; 2023.
Endari [package insert]. Torrance, CA: Emmaus Medical; 2020.

SCD Treatment Options

Voxelotor
(Oxbryta)

- Approval based on increased hemoglobin levels
- Previously approved for 4yo and up
- Voluntarily withdrawn from all markets in late-September, 2024

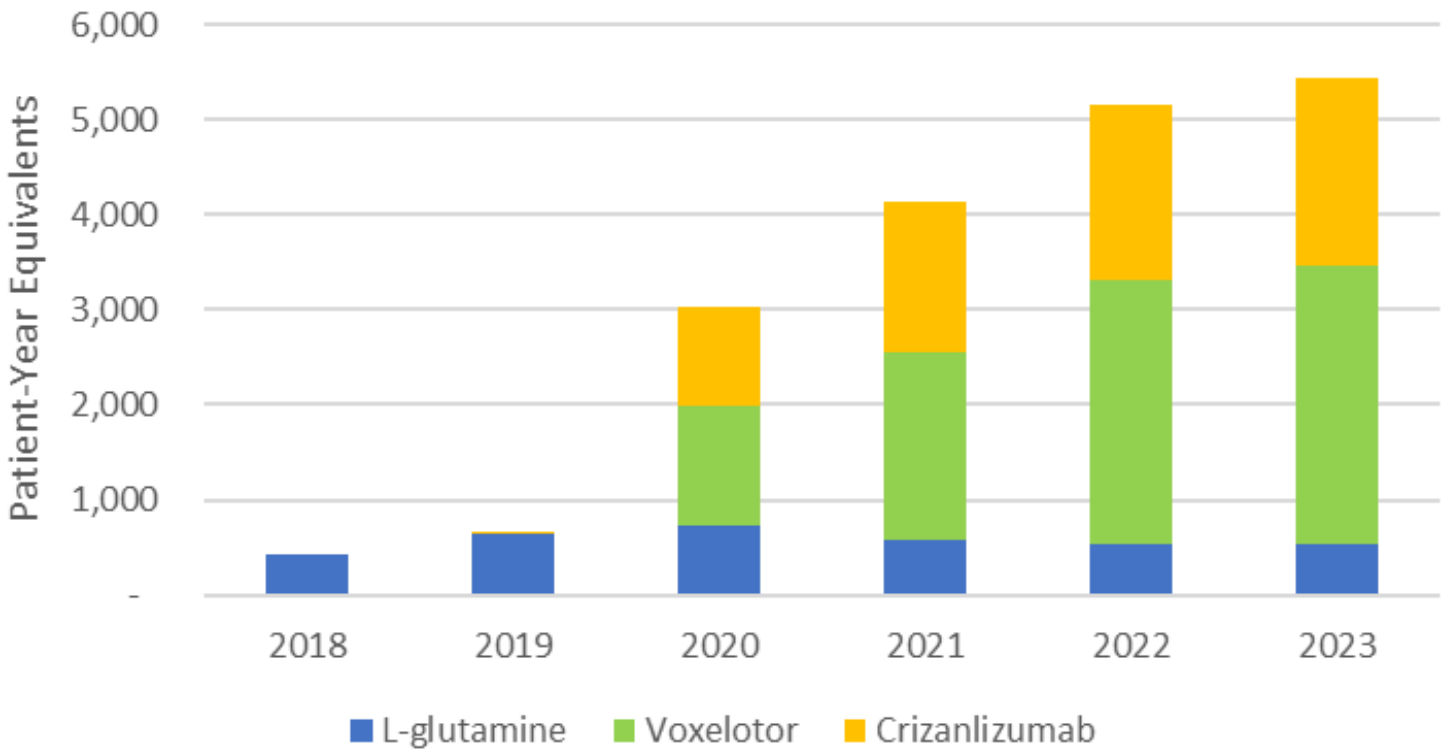
Crizanlizumab-tmca
(Adakveo)

- Approved for 16yo and up
- IV infusion every 4 weeks
- Controversy surrounding clinical utility

Oxbryta [package insert]. South San Francisco, CA: Global Blood Therapeutics; 2023.
Adakveo [package insert]. East Hanover, NJ: Novartis Pharmaceuticals; 2024.
Adakveo – referral. European Medicines Agency. Accessed September 6, 2024. https://www.ema.europa.eu/en/medicines/human/referrals/adakveo

Drug Utilization

Brand Sickle Cell Drug Utilization



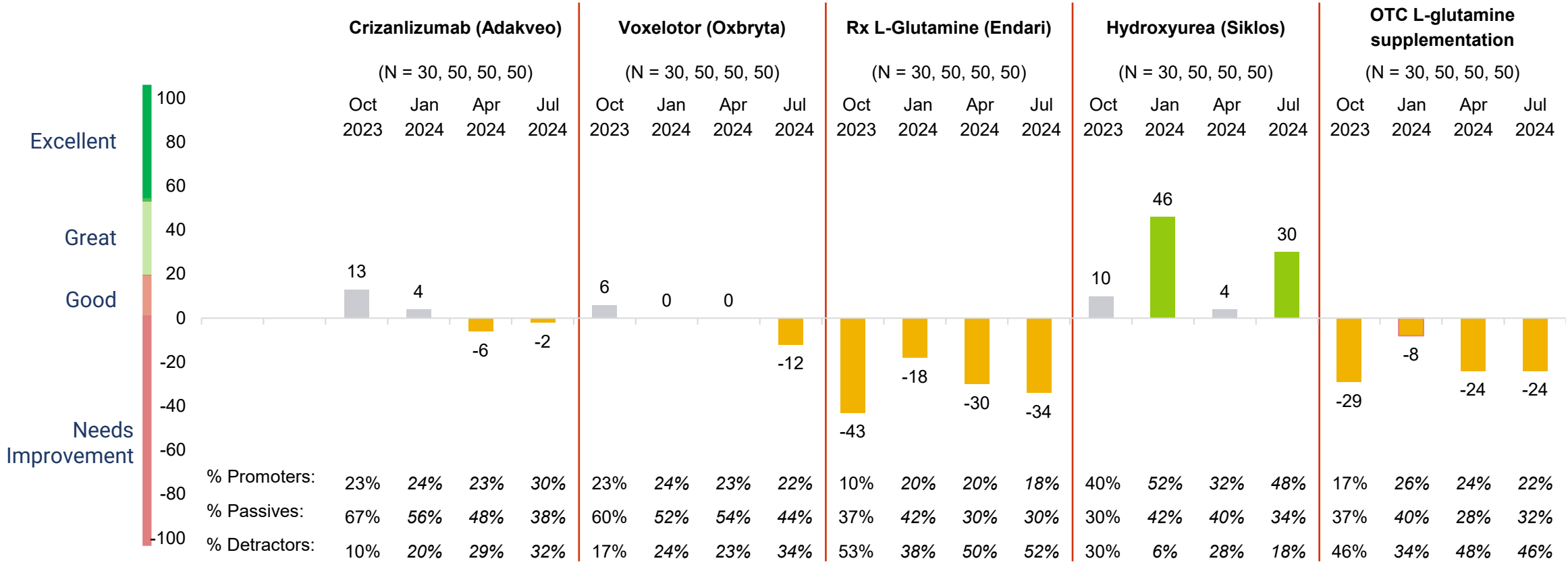
We estimate hydroxyurea therapy to account for an additional 7,000–8,000 patient-year equivalents.

IPD Analytics. Market and Financial Insights. Internal data, August 2024.

Provider Opinions

Physician opinion of established SCD treatments remains stable, with hydroxyurea consistently preferred.

Respondents were asked how likely they would be to recommend a product to their colleague[a] on a scale of 0 to 10. NPS[b] was then calculated based on those responses: **NPS = % Promoters (gave response 9–10) − % Detractors (responded 0–6)**



IPD Analytics. Primary Market Insights. Internal data, August 2024

Abbreviations: OTC, over-the-counter; SCD, sickle cell disease.

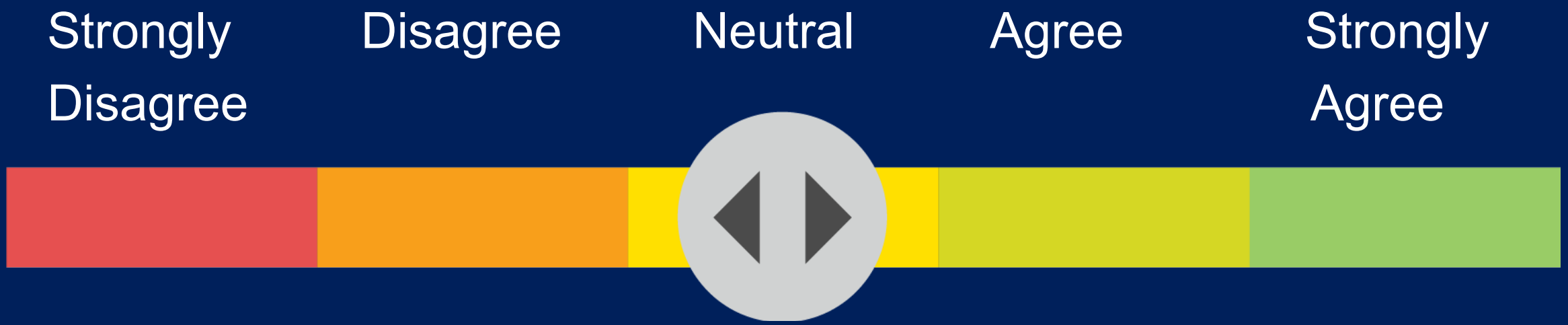
[a] **Q.** On a scale of 0–10, how likely would you be to recommend the following products to your colleagues for the treatment of SCD?

[b] NPS = Net Promoter Score. For additional information on NPS, please refer to: Reichheld FF. *Harvard Business Rev.* 2003.

Interactive Question

Agreement Likert Scale

Gene therapies are poised to be an effective therapy option in sickle cell disease.



SCD Gene Therapies

Exagamglogene autotemcel
(Casgevy, exa-cel)

- Autologous hematopoietic stem cells (HSCs) modified with CRISPR/Cas9
  - Increases production of fetal hemoglobin (HbF)
- 5 to 6 months to manufacture from cell collection to delivery
- CLIMB SCD-121 Trial
  - 29/31 (93.5%) patients had freedom from severe vaso-occlusive crisis (VOC) episodes for ≥12 months
  - 31/31 (100%) patients had freedom from hospitalizations for severe VOC episodes for ≥12 months
- Serious adverse effects (AEs) in 45% of patients

Casgevy [package insert]. Boston, MA: Vertex Pharmaceuticals; 2024.

SCD Gene Therapies

Lovotibeglogene autotemcel
(Lyfgenia, lovo-cel)

- Autologous HSCs modified via lentiviral vector (LVV), adding functional copies of a modified β^A-globin gene
  - Results in production of functional hemoglobin A
- 2.5 to 3.5 months to manufacture from cell collection to delivery
- HGB-206 Trial
  - 28/32 (88.2%) patients had complete resolution of vaso-occlusive events 6 to 18 months after infusion
  - 30/32 (94%) patients had complete resolution of severe vaso-occlusive events 6 to 18 months after infusion
- Serious AEs in 73% of patients
- Boxed Warning related to hematologic malignancy
  - No cases of insertional oncogenesis with Lyfgenia have been reported

Lyfgenia [package insert]. Somerville, MA: bluebird bio; 2024.

Gene Therapy Challenges

Patient-Centric

- Myeloablative conditioning
- Fertility

Logistic and Operational

- Durability
- Better therapies to follow?
- Access
  - Qualified treatment centers (QTCs)

Financial

- High cost → limited coverage

IPD Analytics. Payer and Provider Insights. New Drug Approval Review: Casgevy. January 12, 2024.
IPD Analytics. Payer and Provider Insights. New Drug Approval Review: Lyfgenia. January 5, 2024.

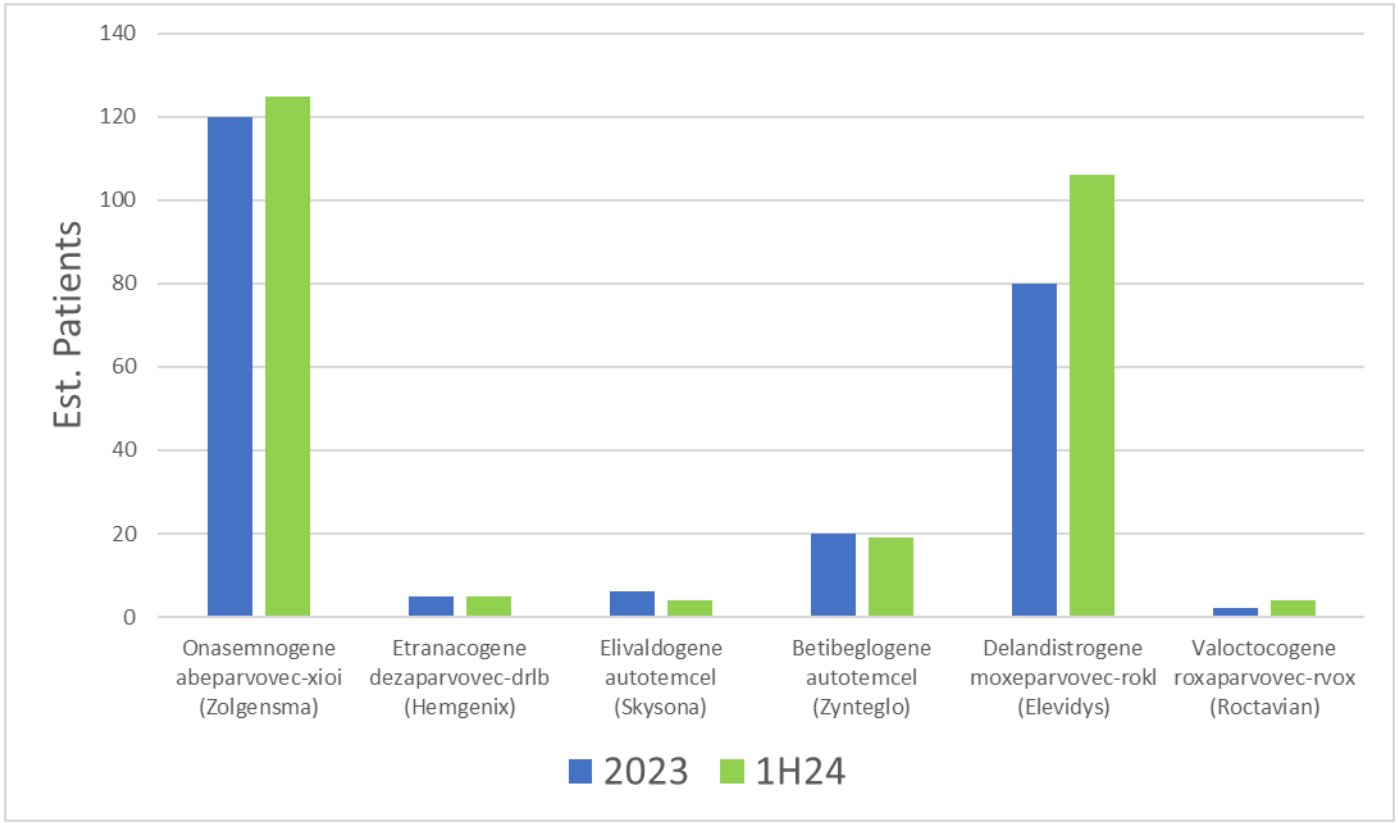
Gene Therapy Utilization

Exa-cel

- CRISPR/Vertex report 20 patients have completed cell collection globally as of mid-July 2024

Lovo-cel

- bluebird bio reports 4 patient starts as of mid-August 2024



IPD Analytics. Market and Financial Insights. Internal data, August 2024.

Coverage Solutions

Outcomes-Based Model (OBA, VBA)

- Aligns cost with value provided
- Ideal for therapies with well-defined and measurable outcomes

Mortgage Model

- Pay over time; no alignment of cost and value
- Geared toward self-insured plans

IPD Analytics. Payer and Provider Insights. RxInsights. Innovative Contracts. June 29, 2022.
IPD Analytics. Market and Financial Insights. Alternative Payment Models. Presentation in February 2024.

Coverage Solutions

Prevalence Model

- Increased utilization triggers rebates
- Controls costs for payers; enhances access for manufacturers

Subscription Model

- Capped annual expense in exchange for preferred or exclusive formulary placement
- Controls costs for payers; enhances access for manufacturers

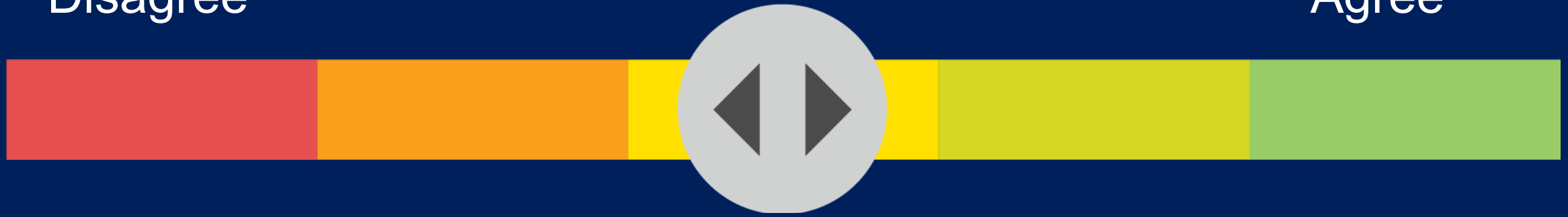
IPD Analytics. Payer and Provider Insights. RxInsights. Innovative Contracts. June 29, 2022.
IPD Analytics. Market and Financial Insights. Alternative Payment Models. Presentation in February 2024.

Medicaid Focus:
Risk Mitigation & The CGT Model

Interactive Question

Agreement Likert Scale

Gene therapy coverage is a topic of conversation in my pharmacy program.



Risk Mitigation

Medicaid Managed Care Considerations

- Is there a risk of uneven distribution across MCOs?
- How predictable is the utilization of the drug?
- What is the prevalence of the condition being treated?
- Is there a concern about overutilization?
- How important is care management to this drug or condition?
- Will the State pay a premium for the plan to manage the risk?
- How administratively complex is the risk mitigation?

Questions and considerations driving the selection of a risk mitigation tool

High-Cost Drug Risk Mitigation Options

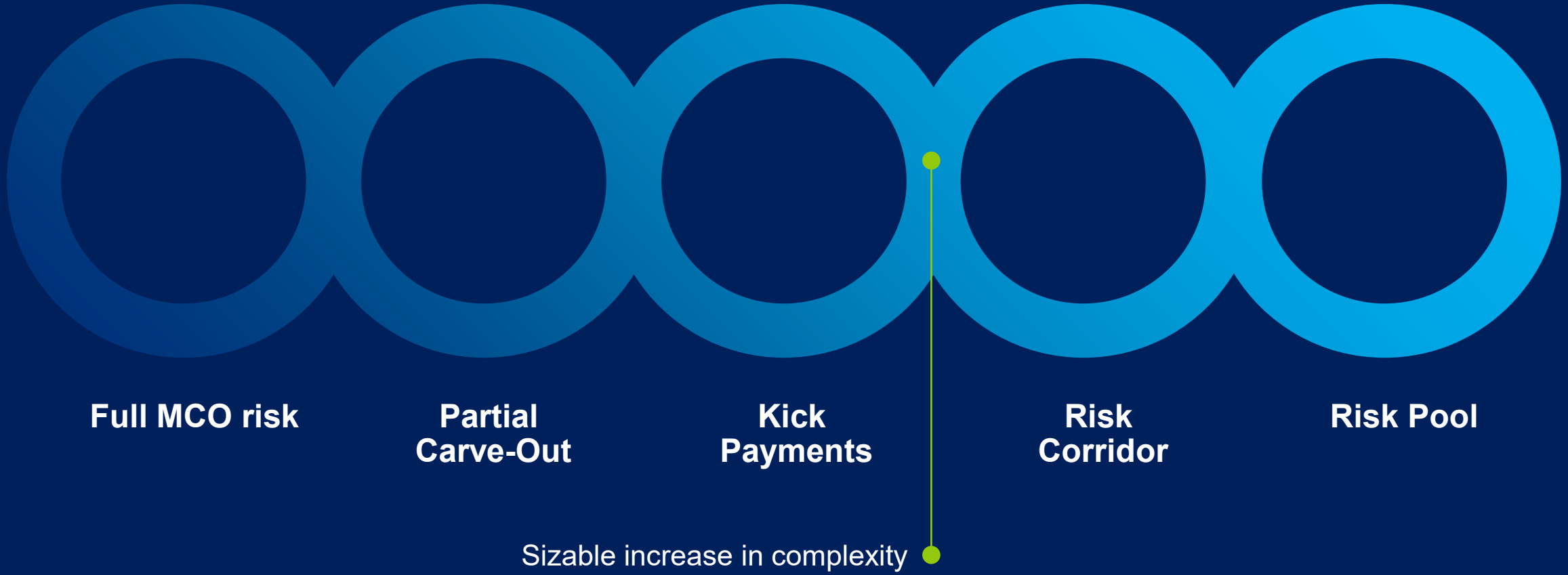
Advantages and Disadvantages

	MCO Full Risk	Limited Carve-Outs	Risk Corridors	Kick Payments	Risk Pools	State Administered Reinsurance
Budget Predictability	+	–	–	–	+	+/–*
Incentive for MCOs to Manage Utilization	+	–	+	–	+	+
Incentive for MCOs to Manage Unit Cost	+	–	+	+	+	+
Directs Funds to MCOs with Highest Utilization	–	–	+	+	+	+
Maintains Integrated Managed Care Model	+	–	+	+	+	+
Requires Maintenance of a High-cost Drug List	–	+	+	+	+	–
VBP Operational Simplicity	–	+	–	–	–	–

* *Dependent on the design of the reinsurance. Capped reinsurance is more predictable than open ended reinsurance arrangements funded by the State.*

Administrative Complexity

Least Complex to Most Complex



Budget Predictability

Least Risk to the State to Most Risk to the State

Full MCO Risk Or Risk Pool

Risk Corridor

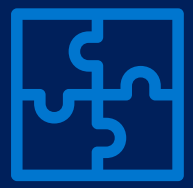
State Administered Reinsurance

Kick Payments

Carve Outs

Cell and Gene Therapy (CGT) Access Model

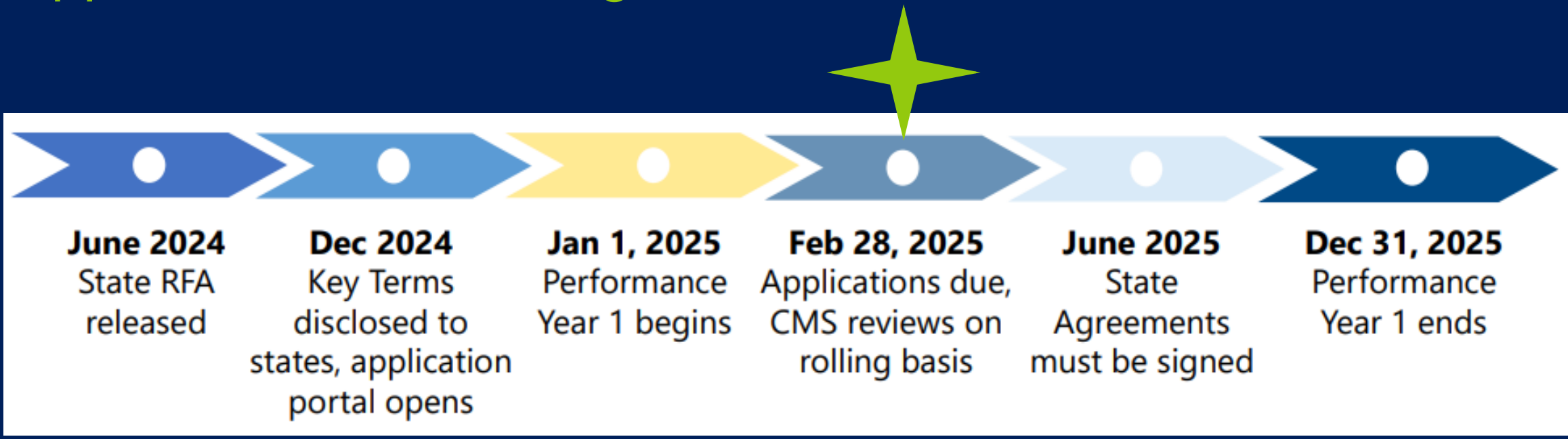
Purpose and Overview

			
Reduce the burden of outcomes-based agreement (OBA) negotiation and implementation	**Facilitate price discounts and flexible OBA structures**	**Centralize data collection and payment reconciliation**	**Improve health outcomes, increase access, reduce long-term health care costs**

Centers for Medicare & Medicaid Services. Cell and Gene Therapy (CGT) Access Model State Request for Applications (RFA) Factsheet; 2024. Accessed September 2, 2024. https://www.cms.gov/files/document/cgt-model-rfa-fact-sheet.pdf

Cell and Gene Therapy (CGT) Access Model

Application and Funding Timelines



Optional: Notice of Funding Opportunity (NOFO) available to support states' participation in the CGT Access model through Cooperative Agreement funding. Separate application is required; states must also apply to the Request for Application (RFA).

Centers for Medicare & Medicaid Services. Cell and Gene Therapy (CGT) Access Model Notice of Funding Opportunity (NOFO) Factsheet; 2024. Accessed September 2, 2024. https://www.cms.gov/files/document/cgt-model-rfa-fact-sheet.pdf

Cell and Gene Therapy (CGT) Access Model

Requirements for Medicaid State Participation

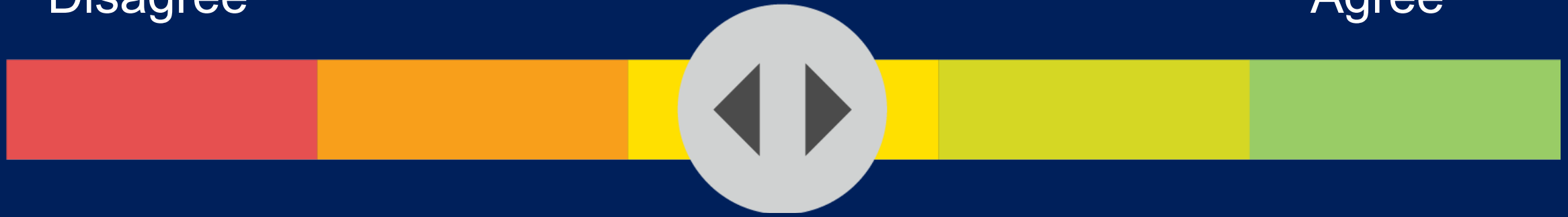
Legal Authority	CMS approval of a State Plan Amendment (SPA) to execute Value-Based Purchasing (VBP)
Bundled Payment Carveout	Carve model drug(s) out of any bundled payment arrangements
Access to Drug	Establish a standard policy to align with final key terms of the model
Access to Care	Ensure access to at least one qualified SCD gene therapy provider
Data and Reporting	Submit claims through Transformed Medicaid Statistical Information System (T-MSIS), other reports to CMS
Provider Reimbursement	Require providers to register and submit claims per model guidance
Managed Care	Confirm managed care policies align with model requirements

Centers for Medicare & Medicaid Services. Cell and Gene Therapy (CGT) Access Model Notice of Funding Opportunity (NOFO) Factsheet; 2024. Accessed September 2, 2024. https://www.cms.gov/files/document/cgt-model-rfa-fact-sheet.pdf

Interactive Question

Agreement Likert Scale

Gene therapies for SCD have financial and operational challenges that may limit access unless addressed.



CGT Medicaid Landscape

What are Medicaid States currently doing for gene therapy coverage?

- Medicaid is required to pay for CGTs if they cover prescription drugs, and the manufacturer participates in the Medicaid Drug Rebate Program (MDRP)
- Several states are preparing to opt-in to the CGT Access Model, contingent on Key Terms defined by CMS
  - Updating SPA language to engage in VBP
  - Gene therapy carve-out of bundled payments
- Some states have negotiated VBP for select gene therapies, or are currently negotiating for SCD gene therapies outside of the CGT Access Model
- Some states are re-evaluating risk mitigation strategies options in the managed care environment

Centers for Medicare & Medicaid Services. Cell and Gene Therapy (CGT) Access Model Notice of Funding Opportunity (NOFO) Factsheet; 2024. Accessed September 2, 2024. https://www.cms.gov/files/document/cgt-model-rfa-fact-sheet.pdf

Post-Test

Polling Question

LQ1: Which of the following is true of gene therapies relative to traditional sickle cell disease treatments?

a) Low cost
b) Limited distribution and access
c) Minimal administration burden
d) Minimal utilization management applied

Polling Question

LQ1: Which of the following is true of gene therapies relative to traditional sickle cell disease treatments?

a) Low cost

b) Limited distribution and access

c) Minimal administration burden

d) Minimal utilization management applied

CORRECT RESPONSE: B, the correct answer can be found on page 8 of the handout.
BRIEF EXPLANATION: Gene therapies are only available through qualified treatment centers (QTCs) authorized by their respective manufacturers.

Polling Question

LQ2: Which is not a potential coverage solution for high-cost therapies?

a) Subscription model
b) Lottery model
c) Outcomes-based model
d) Mortgage model

Polling Question

LQ2: Which is not a potential coverage solution for high-cost therapies?

a) Subscription model

b) Lottery model

c) Outcomes-based model

d) Mortgage model

CORRECT RESPONSE: B, the correct answer can be found on pages 9-10 of the handout.
BRIEF EXPLANATION: Outcomes-based, mortgage, and subscription models have all been implemented in one form of another as solutions to high-cost therapy coverage.

Polling Question

LQ3: Which of the following is NOT a risk mitigation option utilized by state Medicaid programs?

a) Risk Corridor
b) Risk Pool
c) Coverage Exclusion
d) Kick Payment

Polling Question

LQ3: Which of the following is NOT a risk mitigation option utilized by state Medicaid programs?

a) Risk Corridor

b) Risk Pool

c) Coverage Exclusion

d) Kick Payment

CORRECT RESPONSE: C, the correct answer can be found on page 13 of the handout.
BRIEF EXPLANATION: Slide 34. Medicaid is required to cover CGTs if they cover prescription drugs, and the manufacturer participates in the Medicaid Drug Rebate Program (MDRP). Other risk mitigation options are available that can be leveraged in a managed care environment.

Questions

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