A Targeted Literature Review of Value-Based Agreements (VBAs) for Cell and Gene Therapies in the United States

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Introduction

- Cell and gene therapies (CGTs) have increasingly become more expensive in the United States (US), leading to the adoption of various payment types by payers.
- One such type of payment is value-based agreements (VBAs), sometimes referred to as outcomes-based agreements (OBAs), which are performance-based reimbursement agreements between healthcare payers and pharmaceutical manufacturers in which the price, amount, or nature of reimbursement is tied to real-world outcomes.[1]
- VBAs can be beneficial to three stakeholders: patients, payers, and manufacturers.[1]
- For patients, VBAs can provide greater access to new therapies, especially for those with rare diseases. They can also increase earlier access to treatments when treatments have limited clinical data.[1]
- For payers, VBAs can lower the amount of risk a payer takes on when paying for a gene therapy, while also reducing uncertainty regarding clinical value and performance in a real-world setting.[1]
- Lastly, manufacturers can use VBAs to differentiate and demonstrate effectiveness in a crowded therapy class.[1]

Objective

- To conduct a review of literature and sources available in the public domain on the use of VBAs for CGTs in the US.

Methods

- A review of VBAs for CGTs was conducted based on the FDA list of approved CGT products as of September 2024.[2]
- Procedure-related therapies (e.g., cord blood, scaffold products) were excluded from further exploration.
- Literature identified through PubMed, manufacturer/payer press releases, and policy statements were reviewed to identify VBAs.
- VBA terms, such as payer, length of agreement, and outcomes assessed, were extracted where possible.

Results

- From the list of FDA-approved CGTs, 24 fit the inclusion criteria.
- Following a review of identified literature and public sources, 11 CGTs (46%) were found to be covered by VBAs in the US (**Table 1**).
- For 13 CGTs, VBAs in the US were not identified (**Table 2**).
- The CGTs with VBAs in place included: Beqvez, Casgevy, Hemgenix, Kymriah, Lenmeldy, Luxturna, Lyfgenia, Roctavian, Vyjuvek, Zolgensma, and Zynteglo.
- Details on VBA terms were publicly disclosed for select CGTs only.
- Specific outcomes detailed in the VBAs ranged from measures of clinical efficacy (e.g., symptom improvement, patient response) to healthcare resource utilization (e.g., transfusion independence, hospitalizations).

References

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Results

Table 1. Characteristics of Publicly Disclosed VBAs for CGTs in the US

Therapy	Manufacturer*	Indication*	Delivery*	WAC[3†]	Payer	VBA Terms	Outcome Measure
Beqvez *Fidanacogene elaparvovec-dzkt*	Pfizer	Hemophilia B	AAV vector	$3.5M	Not specified	• Novel warranty program: Offers refunds or financial offsets if the therapy does not meet certain efficacy thresholds over a specified period.[4] • Aims to reduce financial risks associated with the therapy's performance and ensure broader access and acceptance.[4,5]	Durability of patient response to treatment[5]
Casgevy‡ *Exagamglogene autotemcel*	Vertex	SCD, transfusion-dependent beta-thalassemia	Genome-edited stem cells	$2.2M	Medicaid[6]	• If the therapy does not work as promised within a certain time frame, a rebate will be issued.[6]	Not specified
Hemgenix *Etranacogene dezaparvovec-drlb*	CSL Behring	Hemophilia B	AAV vector	$3.5M	Not specified	• Warranty: 20-30% value-based discounts to be given in the event of poor patient response.[7]	Not specified
Kymriah‡ *Tisagenlecleucel*	Novartis	B-cell precursor ALL, follicular lymphoma, large B-cell lymphoma	Genetically modified T-cells	$593,533	Not specified	• 30-day outcomes guarantee with cost of therapy wiped if poor response; now discontinued.[4,8,9] • Therapy is shipped without an invoice; invoice only sent once 30-day period is reached.[9]	Outcomes at 30 days (for only one of its indications, B-cell precursor ALL) with certified treatment centers or providers[4,8,9]
Lenmeldy‡ *Atidarsagene autotemcel*	Orchard Therapeutics	Pre- or early symptomatic metachromatic leukodystrophy	Stem cells	$4.25M	Undisclosed private and government insurers[10]	• Outcomes- and value-based agreements[10]	Not specified
Luxturna‡ *Voretigene neparvovec-rzyl*	Spark Therapeutics	Biallelic *RPE65* mutation-associated retinal dystrophy	AAV vector	$456,875 per 0.5 mL (per eye)	• Cigna[11] • Express Scripts[11] • Harvard Pilgrim[11]	• Milestone-based (90-day and 30-month): Outcomes-based rebates if the therapy does not meet certain efficacy thresholds over specific periods, up to 30 months.[4,9] • Novel contracting model: Changes the traditional buy and bill model by having the payer or their specialty pharmacy purchase the therapy directly.[4] • Extended payment options: Allows payers to spread payments over several years to manage the high upfront costs, with the potential for larger rebates based on the therapy's long-term success.[4]	Short-term efficacy and long-term durability based on light-sensitivity testing scores[9]
Lyfgenia‡ *Lovotibeglogene autotemcel*	bluebird bio	SCD	Stem cells	$3.1M	• Medicaid[12] • Undisclosed national payers[12]	• Graduated 3-year: OBAs offering a discount if a patient is hospitalized due to vaso-occlusive events within three years after treatment.[12]	Hospitalizations related to vaso-occlusion events within 3 years after treatment[12]
Roctavian *Valoctocogene roxaparvovec-rvox*	BioMarin Pharmaceutical	Hemophilia A	AAV vector	$2.9M	Not specified	• Warranty/milestone-based: 25% refund for lack of response after 3 years.[7] • 4-year warranty being offered to all US payers.[13]	Hemophilia-related metrics[13]
Vyjuvek‡ *Beremagene geperpavec*	Krystal Biotech	Wounds in patients with dystrophic epidermolysis bullosa with mutations in *COL7A1* gene	HSV-1 vector	$25,230 per 2.5 mL (max. dose 0.8-1.6 mL per week)	Undisclosed commercial and public payers[14]	• Since Vyjuvek is re-dosed, a different payment model was utilized by the manufacturer, Krystal Biotech.[14‡‡] • Krystal Biotech is offering all commercial payers a price cap of $900,000 per patient per year to account for patients requiring large numbers of vials of treatment.[14]	Not specified
Zolgensma‡ *Onasemnogene abeparvovec-xioi*	Novartis	Spinal muscular atrophy with biallelic mutations in *SMN1 gene*	AAV vector	$2.4M	• Cigna[11,15] • Harvard Pilgrim[11,15] • Mass Health[16]	• Milestone-based, evolving: Pay-over-time option up to 5 years.[4] • A portion of the cost at risk based on the therapy's performance over that period.[4] • Mass Health: Outcomes-based rebates of up to 100% (based on individual patient data) over a period of 5 years.[16]	Not specified
Zynteglo‡ *Betibeglogene autotemcel*	bluebird bio	Beta-thalassemia	Stem cells	$2.8M	• Medicaid[4,17] • Undisclosed commercial payer[17]	• Graduated 2-year: Payers are reimbursed up to 80% for patients who do not achieve and maintain transfusion independence, up to 2 years.[4] • OBAs with certain state Medicaid agencies.[4]	Transfusion independence[4]

Table 2. CGTs for Which VBAs in the US Were Not Identified

Therapy	Manufacturer*	Indication*	Delivery*	WAC[2†]
Abecma *Idecabtagene vicleucel*	Celgene/Bristol-Myers Squibb	Multiple myeloma	Genetically modified T-cells	$528,312
Adstiladrin *Nadofaragene firadenovec-vncg*	Ferring Pharmaceuticals	NMIBC	AAV vector	$60,000 for 4 vials
Amtagvi *Lifileucel*	Iovance Biotherapeutics	Unresectable or metastatic melanoma	Tumor-derived autologous T-cells	$562,000
Breyanzi *Lisocabtagene maraleucel*	Juno Therapeutics/Bristol-Myers Squibb	CLL/SLL, follicular lymphoma, large B-cell lymphoma, MCL	Genetically modified T-cells	$531,350
Carvykti *Ciltacabtagene autoleucel*	Janssen Biotech	Multiple myeloma	Genetically modified T-cells	$555,310
Elevidys‡ *Delandistrogene moxeparvovec-rokl*	Sarepta Therapeutics	Duchenne muscular dystrophy	AAV vector[8]	$3.2M
Imlygic *Talimogene laherparepvec*	BioVex/Amgen	Melanoma	Genetically modified oncolytic viral therapy	$6,986 per 1 mL
Omisirge‡ *Omidubicel-onlv*	Gamida Cell	Hematologic malignancies	Modified allogeneic hematopoietic progenitor cell therapy	$512,070
Provenge *Sipuleucel-T*	Dendreon Corporation	Metastatic castrate-resistant prostate cancer	Autologous cellular immunotherapy	$64,850 per 250 mL
Skysona‡ *Elivaldogene autotemcel*	bluebird bio	Cerebral adrenoleukodystrophy	Stem cells	$3M
Tecartus *Brexucabtagene autoleucel*	Kite Pharma	ALL, MCL	Genetically modified T-cells	$462,000
Tecelra *Afamitresgene autoleucel*	Adaptimmune	Unresectable or metastatic synovial sarcoma	Genetically modified T-cells	$727,000
Yescarta *Axicabtagene ciloleucel*	Kite Pharma	Follicular lymphoma, large B-cell lymphoma	Genetically modified T-cells	$503,580

Conclusions

- This review demonstrates that VBAs are used for multiple CGTs, across multiple therapy areas, in the US.
- Outcome measures linked to VBAs were often not publicly disclosed.
- Many of the disclosed outcome measures can be sourced from routine patient visits and/or adjudicated claims, placing no additional burden on healthcare providers to collect data for the sole purpose of the VBA.
- VBAs continue to evolve with emerging approaches (e.g., annuities), and initiatives such as the Center of Medicare and Medicaid Innovation's CGT Access Model will shape a multi-stakeholder approach to the use of VBAs.

Footnotes

*According to fda.gov and FDA Package Inserts.
†Prices accurate as of April 3, 2025.
‡Therapy FDA-approved for use in pediatric patients.
‡‡ Price being capped per patient did not have any terms tied to outcomes.
Abbreviations: AAV, adeno-associated virus; ALL, acute lymphoblastic leukemia; CGT, cell and gene therapy; CLL, chronic lymphocytic leukemia; DLBCL, diffuse large B-cell lymphoma; FDA, United States Food and Drug Administration; HSV, herpes simplex virus; max., maximum; MCL, mantle cell lymphoma; NMIBC, non-muscle-invasive bladder cancer; OBA, outcomes-based agreement; SCD, sickle cell disease; SLL, small lymphocytic lymphoma; SMN1, survival motor neuron 1; TTR, transthyretin; US, United States; VBA, value-based agreement; WAC, wholesale acquisition cost.

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