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Variation in Medicaid and commercial coverage of cell and gene therapies

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ABSTRACT

Growth in the availability of cell and gene therapies (CGTs) promises significant innovation in the treatment of serious diseases, but the high cost and one-time administration of CGTs has also raised concern about strain on health plan budgets and inequity in access. We used coverage information from the Tufts Medical Center Specialty Drug Evidence and Coverage (SPEC) database for 18 large commercial health plans in the US and information from state Medicaid websites to examine variation in coverage of 11 CGTs in August 2021. We found that US commercial and Medicaid health plans imposed restrictions in 53.5 % and 68.3 % of their coverage policies for the 11 included CGTs, respectively. In addition, we identified significant variation in access to CGTs across commercial plans and across Medicaid plans. Coverage restrictions for certain CGTs were more common than others; clinical requirements were often (but not always) consistent with the inclusion criteria for the clinical trial central to the drug's approval. We conclude that there is variation in access to CGTs, creating differential patient access.

1. Introduction

Cell and gene therapies (CGTs) promise potentially transformative treatments for a growing array of diseases, ranging from rare diseases such as spinal muscular atrophy to more common diseases such as advanced prostate cancer [1]. CGTs use living cells or genes to treat or prevent disease. The Food and Drug Administration (FDA) describes cell therapy as the transfer of cells from one person to another (allogeneic) or from the same person (autologous), and gene therapy as the transfer of genes into cells to correct or replace a defective gene [2].

CGTs pose a challenge to health care payers due to their one-time administration, high costs and uncertain long-term benefits. Payer coverage policies play a critical role in determining patient access to CGTs. Due to the age of disease onset, many patients who are eligible for CGTs are covered by Medicaid or commercial health plans [3]. As Medicaid provides health insurance for high-need populations, it pays a disproportionate share of some high-cost specialty therapies [4]. Previous research demonstrated significant variation in health plan coverage for CGTs, creating differential access [5]. It is unclear to what extent CGT access differs between Medicaid and commercial plans.

To address this issue, we investigated CGT market access for Medicaid and commercial plans by reviewing publicly available coverage policies. We focused specifically on clinical requirements and whether these restrict the eligible patient population relative to the corresponding FDA labeled indication. We examined coverage differences across CGTs among Medicaid plans, among commercial plans, and between Medicaid and commercial plans.

2. Study data and methods

We created a database of coverage policies for 11 FDA-approved CGTs issued by 18 of the largest US commercial health plans and Medicaid fee-for-service programs (50 states and DC) (Appendix 1) [6]. Coverage policies were current as of August 2021. To identify coverage policies, we used the Tufts Medical Center Specialty Drug Evidence and Coverage (SPEC) Database [7] for commercial health plans and searched state websites for Medicaid program information. We benchmarked coverage policies to each drug's FDA label indication. We categorized coverage restrictions, i.e., coverage requirements that go beyond a drug's label indication, as: (1) restrictions based on frailty or function, (2) restrictions based on life expectancy, or (3) restrictions based on prior therapy.

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We evaluated variation in coverage restrictions for CGTs both across and within commercial and Medicaid plans. We present two analyses.

First, we report on coverage differences between commercial and Medicaid plans for the same CGT. For this analysis we categorized policies as either: (1) having no restrictions (i.e., the plan covered the therapy for all patients for which the FDA approved the therapy), or (2) as having any restriction (i.e., plan coverage excludes some portion of the population for which the FDA approved the drug).

Second, we report differences in frequency and type of specific clinical criteria (e.g., patient must be of a certain age, frailty score, have a certain genetic profile, etc.) across commercial plans and across Medicaid plans. For this analysis, we report on chimeric antigen receptor T-cell (CAR-T) and immunotherapy products separately from adeno-associated virus (AAV)-based gene replacement therapy products due to their unique clinical requirements.

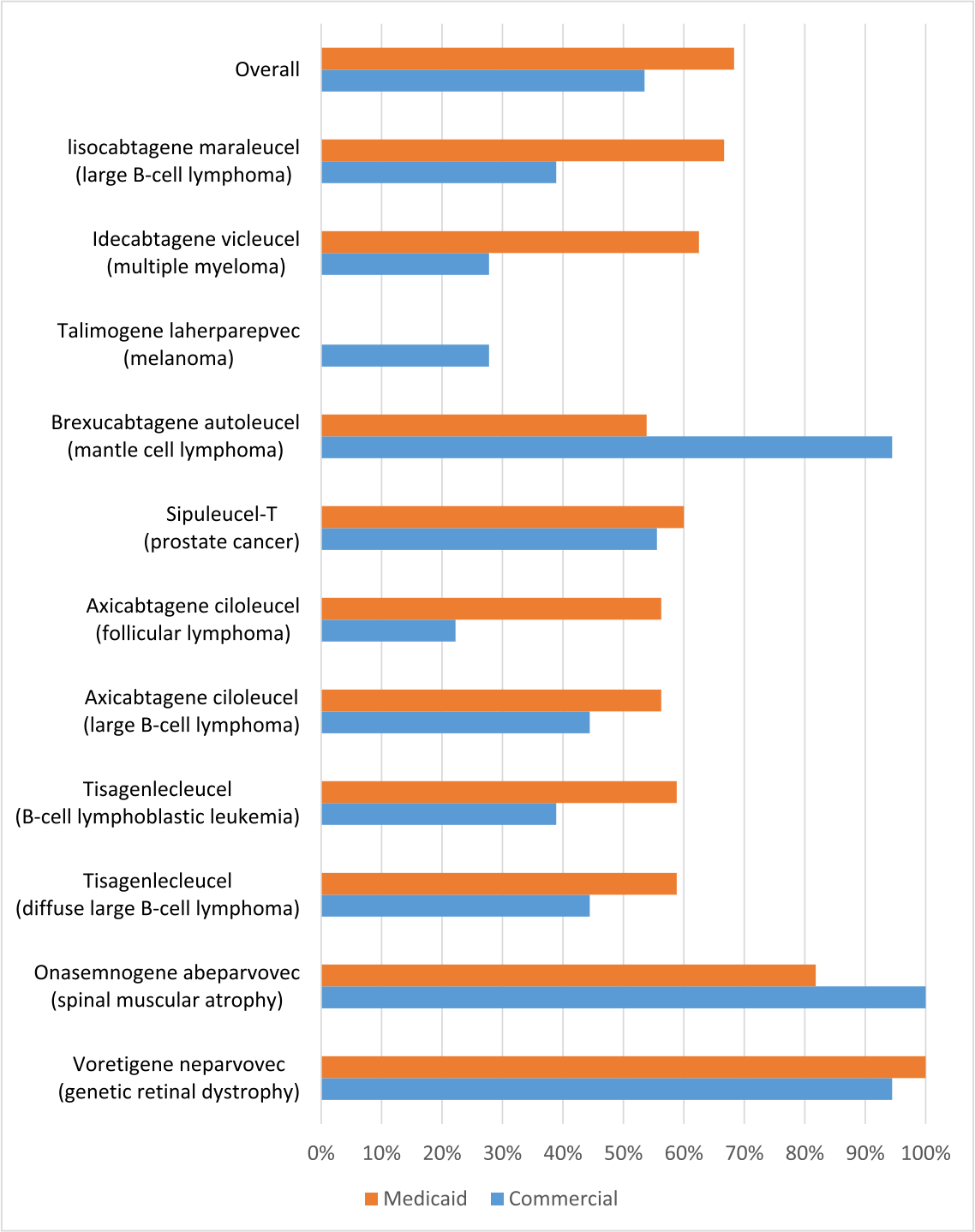

Fig. 1. Proportion of Cell and Gene Therapy Coverage Policies More Restrictive than FDA Label, Commercial vs Medicaid Health Plans, 2021. Source/Notes: Source: SPEC Database. Notes: Inclusion criteria requires US Medicaid and Commercial health plans to have a coverage policy present in August 2021. A coverage restriction includes at least one of the following coverage requirements that go beyond a drug's label indication: clinical requirement, step therapy protocols, prescriber requirements, and/or other requirements.

3. Study results

We identified 198 Commercial and 167 Medicaid policies for the included 11 CGTs (Fig. 1). Overall, Medicaid policies included coverage restrictions more often than did commercial policies (68.4 % vs 53.5 % of policies). Medicaid policies were more restrictive than commercial policies for 8 out of the 11 CGTs. The proportion commercial and Medicaid plans imposing coverage restrictions differed most for axicabtagene ciloleucel (Yescarta) to treat follicular lymphoma, idecabtagene vicleucel (Abecma) to treat multiple myeloma, and lisocabtagene maraleucel (Breyanzi) to treat large B-cell lymphoma (Fig. 1).

How often health plans imposed coverage restrictions varied across CGTs. Restrictions were most common for voretigene neparvovec (Luxturna) to treat retinal dystrophy (imposed in 17/18 and 26/26 commercial and Medicaid policies, respectively) and for onasemnogene abeparvovec (Zolgensma) to treat spinal muscular atrophy (imposed in 18/18 and 27/33 commercial and Medicaid policies, respectively). Conversely, restrictions were least common for talimogene laherparepvec (Imlygic) to treat melanoma (included in 5/13 and 0/4 commercial and Medicaid policies, respectively) and for axicabtagene ciloleucel (Yescarta) to treat follicular lymphoma (included in 4/18 and 9/16 commercial and Medicaid policies, respectively) (Fig. 1).

Clinical criteria for access to the 11 CGTs varied across health plans. A total of 35.6 % of included policies for CAR-T and AAV products imposed restrictions based on patient frailty or function, as measured by the Eastern Cooperative Oncology Group (ECOG) Performance Status, the Karnofsky/Lansky scale, or both (Table 1). Plans that included restrictions based on frailty or function were most likely to exclude patients with ECOG status exceeding 1 or 2, a Karnofsky/Lansky score exceeding 50 or 70 %, or both. These requirements imply that to gain access to the covered treatments, patients must be symptomatic and capable of self-care but be bed-bound less than 50 % of the time, criteria that exclude the patients with the greatest frailty [8]. A total of 16.3 % of policies for CAR-T and AAV products imposed restrictions based on life expectancy; life expectancy cutoffs were consistent across plans that included this restriction. For access to brexucabtagene autoleucel (Tecartus) to treat mantle cell lymphoma, plan requirements for previous lines of therapy varied, with 46.7 % requiring 2 previous lines of therapy and 36.7 % requiring 3 previous lines (Table 1).

Restrictions based on disease severity, genetic factors, and age were common for AAV products; however, applied thresholds varied across plans (Table 2). Restrictions based on a retinal thickness (100 μm) were consistent across the 75 % of plans that included this requirement for access to voretigene neparvovec (Luxturna) to treat genetic retinal dystrophy. However, age requirements varied, with one-quarter of plans requiring patients be age 1–65, 13.6 % requiring patients be older than 3 or 4, and 4.5 % requiring patients be age 3–65. Clinical requirements for access to onasemnogene abeparvovec (Zolgensma) to treat spinal muscular atrophy (SMA) varied considerably in terms of the required number of survival of motor neuron 2 (SMN2) gene copies (1–3 copies), SMA Type (1, 2, or 3), patient age (6 months-2 years), and time since symptom onset (0–6 months) (Table 2).

4. Discussion

US commercial and Medicaid health plans imposed restrictions in 53.5 % and 68.3 % of their coverage policies for the 11 included CGTs, respectively. In comparison, research has found that commercial plans impose coverage restrictions for specialty drugs roughly one-third of the time and for orphan drugs roughly 30 % of time [9,10]. This difference is

Table 1
Clinical Coverage Restrictions Required by Commercial and Medicaid Plans, Chimeric Antigen Receptor T-cell (CAR-T) and Immunotherapy Products, 2021

Therapy (Indication)	Restrictions based on frailty or function (n/N, %)		Restrictions based on life expectancy (n/N, %)		Restrictions based on prior therapy (n/N, %)	
	Commercial	Medicaid	Commercial	Medicaid	Commercial	Medicaid
Idecabtagene vicleucel (multiple myeloma)	ECOG: • ≤1 (4/13, 31 %) • ≤2 (1/13, 8 %)	ECOG: • ≤1 (2/8, 25 %) • ≤2 (1/8, 13 %)	None	None	5 drugs from 3 classes (1/13, 8 %)	None
lisocabtagene maraleucel (large B-cell lymphoma)	ECOG: • ≤1 (2/15, 13 %) • ≤2 (3/15, 20 %)	ECOG: • ≤1 (1/12, 8 %) • ≤2 (2/12, 17 %)	None	None	None	None
Talimogene laherparepvec (melanoma)	None	None	None	None	None	None
Tisagenlecleucel (B-cell acute lymphoblastic leukemia)	Karnofsky/Lansky: • ≥50 % (2/17, 12 %) • ≥70 % (1/17, 6 %) ECOG ≤ 2 (2/17, 12 %) Karnofsky/Lansky ≥50 % OR ECOG ≤ 2 (1/17, 6 %) Karnofsky/Lansky ≥70 % AND ECOG ≤ 2 (1/17, 6 %)	Karnofsky/Lansky ≥50 % (3/16, 19 %) ECOG ≤ 3 (1/16, 6 %)	12 weeks (2/17, 12 %)	12 weeks (1/16, 6 %)	None	None
Tisagenlecleucel (diffuse large B-cell lymphoma)	ECOG: • ≤1 (6/8, 75 %) • ≤2 (1/8, 13 %)	ECOG ≤ 1 (3/17, 18 %) Karnofsky/Lansky ≥50 % (1/17, 6 %)	None	12 weeks (1/17, 6 %)	None	None
Sipuleucel-T (prostate cancer)	ECOG ≤ 1 (11/17, 65 %)	ECOG ≤ 1 (2/5, 40 %)	6 months (8/17, 47 %)	6 months (3/5, 60 %)	None	None
Brexucabtagene autoleucel (mantle cell lymphoma)	ECOG: • ≤1 (3/18, 17 %) • ≤2 (1/18, 6 %)	ECOG ≤ 1 (2/12, 17 %)	None	None	2 prior lines (9/18, 50 %) 3 prior lines (7/18, 39 %)	2 prior lines (5/12, 42 %) 3 prior lines (4/12, 33 %)
Axicabtagene ciloleucel (large B-cell lymphoma)	ECOG: • ≤1 (6/17, 35 %) • ≤2 (1/17, 6 %)	ECOG ≤ 1 (3/16, 19 %)	None	12 weeks (1/16, 6 %)	None	None
Axicabtagene ciloleucel (follicular lymphoma)	ECOG ≤ 1 (4/11, 36 %)	ECOG ≤ 1 (3/16, 19 %)	None	12 weeks (1/16, 6 %)	None	None

Source: SPEC Database.
ECOG: Eastern Cooperative Oncology Group.

Table 2
Coverage Restrictions Required by Commercial and Medicaid Plans, Adeno-Associated Virus (AAV)-Based Gene Replacement Therapy Products, 2021

Therapy (Indication)	Restrictions based on gene requirements (n/N, %)		Restrictions based on disease severity (n/N, %)		Restrictions based on age (n/N, %)	
	Commercial	Medicaid	Commercial	Medicaid	Commercial	Medicaid
Voretigene neparvovec (genetic retinal dystrophy)	None	None	Retinal thickness: • ≥100μm OR ≥3 disc areas without atrophy OR visual field within 30° of fixation (16/18, 89 %) • ≥100μm (1/18, 6 %)	Retinal thickness: • ≥100μm OR ≥3 disc areas without atrophy OR visual field within 30° of fixation (16/26, 62 %)	Age: • 1–65 (7/18, 39 %) • 3–65 (2/18, 11 %) • ≥3 (2/18, 11 %) • ≥4 (1/18, 6 %)	Age: • 1–65 (4/26, 15 %) • ≥3 (1/26, 4 %) • ≥4 (2/26, 8 %)
Onasemnogene abeparvovec (spinal muscular atrophy [SMA])	SMN2 gene copies: • ≤3 (11/18, 61 %) • ≤2 (3/18, 17 %) • 1–2 OR 3 without c.959G>c single base substitution (1/18, 6 %) • 2–3 (1/18, 6 %)	SMN2 gene copies: • ≤3 (8/33, 24 %) • ≤2 (4/33, 12 %) • 1–2 OR 3 without c.959G>c single base substitution (3/33, 9 %) • 2–3 (1/33, 3 %)	SMA Type: • 1 (4/18, 22 %) • 1 or 2 (1/18, 6 %)	SMA Type: • 1 (8/33, 24 %) • 1 or 2 (2/33, 6 %) • 1, 2, or 3 (1/33, 3 %)	Age: • ≤9 months (1/18, 6 %) • ≤6 months (1/18, 6 %)	Age: • ≤9 months (1/33, 3 %) • ≤6 months (1/33, 3 %) • ≤2 years, symptom onset ≤6 months (1/33, 3 %) • ≤1 year, symptom onset ≤6 months (2/33, 6 %)

Source: SPEC Database
SMN2: Survival of Motor Neuron 2.

likely a consequence of the high upfront cost of CGTs; as more CGTs are approved, the total costs of treatment could exceed health plan budgets [11].

We found notable coverage differences both between and among commercial and Medicaid health plan policies. Medicaid plans were more likely than commercial plans to impose coverage restrictions. Reasons for this finding are unclear, but are likely due to budget and patient population differences. Coverage restrictions for certain CGTs were more common than others. For some CGTs, the restrictions are clinically appropriate. For example, almost all coverage policies for voretigiene-neparovec (Luxturna) included specific definitions of viable retinal cells that are consistent with the inclusion criteria for the clinical trial central to the drug's approval [12]. Age requirements for voretigene-neparovec (Luxturna) often lacked clear justification; while the clinical trial included patients age 3 years and older, 10 commercial and 6 Medicaid plans imposed further restrictions based on age (with varying requirements). In contrast, the FDA label does not recommend use of the therapy in patients under 12 months of age [13].

Restrictions based on patient frailty or function varied considerably across coverage policies for CAR-T and immunotherapy products. Some plans appear to be using patient frailty or function (based on ECOG and/or Karnofsky/Lansky scores) as a proxy measure for selecting which patients would be most likely to benefit from CGTs. Restrictions based on gene status, age, and disease severity were common for AAV-based gene products, suggesting a lack of clinical consensus on optimal patient populations for these therapies. This variation means that a patient's access to some CGTs depends on their commercial insurer, or on where they live.

Our analysis is limited by the fact that not all plans issued a coverage policy for each therapy. The commercial health plan sample represents 188 million lives, or approximately 70 % of the US commercial market and the availability of Medicaid coverage policies limits the generalizability of our findings [14]. Because policies for certain CGTs, such as sipuleucel-T (Provenge) for prostate cancer, are not as relevant to the Medicaid population, fewer coverage policies are available. Nor did this study account for other factors that can affect patient access, such as cost sharing.

Future research should examine if and how plans adjust their coverage in response to emerging evidence. Real-world data are needed to establish which patients will most likely benefit from CGTs and to characterize long-term outcomes, as evidence for CGT products at the time of their approval is often less robust than corresponding data for other therapies. As the evidence for individual CGTs matures, we expect variation in coverage criteria to decrease. Furthermore, as more CGTs emerge, further straining health plan budgets, it is crucial to assess how coverage evolves. Finally, future research should examine whether innovative payment mechanisms such as outcomes-based contracts or advanced payment models promote access as fiscal pressure mounts on payers to cover these increasingly expensive therapies.

5. Conclusions

Patient access to CGTs varies across commercial plans, across Medicaid plans, and between commercial and Medicaid plans. Our findings suggest that Medicaid plans impose more restrictions on access than do commercial plans. This pattern most likely reflects differences in health plan budgets and patient populations. Differences in the type of restrictions imposed suggest a lack of consensus regarding the ideal patient populations for these therapies.

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CRediT authorship contribution statement

Molly T. Beinfeld: Writing – review & editing, Writing – original draft, Supervision, Project administration, Investigation. **Julia A. Rucker:** Writing – review & editing, Formal analysis, Data curation. **Nola B. Jenkins:** Investigation, Data curation, Conceptualization. **Lucas A. de Breed:** . **James D. Chambers:** Writing – review & editing, Supervision, Project administration, Methodology, Investigation, Data curation, Conceptualization.

Declaration of Competing Interest

The authors declare that they have no known competing financial

interests or personal relationships that could have appeared to influence the work reported in this paper.

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