Gene Therapy Legislation Codifies Best Price(s)

Institute for Gene Therapy Hosts Capitol Hill Briefing, Works with CMMI on CGT Pilot

On February 21 the Institute for Gene Therapies (IGT) hosted a Capitol Hill briefing on the potential of gene therapies in treating rare and ultra-rare diseases as well as their policy asks for the new Congress. Panelists included IGT Chair Erik Paulsen (former House member, R-MN) as moderator, Dr. Sudha Sharma from National Genome Center at Howard, Nate Plasman, a patient advocate for Duchenne muscular dystrophy, and John Feore, the IGT Policy Director.

- **Cell & gene therapies have garnered attention in Washington this year for not only curative traits but also concern over pricing/reimbursement by the government**. Gene therapies are curative treatments that target the genetic causes of a disease by introducing genetic material through a viral vector, while cell therapies involve the transfer of live, intact cells to help lessen or cure a disease.

- **The Institute for Gene Therapies (IGT) is a stakeholder organization that advocates for a modern regulatory and reimbursement framework for gene therapies.** Members of the IGT advisory council include manufacturers (SRPT, PTCT), patient advocacy groups (Cure SMA, American Autoimmune Related Diseases Association), and various research organizations (National Genome Center). IGT is pushing for legislators and payers to consider the lifetime value and curative nature of gene therapies in determining reimbursement to justify the costs of treatments. Gene therapies cost payers millions for a single treatment. Zolgensma (NVS) is priced at $2.1 M. Hemegenix (CSL Behring), launching this year, is priced at $3.5 M per treatment. Therapies have found willing payers in the commercial space, but Medicaid reimbursement is harder to reach.

- **IGT has two (2) major policy requests for gene therapies.**

    - **increased FDA cell and gene therapy review funding.** In the 2022 FDA prescription drug user fees, Center for Biologics (CBER) received a significant boost in funding ($348.7 M over 5 years) to address the complexity and increased demand for review of cell & gene therapies. Despite the increase, the agency remains understaffed and under-resourced. There are >800 gene therapy clinical trials in the U.S. alone, and CBER head, Peter Marks, acknowledges that there are more than 1,300 active investigational new drug (IND) applications for gene therapies, and over 1,200 active IND applications for cell therapies. The retirement of FDA's Director of the Office of Therapeutic Products, Wilson Bryan, may also burden the agency with a leadership vacuum as the agency looks for his replacement. IGT is advocating for increased FDA funding in future user fees and finding ways to increase expertise at the FDA to accelerate approval timelines.
    - **The *Medicaid VBPs for Patients (MVP) Act* is expected to be reintroduced this year (another IGT priority).** The MVP Act codifies 2022 guidance that allows state Medicaid programs to voluntarily enter value-based purchasing (VBP) arrangements with drug manufacturers and allows manufacturers to use varying best price points for Medicaid. It was introduced in the House by Rep Kurt Schrader (D-OR). Cosponsors include Reps. Brett Guthrie (R-KY), Markwayne Mullin (R-OK), and John Joyce (R-PA). The bill has no CBO cost estimate and no Senate equivalent yet but we anticipate a bipartisan and bicameral bill in 2023..

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- **IGT is meeting with CMS next month to discuss the implementation of the HHS cell & gene payment model**. Last week, HHS released the drug pricing models selected for CMMI testing. See below for details.

- **CMS's Center for Innovation (CMMI) unveiled three new drug coverage models, one that could be beneficial to cell and gene therapies.**

  - **(*Positive*) A Medicaid model that establishes an outcomes-based agreement between CMS, CGT manufacturers, and state agencies (2026).** It would test outcomes-based agreements (OBAs) to help increase Medicaid access to high-cost specialty drugs. CMS would take the lead in coordinating multi-state OBAs with manufacturers and take responsibility for implementation. CMS aims to start model development this year, aims to announce in 2024-2025, and testing will start in 2026. While OBAs are not expected to work for all gene therapies, IGT is working to ensure that it remains a reimbursement option.

  - **Companies impacted.** This model has the potential to impact sickle cell anemia (BLUE, NOVN, CRSP, VRTX, SGMO, others) and cancer (BMY, NVS, JNJ, GILD, GSK, IOVA, others) The report states that CMMI will focus on treatments like sickle cell and cancer. We expect treatments for hemophilia to also be a target with several gene therapies (BMRN, CSL Behring, SNY, others) approved/expected. There are 3 potential ways that CMMI could address cell and gene therapies, though we note this is a voluntary program. CMMI wants to explore CGT access in Medicare FFS as well (in the future). (1) Outcomes-Based Payments, with a portion of payment up front, and the remainder based on clinical milestones (2) Outcomes-Based Rebates, with payment up front and a rebate if a specific clinical outcome is not achieved (currently used by BLUE with commercial payers) and (3) Outcomes-Based Annuities, with fixed price payments spread over time if beneficiaries receiving treatment continue to achieve specific clinical outcomes.

- **Currently, there are 5 FDA approved gene therapies**: Hemegenix (CSL Behring) for Hemophilia B, Luxturna (NVS) for vision loss, Skysona (BLUE) to treat cerebral adrenoleukodystrophy, Zynteglo (BLUE) to treat beta-thalassemia, and Zolgensma (NVS) for spinal muscular atrophy. Anticipated 2023 FDA approvals include a treatment for hemophilia A (BMRN), another treatment for hemophilia B (uniQure/CSL Behring), and treatments for sickle cell disease (CRSP & VRTX, BLUE).

- **OUR TAKE/ NEXT UP: The Capitol Hill Cell & Gene Therapy briefing was the first of three that will be hosted by IGT.** Future meetings will likely include discussions on reimbursement options. CMMI is conducting stakeholder meetings on cell & gene therapies to help shape their Medicaid model. We wait to see what the model will look like in 2024/2025. By then, the number of FDA approved treatments is also expected to significantly increase. Cell and gene therapies still face significant hurdles in development and struggle to address safety and long-term efficacy. (1) To quality for gene therapies, genetic testing is often required, presenting an initial barrier. Additionally, manufacturers are struggling to provide long-term durability data due to the small number of patients in their clinical trials and difficulty in maintaining long-term data collection methods. (2) Clinical trials have also struggled to advance due to serious safety concerns from treatments. Most recently, Graphite Bio ended development of its sickle cell gene therapy due to serious adverse events in the first patient dosed. (3) There are also human factors that impact the success of treatments which complicate gene therapies. e.g., Luxturna (NVS) has CMS coverage through a local coverage determination (LCD), but many older adult patients do not qualify for treatment due to the possible lack of viable retinal cells.

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BACKGROUND

On Feb 14, HHS released an Executive Order mandated report on drug pricing models selected by the CMMI leader (Liz Fowler, PhD). The models -- Medicare $2 Drug List, Cell and Gene Therapy Access Model, Accelerating Clinical Evidence Model – are intended to complement the *Inflation Reduction Act* (IRA) drug pricing provisions with each model addressing a different cost issue (Here).

- **The pilots seek to improve Part D price transparency, high cell & gene therapy prices, and improving Accelerated Approval clinical trial completion**.
    - **NOT IMPACTFUL Medicare $2 Generic Drug List (no start date provided, possibly mandatory for PDPs)** – *This reminds us of the Amazon RxPass ($5 per mo.*) Medicare Part D model that allows plan sponsors to offer 150 high-value generic drugs with a maximum co-pay of $2 per month per drug. Included drugs will target chronic conditions, like hyperlipidemia and hypertension, and would not be subject to step therapy, prior authorization, quantity limits, or pharmacy network restrictions.
    - **IMPACTFUL Cell and Gene Therapy Access Model (2026 start, voluntary)** – *Medicaid model that establishes an outcomes-based agreement between CMS, manufacturers and state agencies*. It would test a new approach for administering outcomes-based agreements (OBAs) to help increase Medicaid access to high-cost specialty drugs. CMS would take the lead in coordinating multi-state OBAs with manufacturers and take responsibility for implementation. CMS aims to start model development this year and aims to announce in 2024-2025. The model would be tested in 2026.
    - **POTENTIALLY IMPACTFUL Accelerated Approval Model (Likely 2025/26, CMS rulemaking necessary, consultation with FDA)** – Part B model that adjusts Medicare pay for Accelerated Approval approved (AAP) drugs to give co's an incentive to complete confirmatory clinical trials. CMS states any changes will attempt to avoid penalizing physicians or beneficiaries (i.e., not likely to impact ASP+6%). Implementation will be explored with the FDA in 2023 with no launch date described.
- **IMPACTFUL Recall we noted that cell & gene therapy payment models may be included here in our HHS drug report preview (Jan 18, 2023).** This model has the potential to hurt sickle cell anemia (BLUE, NOVN, CRSP, VRTX, SGMO, others) and cancer (BMY, NVS, JNJ, GILD, GSK, IOVA, others) The report states that CMMI will focus on treatments like sickle cell and cancer. We expect treatments for hemophilia to also be a target with several gene therapies (BMRN, CSL Behring, SNY, others) approved/expected. There are 3 potential ways that CMMI could address cell and gene therapies, though we note this is a voluntary program. CMMI wants to explore CGT access in Medicare FFS as well (in the future).
    - Outcomes-Based Payments, with a portion of payment up front, and the remainder based on clinical milestones
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- **POTENTIALLY IMPACTFUL Accelerated approval payment under Part B is addressed (negative for breakout or novel therapies).** Recall in 2021, MACPAC explored raising Medicaid

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rebates for drugs with accelerated approval and reimbursement in Part B was explored in the recent MedPAC meeting. MACPAC options: 1. increased minimum rebate amount on accelerated approval drugs with rebates reverting to standard amount on full approval and 2. increased inflationary rebate on accelerated approval drugs if the manufacturer has not yet completed the confirmatory trial within a certain number of years with rebates reverting back on full approval. MedPAC similarly explored ways to cap reimbursement with no consensus and we may see CMMI choose rebating to limit the impact on providers.

- **NOT IMPACTFUL Part D Drug List model builds off of the Part D Senior Savings (PDSS) model.** PDSS operates from 2021 to 2023 and allows plans to cap copayments for insulin at $35 (or less). Recall that this model was the basis for IRA's insulin co-pay cap for Medicare beneficiaries. Capping co-pay is a low hanging fruit for Medicare and appears to be easier to implement due to simplicity. It is also reminiscent of the generic drug discount program launched by Amazon on January 24th. The subscription service, called RxPass, is $5 per month for Prime customers to fill as many prescriptions as needed from a list of about 50 generic medications, including delivery to their doorstep.

- **BACKGROUND: Policies are intended to complement IRA drug policies (inflationary rebates, Rx negotiation, Part D restructuring),** CMMI solicited input from over 40 external stakeholders (trade associations representing manufacturers; payers and pharmacy benefit managers (PBMs); hospital systems; provider groups) to develop their recommendations and their feedback is incorporated. Cell & gene therapies struggled with coverage and the models may serve as a route to gathering data and future coverage. Part D model focuses on generics, relieving some of the pressure for brand manufacturers and its low impact for plans which already encourage the use of generics.
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- **NEXT UP: As we predicted, we don't expect any CMMI drug pricing demo to start before 2025/26.** The CMS Innovation Center is moving cautiously in design and implementation and we expect CMMI to garner additional stakeholder feedback as they work out key details. We expect regulations on the Accelerated Approval reform model later this year. CMMI was also directed to explore potential models in other topics of interest include accelerating biosimilar adoption, improving Medicare beneficiary data access on drug prices, and increasing cell & gene therapy access in Medicare fee-for-service. We may see additional details on these topics as CMMI fleshes out details.

Background

- **Recall that CMMI was directed to explore drug pricing models per Biden's prescription drug Executive Order (EO) in October 2022 here**. HHS reported to the White House on which models

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complement the IRA in lowering drug costs for patients, as well as CMMI's plan and timeline to test such models.

- **We said on Jan 18 in our preview that we think that potential reforms are more likely to hit on Part B versus D, and Medicaid is likely off the table**. We could see some broader concepts as well as specific ideas with a timeline for stakeholder input and reform. Our take:
  - Part D is addressed by *Inflation Reduction Act*, therefore less likely a place to look for reform via HHS report
  - Part B is known to be in dire need of reform but tough to enact given that physicians/providers cry poor when ASP + 6% is addressed/modified
  - Reimportation is unlikely to come back
  - CMMI based value based care models / alternative payment models (APMs) are likely
  - Cell & gene therapy price & payment models may be floated
  - We do not view IP reforms or March-In Rights as likely for inclusion (though we note HHS Secretary Becerra is a supporter)

- **MedPAC, a non-partisan commission of experts that provides pay & policy recommendations, met to discuss Part B reform last week & provided signs of where CMMI may go**. Link to slides here. Their policy approaches address (1) high prices for new drugs with limited clinical evidence, (2) lack of price competition for drugs with similar health effects, and (3) financial incentives associated with the percentage add-on payment rate. CMMI typically takes guidance from MedPAC, as well as other stakeholders & think tanks.

- **Part B reform is likely to be a CMS Pilot target.** This is mainly due to the dire need for reform, and lack of impact via *Inflation Reduction Act* (until 2028). Part B covers outpatient drugs administrated by providers or at a hospital outpatient, including most injectable and infused drugs. The cost of Part B has risen year over year (+9% on average) with price being the largest driver of Part B drug spending growth.

- **Top Part B therapies, by spend**. CMMI may target Part B reform as those specialty medications and biologics will not be subject to negotiation until 2028, while Part D restructuring starts in 2025 and Medicare Part D negotiation in 2026.

  - The top 10 Part B drugs by Medicare spend (2020) are Keytruda (oncology – MRK), Eylea (macular degeneration – Regeneron), Prolia (osteoporosis – AMGN), Opdivo (oncology – BMY), Rituxan (autoimmune - Roche), Lucentis (macular degeneration – Roche), Orencia (autoimmune – BMY), Neulasta (oncology – AMGN), Darzalex (oncology - JNJ), Avastin (oncology – Roche). *Source. CMS/Office of Enterprise Data & Analytics (OEDA), Medicare Part B Drugs, 2022.*

- **CMMI will be cautious for sure: a 2016 Part B demo fell flat**. Recall that in 2016, CMMI proposed a Part B pilot that would have eliminated ASP + 6%, replaced it with ASP + 2.5% + a flat fee, and introduced value-based purchasing tools (reference-based pricing, indications-based pricing). The model drew significant criticism from physicians, lawmakers, and patient groups due to the negative impact on drug access and it was nixed before implementation. Other CMMI Part B demonstrations (most favored nation, international pricing index) have similarly been withdrawn before the models ever started.

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- **MedPAC's options reflect what CMMI *may* attempt to mimic in a pilot as they address long-standing Part B pricing issues**. While recommendations are not baked, CMMI looks to MedPAC for guidance on their models. The policy options below serve as indicators on key pricing issues that CMS may focus on and what solutions will be considered in a drug pricing pilot. Policy options A (single ASP based rate) & B (reducing add-on pay) are strongly supported by Commissioners.

  - **Policy A: Establish a single ASP-based payment rate for groups of drugs and biologics with similar health effects.** Each product would remain in its own billing code and CMS would base payment on the volume-weighted ASPs of all products in reference group. Drug reference groups would have to be defined by CMS (likely by clinical indications and drug classification and ease of implementation). Recall in 2017, the Commission recommended a type of reference pricing for biosimilars and originator biologics.

  - **Policy B: Reduce the add-on payment for drugs and biologics paid ASP and eliminate the add-on payment for drugs and biologics paid WAC**. This policy maintains current add-on for lower-priced drugs, converts part of percent add-on to flat fee for higher-priced drugs, and caps add-on for most expensive drugs. ASP Add-on = Lesser of 6%, 3%+ $24, $220 per drug per day.

- **Policy C: Reform pay for accelerated approval (AA) drugs**. See below.

  - **MedPAC Commissioners are refining a policy around accelerated approval (AA) pathway drugs (think Aduhelm).** Policy C gives the Secretary the authority to cap Medicare payment of drugs and biologics that receive accelerated approval until the product has converted to full approval. The AA pathway is under scrutiny and lawmakers have called for increased guardrails due to reports of unfinished confirmatory trials. The Commission seeks to ensure that confirmatory trials are completed in a timely way by linking full approval with a pricing incentive. However, there is uncertainty on how to apply the cap and when the cap would begin. The implementation complexity was further highlighted by disagreements on how to address AA indications of previously approved drugs. MedPAC does not want pricing incentives to discourage manufacturers from pursuing new indications.

  - **Commissioners are concerned about the policy impact on physicians and oncologists in particular.** For option C, implementation could add an administrative burden on providers if AA drugs must be coded using a modifier. This was not considered a reliable solution as it relies on incentivizing providers and the low provider uptake on drug wastage modifier was noted as an example. For option B, oncology practices benefit financially from the current add-on payments. Lowering the ASP add-on and eliminating the WAC add-on, is expected to drive up consolidation of private oncology practices to hospitals.

- **Separately, Commissioners discussed unintended consequences for Part D restructuring, slated for 2025: Part D prices could actually *increase*.** Medicare spending in protected specialty classes is predicted to increase. Note that Part D plans are required to cover all drugs in six so-called "protected" classes: immunosuppressants, antidepressants, antipsychotics, anticonvulsants, antiretrovirals, and antineoplastic. The spending in these classes is expected to grow as plans have few tools to manage costs under the new Part D structure (while navigating increased plan liability). Costs are also expected to grow due to beneficiary behavior changes from the $2K OOP cap.