Navigating reimbursement and access challenges for novel cell and gene therapies

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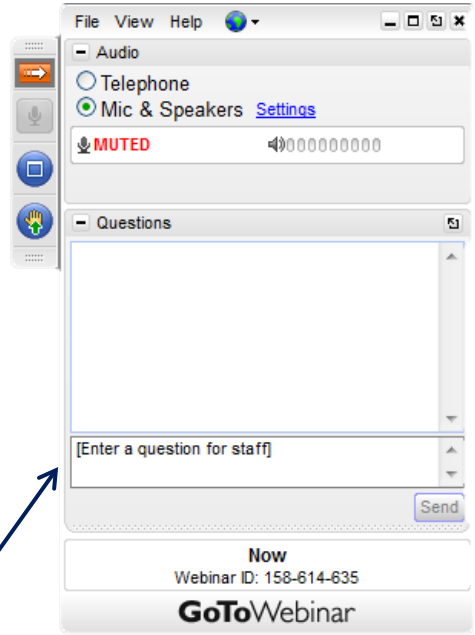

Type your question in the “Questions” area, then click “Send”

Panelists

Moderator

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Webinar overview

In this session, you will learn:

- Cell and gene therapy (CGT) pipeline trends
- CGT reimbursement and patient access challenges including an inpatient case study
- Potential strategies that may help mitigate these challenges

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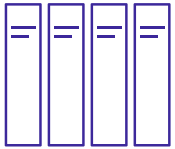
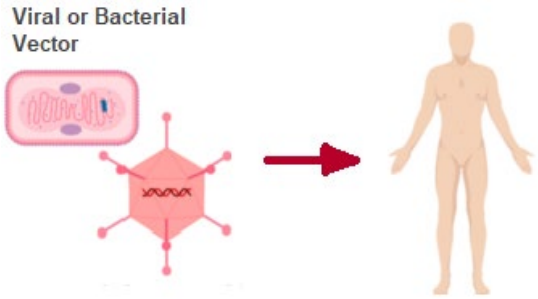
CGT pipeline

Disclaimers



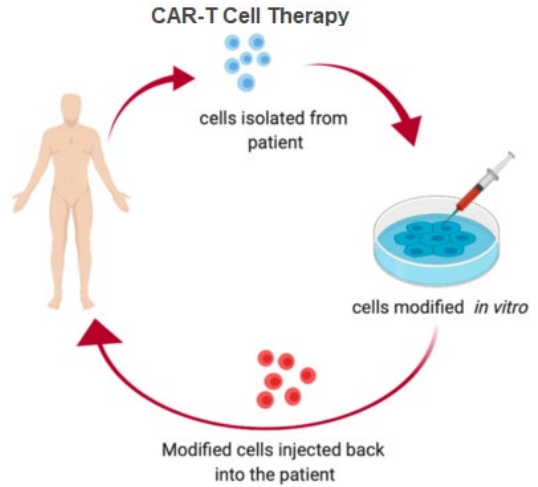
- Non-biased overview of pipeline trends
  - Speakers have nothing to disclose
  - May discuss off-label uses of marketed therapies
  - Not intended to speculate Food and Drug Administration (FDA) actions
  - Not an all-inclusive review of the pipeline

CGTs: Brief overview



Gene therapy

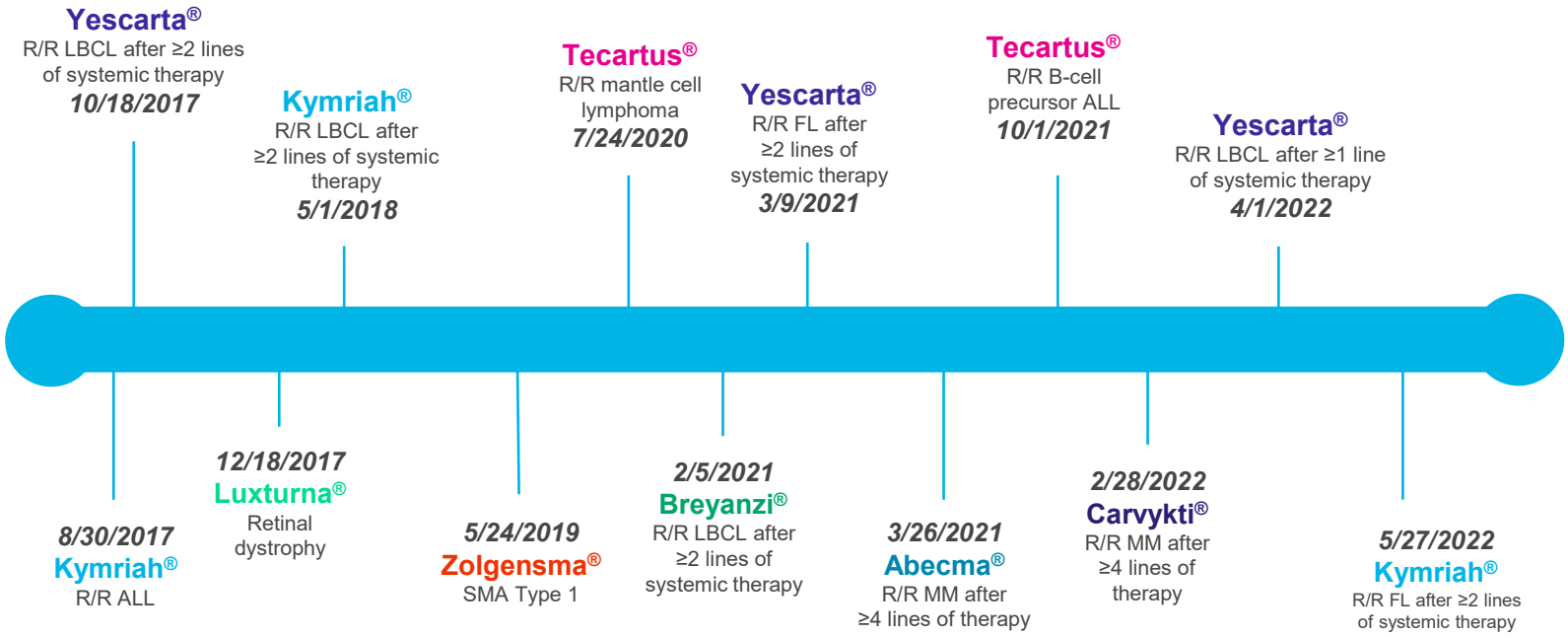
- Replaces, inactivates, or introduces genes into cells via a vector



Cell therapy

- Cells are cultivated or modified outside the body before being injected into the patient
- Cells may originate from the patient (autologous cells) or a donor (allogeneic cells)

CAR-T and gene therapies: Timeline of FDA approvals



Key: ALL – acute lymphoblastic leukemia; FDA – Food and Drug Administration; FL – follicular lymphoma; LBCL – large B-cell lymphoma; R/R – relapsed or refractory; SMA – spinal muscular atrophy.

FDA-approved CAR-T and gene therapies: Cost

Drug class	Therapy name	Indications	Cost of therapy
Gene therapy	Luxturna® (voretigene neparvovec-rzyl)	Biallelic RPE65 mutation-associated retinal dystrophy	$850,000
	Zolgensma® (onasemnogene abeparvovec-xioi)	Spinal muscular atrophy type 1	$2,125,000
CAR-T cell therapy	Abecma™ (idecabtagene vicleucel)	R/R multiple myeloma	$419,500
	Breyanzi® (lisocabtagene maraleucel)	R/R large B-cell lymphoma	$410,300
	Carvykti™ (ciltacabtagene autoleucel)	R/R multiple myeloma	$465,000
	Kymriah® (tisagenlecleucel)	- R/R large B-cell lymphoma - R/R B-cell acute lymphoblastic leukemia - R/R follicular lymphoma	$373,000 or $475,000
	Tecartus® (brexucabtagene autoleucel)	- R/R mantle cell lymphoma - R/R B-cell precursor acute lymphoblastic leukemia	$399,000
	Yescarta® (axicabtagene ciloleucel)	- R/R large B-cell lymphoma - R/R follicular lymphoma	$399,000

Key: FDA – Food and Drug Administration; R/R – relapsed or refractory.

Trends in clinical research

Position 2021 (2020)	Therapy	Number of R&D products in 2020	Number of R&D products in 2021	% Change 2020 to 2021
1 (1)	Anticancer, immunological	3,434	3,712	+8%
2 (2)	Anticancer, other	2,510	2,680	+7%
3 (3)	Gene therapy	1,273	1,589	+25%
4 (4)	Monoclonal antibody, other	1,009	1,136	+13%
5 (28)	Antiviral, other	380	858	+126%
6 (6)	Prophylactic vaccine, anti-infective	698	843	+21%
7 (5)	Ophthalmological, other	756	781	+3%
8 (7)	Neurological	666	781	+17%
9 (10)	Anti-inflammatory	529	639	+21%
10 (14)	Cellular therapy, CAR-T	491	612	+25%

Key: R&D – research and development.

Investigational cell and gene therapies

Therapeutic area	Therapy name	Indication	Status/FDA decision
Hematology	Betibeglogene autotemcel	Transfusion-dependent β-thalassemia	8/19/22
	Lovotibeglogene autotemcel	Sickle cell disease	2023
	CTX001	Beta thalassemia and sickle cell disease	2023
	Valoctocogene roxaparvovec	Hemophilia A	2022/2023
	Etranacogene dezaparvovec	Hemophilia B	2022
	Fidanacogene elaparvovec	Hemophilia B	Phase 3
Other rare diseases	Elivaldogene autotemcel	Cerebral adrenoleukodystrophy	9/16/22
	Lenadogene nolparvovec	Leber hereditary optic neuropathy	2022/2023
	Beremagene geperpavec	Dystrophic epidermolysis bullosa	2023
	EB-101	Recessive dystrophic epidermolysis bullosa	2023
	Dabocemagene autoficel	Recessive dystrophic epidermolysis bullosa	Phase 3

Key: FDA – Food and Drug Administration.

Investigational cell and gene therapies (cont.)

Therapeutic area	Therapy name	Indication	Status/FDA decision
Other rare diseases	Eladocagene exuparvovec	Aromatic L-amino acid decarboxylase deficiency	2023
	OTL-200	Metachromatic leukodystrophy	2023
	Olenasufligene relduparvovec	Mucopolysaccahridosis III type A	2023

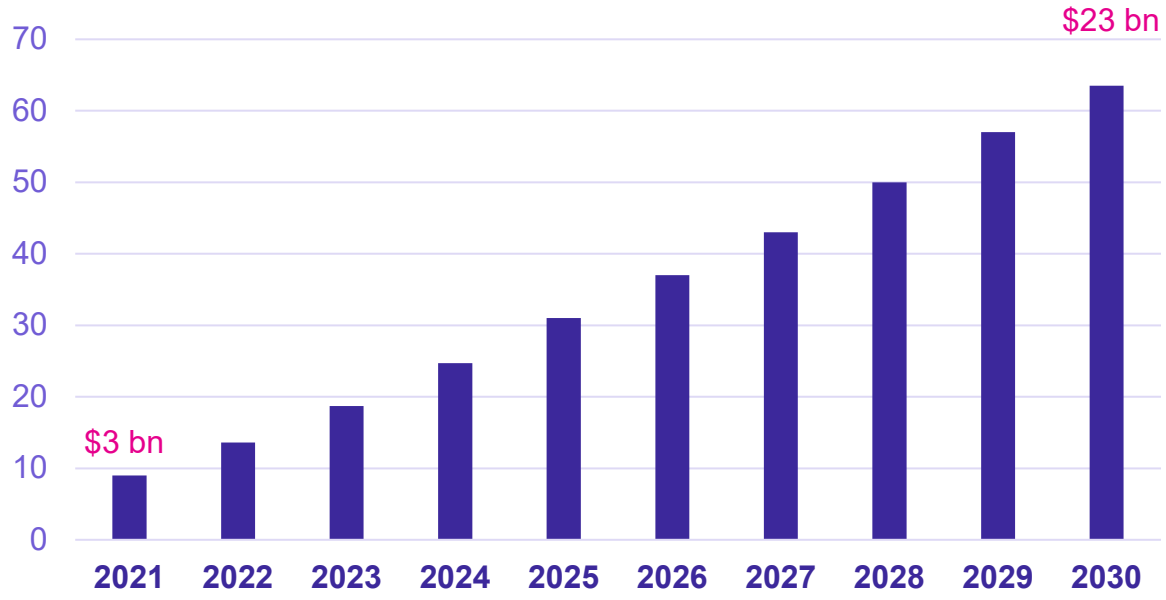
Drug class	Therapy name	Indications	Status/FDA decision
CAR-T Cell Therapies	Breyanzi® (lisocabtagene maraleucel)	Large B-cell lymphoma (2nd line)	06/24/22
	Teclistamab	Relapsed and refractory multiple myeloma	2022
	Tabelecleucel (tab-cel)	EBV+ post-transplant lymphoproliferative disease	2023

Key: EBV – Epstein-Barr virus; FDA – Food and Drug Administration.

Drug pipeline monitoring

Growth in CGTs in development

Total approved indications for CGTs



8
Approved therapies

>100
Diseases explored

60+
Approved indications by 2030

Key: CGT – cell and gene therapy.
Source: Young CM, et al. *Drug Discov Today*. 2022 Jan;27(1):17-30.

Product Snapshots

Product Overview

Manufacturer	Funentech, Inc.
Status	PDUFA date: 05/10/2030
Proposed indication	Miracles in patients with miracle deficiency
Therapeutic class	Miracle receptor agonist (MRA)
Mechanism of action	Pharmacodynamic studies have shown that miraculate selectively binds and agonizes the miracle receptor in the central nervous system (CNS), which activates downstream miracle signaling in patients with miracle deficiency[1]
Formulation	Oral tablet
Dose and administration	• Dosing: 300 mg twice daily • Route of administration: oral • Setting of administration: outpatient

Curated by clinical pharmacists, **Product Snapshots** are a product information source to help jumpstart the product review, with a focus on pre-approval products

- Manufacturer
- PDUFA date
- Approved indication(s)
- Therapeutic class
- Mechanism of action
- Dose and administration
- Epidemiology of disease
- Distinguishing factors of product
- Relevant disease background and treatment guidelines
- Key comparators
- Clinical trials overview
- P&T considerations

Key: PDUFA – Prescription Drug User Fee Act; P&T – pharmacy and therapeutics.

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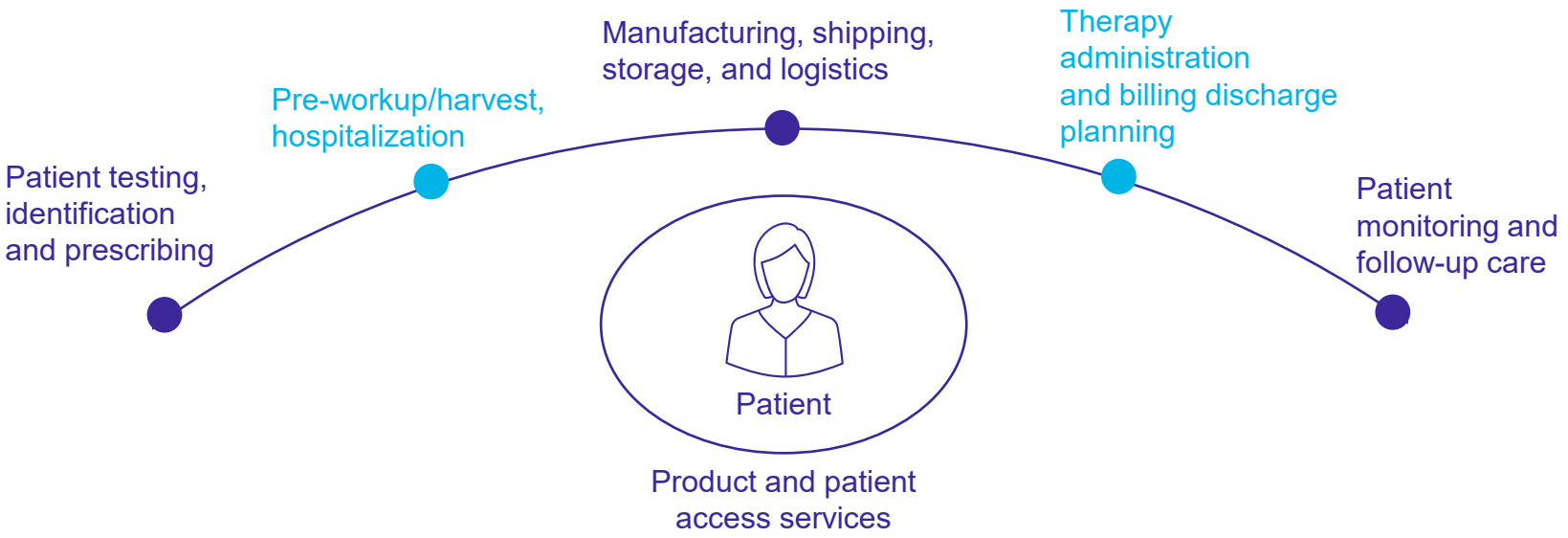
Reimbursement and patient access challenges in CGTs

Overview of the patient access journey in CGT



Administrative tasks at every step

- Insurance coverage and eligibility
- Benefit verifications
- Referral processes
- Payer contracts

Payer concerns throughout this journey

Identifying "the right patient"

In terms of what the general clinician community is aware of? They have no idea… – Payer Advisor

Managing patient populations

If we have a large population, we can do a contract on them. Otherwise for plans, if you have a handful of patients for a value-based contract, it doesn't make sense to do something like that for 10 patients, but it would for 1,000 patients. – Payer Advisor

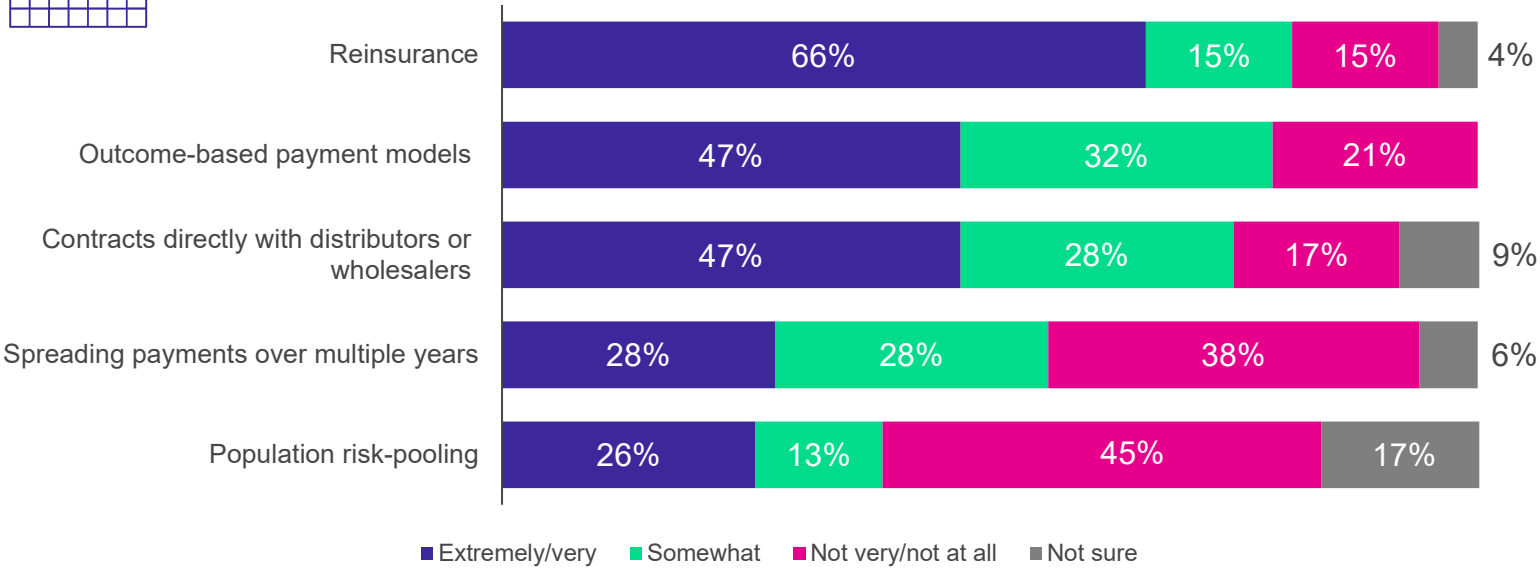
Obtaining the necessary data

We need to address practice gaps, get treatments to patients more quickly, and develop evidence that will be beneficial in the long run. But, to get evidence, we need to factor in practice gaps. We are looking for practice-based evidence, showing economic value for treatment strategy…We have started to set up models by populating with real-world evidence, we can show what the situation is (ie, if we didn't have practice gaps, and all patients got treatment in a timely fashion, then the value would be this). Coverage shouldn't be a barrier. – Payer Advisor

Source: Xcenda Ad Board. May 2019.

Payers are open to other methodologies over the next 12 months, but these may still be problematic for CGTs

Likely use of these CGT payment approaches next 12 months



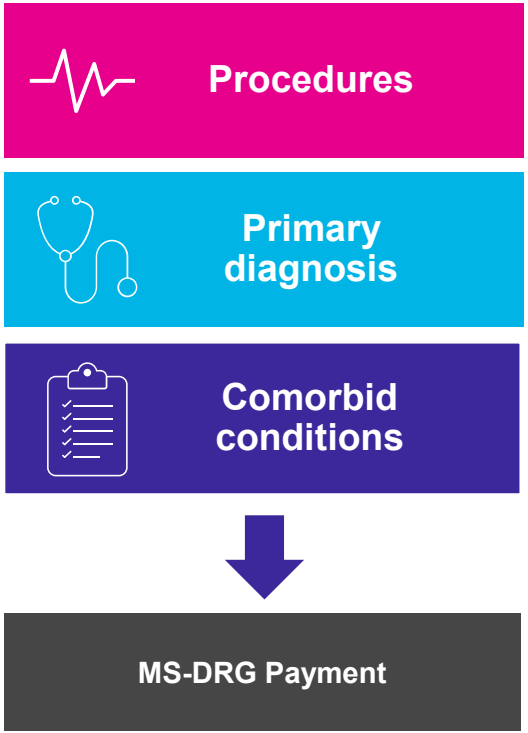
Key: CGT – cell and gene therapy.
Source: Xcenda Survey. October 2020.
Note: Totals do not always add to 100% due to rounding.

Medicare Inpatient Prospective Payment System (IPPS) overview

- Medicare uses Medicare Severity Diagnosis Related Groups (MS-DRGs) that are receive a single lump-sum payment per discharge

- Three potential options could alleviate the costs:

Approval of a new technology add-on payment (NTAP) added to the current MS-DRGs payment	Assignment of a new MS-DRG for new CGTs	Outlier payments for patients receiving CGTs could also be made in addition to MS-DRG and NTAP



Key: CGT – cell and gene therapy.

Inpatient payment for CGTs is affected by coding and billing

- Historical coding and Medicare payment for KYMRIAH® and YESCARTA® over several years since launch; all claims eligible for Outlier

	2018	2019 2020	2021	2022
MS-DRG (Payment Amount)	**840-842** Lymphoma and non-acute leukemia ($6,198.32-$17,159.49)	**016** Autologous bone marrow transplant with CC/MCC or T-Cell Immunotherapy (2019: $34,837.32; 2020: $37,906.48)	**018** CAR T-cell Immunotherapy ($222,529.74)	**018** Chimeric Antigen Receptor (CAR) T-cell & other immunotherapies ($229,256.40)
NTAP Status	No NTAP (application withdrawn)	**NTAP maximum 2019 $186,500 2020 $242,450**	NTAP expired	No NTAP
ICD-10-PCS Code HCPCS Code	3E033GC Introduction of other therapeutic substance into peripheral vein, percutaneous approach 3E043GC Introduction of other therapeutic substance into central vein, percutaneous approach **Q2041** Yescarta (effective 04/01/2018)	XW033C3 Introduction of engineered autologous chimeric antigen receptor t-cell immunotherapy into peripheral vein, percutaneous approach, new technology group 3 XW043C3 (Introduction of engineered autologous chimeric antigen receptor t-cell immunotherapy into central vein, percutaneous approach, new technology group 3) **Q2042** Kymriah (effective 01/01/2019)		XW033H7 Introduction of Axicabtagene Ciloleucel Immunotherapy into Peripheral Vein, Percutaneous Approach, New Technology Group 7 XW033J7 Introduction of Tisagenlecleucel Immunotherapy into Peripheral Vein, Percutaneous Approach, New Technology Group 7

Medicare inpatient CAR-T claims (2019–2020)

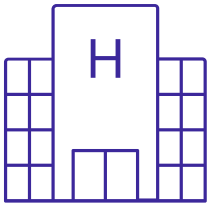
	Claim descriptive stats			Mean charges and payments			
Inclusion criteria*	# of claims	% of claims with NTAP	# of claims with outlier	Total charges	NTAP payment	DRG payment	Outlier payment
MS-DRG and ICD-10-PCS	802	36%	32%	$918,162	$65,052	$118,326	$36,017
ICD-10-PCS	88	3%	38%	$1,377,550	$4,977	$263,926	$55,984
MS-DRG, ICD-10-PCS, and Drug	<11	100%	100%	$2,210,294	$229,829	$213,310	$194,954
ICD-10-PCS and Drug	<11	50%	100%	$2,659,145	$126,202	$470,667	$230,704

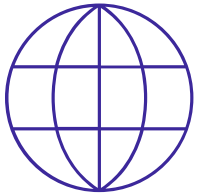
Key: ICD-10-PCS – International Classification of Diseases, 10th Revision, Procedure Coding System; MS-DRG – Medicare Severity Diagnosis Related Group; NTAP – new technology add-on payment.

*Inclusion criteria may also include codes for drug administration.

Note: Inpatient claims were excluded from the analysis if Medicare did not make a base payment. All payments from 2019 were adjusted to 2020 USD.

Case study findings





- Within existing reimbursement methodologies, hospitals may not have received adequate or appropriate reimbursement for CAR-Ts
  - Hospitals may not have been reporting the ICD-10-PCS XW0 codes on the claim form to receive NTAP
  - Hospital charges may not have adequately reflected costs when the cost-to-charge ratio was applied
  - Hospital systems such as the chargemaster may not have been updated with the appropriate data
  - The therapy may not have been documented or communicated appropriately between the clinical staff administering the therapy and the coding and billing staff
  - Aspects of reimbursement (eg, NTAP status, coding, MS-DRG assignment) changed over several years which may have caused confusion to hospitals
- We continue to monitor MS-DRG 018 to see how hospital reimbursement may continue to change

Key: ICD-10-PCS – International Classification of Diseases, 10th Revision, Procedure Coding System; MS-DRG – Medicare Severity Diagnosis Related Group; NTAP – new technology add-on payment.

Considerations

Engage payers

- Payer mix
- Reimbursement and coding assessment
- Evidence generation needs
- Market research
- Resources

Hospital and other providers

- Stakeholder mapping and market research
- Evidence generation needs
- Targeted education and tools

Patients

- Stakeholder mapping and market research
- Evidence generation needs
- Targeted education and tools

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Evidence and landscape review

Insights, preferences, and attitudes

HCDM community

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Key: HCDM – healthcare decision maker.

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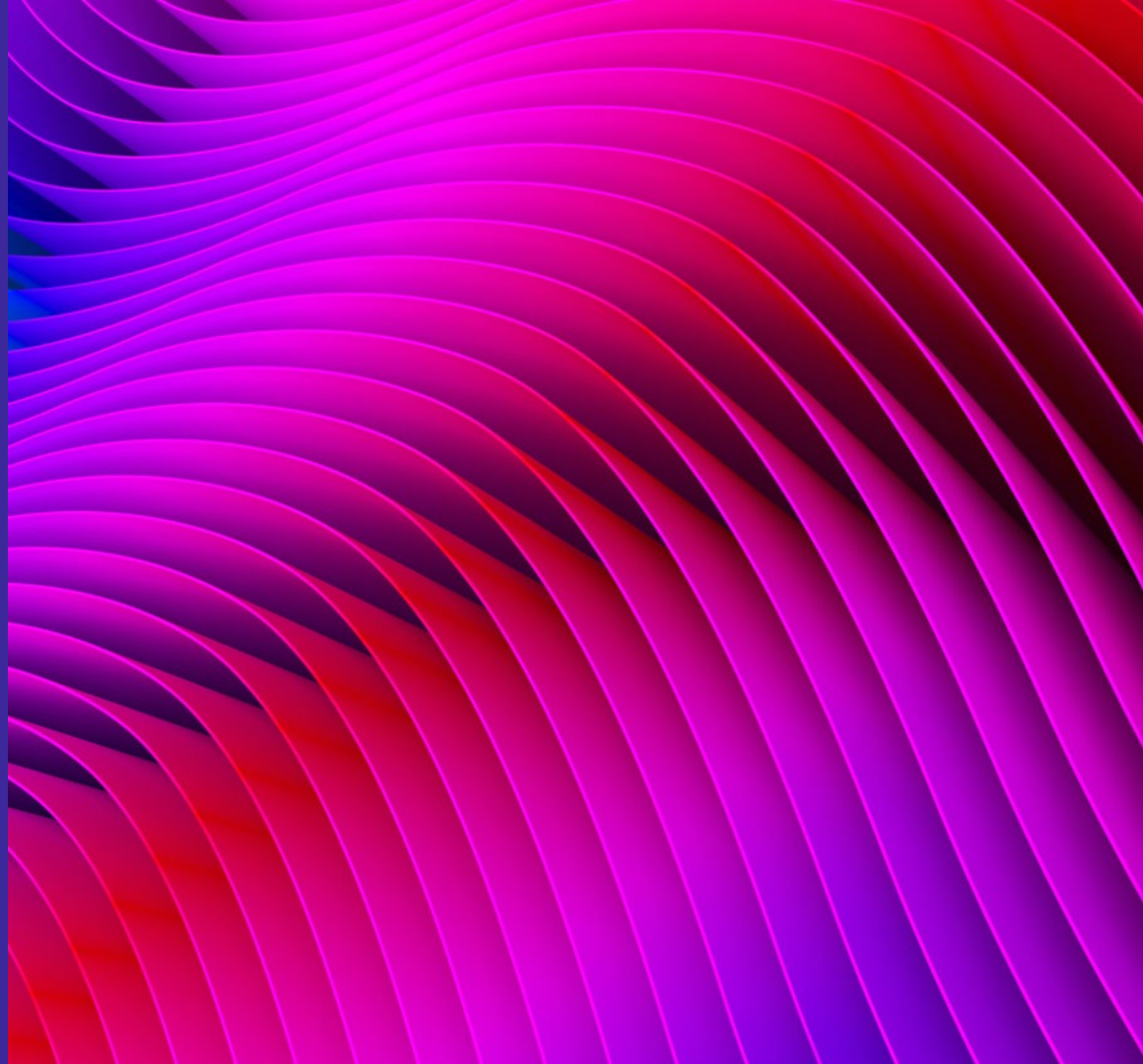

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Questions and discussion

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