Putnam
Inizio Advisory

WHITE PAPER

Navigating IRA Negotiations: Lessons from Round One and Strategies for Future Success.

Authored by

Scott Briggs, Partner – VPA Practice, Ethan Johnson, Principal, Alex Salomon, Consultant, Jasmine Wu, Associate Consultant

May 2025

Content

Introduction

On August 15, 2024, the Centers for Medicare and Medicaid Services (CMS) announced negotiated drug prices, known as Maximum Fair Prices (MFPs) for the first ten drugs negotiated under the Inflation Reduction Act (IRA)[1] **(Figure 1).** Initial headlines reported average MFP discounts of approximately 62% off pre-negotiation list prices, with estimated Medicare savings of $6 billion[1]. However, this figure overestimates the true financial impact. When accounting for pre-existing manufacturer discounts and rebates, a Brookings analysis suggests the average net price reduction was closer to 22%[2].

The IRA mandates CMS to consider a range of clinical and financial factors when determining MFPs[3] **(Figure 2)**. However, the law does not specify how these factors should be weighted, leaving room for interpretation in how CMS applied them in negotiations.

In this report, we build upon Putnam's previous IRA thought leadership Medicare price negotiation: Putnam's round one picks to assess the key factors that shaped MFP outcomes in the first round of IRA negotiations. We identify emerging patterns in CMS' approach, highlighting strategic considerations for manufacturers, and outline steps to strengthen future positioning in Medicare price negotiations.

Fig. 1

DRUGS SELECTED FOR FIRST ROUND OF PRICE NEGOTIATION

Medicare Part D Drugs Negotiated for Price Applicability Year 2026

Brand Name	Manufacturer	Disease Area	FDA Approval Year	Medicare Part D Spend (2022)
Eliquis	BMS	Cardiovascular / Hematologic	2012	$18.3B
Jardiance	Eli Lily / Boehringer-Ingelheim	Cardiovascular/ Metabolic	2014	$8.8B
Xarelto	Janssen	Cardiovascular / Hematologic	2011	$6.3B
Farxiga	AstraZeneca	Cardiovascular / Metabolic	2014	$4.3B
Januvia	Merck	Endocrine	2006	$4.1B
Entresto	Novartis	Cardiovascular	2015	$3.4B
Stelara	Janssen	Immunology / Inflammatory	2009	$3.0B
Enbrel	Amgen	Immunology / Inflammatory	1998	$3.0B
Novolog/Fiasp	Novo Nordisk	Endocrine	2000	$2.6B
Imbruvica	Janssen and Pharmacyclics LLC	Oncology	2013	$2.4B

Source:
"Medicare Drug Price Negotiation Program: Final Guidance" (Oct 2024); Inflation Reduction Act of 2022 (H.R.5376 – 117th Congress); Putnam Analysis 2025

Fig. 2

CMS CONSIDERED SEVERAL FACTORS IN PRICE NEGOTIATIONS

Factors	Explanation
Pre-IRA Market Exclusivity	• Drugs with prolonged exclusivity and historically low commercial discounts **see steeper price cuts**, especially with anticipated future competition
Unmet Need	• Extent to which a drug addresses an **unmet need relative to its therapeutic alternatives, particularly in the Medicare population**
Clinical Data & RWE	• CMS prioritizes **head-to-head clinical trial data to therapeutic alternatives** where applicable • Real-world outcomes, such as **hospitalization, mortality, and cost-effectiveness analysis** are considered • Note: CMS has prohibited use of cost/QALY as a CEA metric, but other methods may be used
Safety Profile	• Safety of a drug compared to its therapeutic alternatives, **particularly in Medicare or high-risk populations**
Non-Clinical Manufacturer Data	• R&D costs **and the extent to which they have been recouped** and cost of goods sold (COGs) • **Prior federal financial support** received in developing the selected drug • Pending or approved **patent applications** • **Market data,** including revenue and sales volume

Source:
"Medicare Drug Price Negotiation Program: Final Guidance" (Oct 2024); Inflation Reduction Act of 2022 (H.R.5376 – 117th Congress); Putnam Analysis 2025

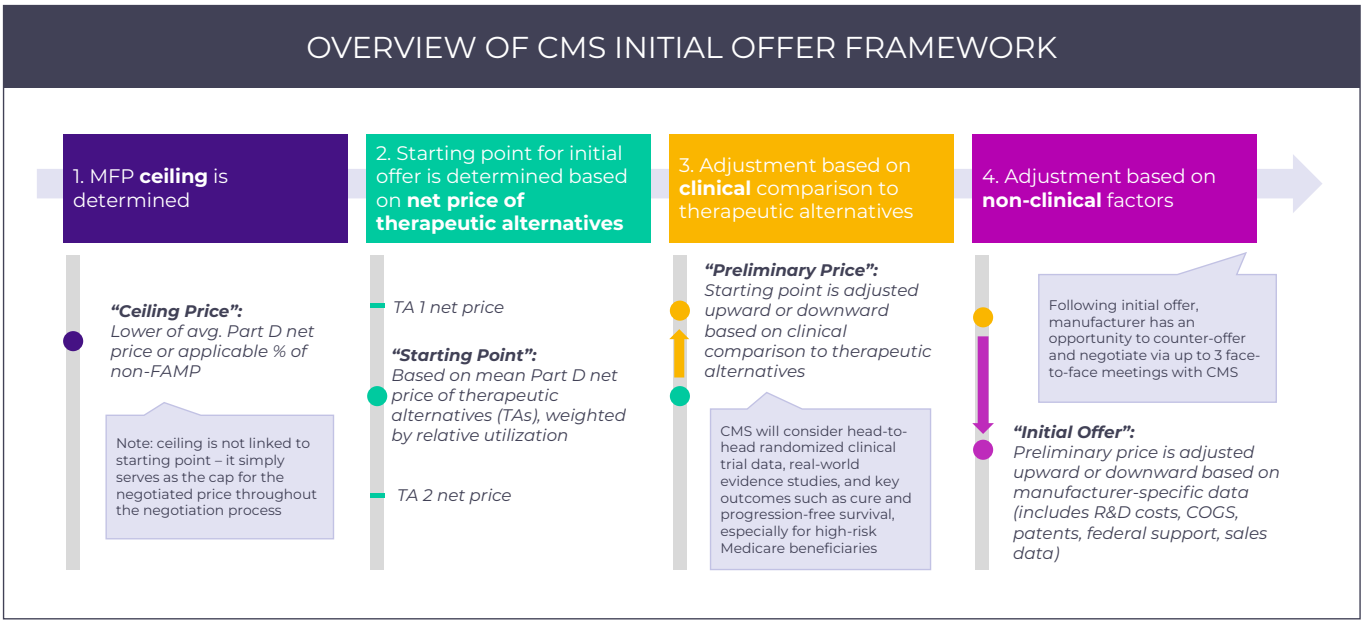
Price Negotiation Overview

The IRA outlines a structured framework for determining MFPs (detailed in **Figure 3**), incorporating clinical comparisons, therapeutic alternatives, and manufacturer-submitted financial information. A key feature of this framework is the ceiling price, which sets the upper bound for negotiations[3].

For Part D drugs, this ceiling is defined by the lower of:

1. The average Part D price, or
2. An applicable percentage of the drug's non-federal average manufacturer price (non-FAMP). This percentage is determined based on the time since FDA approval, as of the MFP applicability date:
   - Short monopoly (9 to <12 years post FDA approval): 75% of non-FAMP
   - Extended monopoly (12 to <16 years post FDA approval): 65% of non-FAMP;
   - (Note: This category did not apply in round one but will be relevant for drugs with price applicability years 2030 and after. For drugs selected in round one with FDA approval dates within this range, the "short monopoly" drug ceiling price applies.)
   - Long monopoly (≥16 years): 40% of non-FAMP

Fig. 3



Abbreviations:
CMS=Centers For Medicare And Medicaid Services; COGS=Cost Of Goods Sold; FAMP=Federal Average Manufacturer Price; MFP=Maximum Fair Price; R&D=Research And Development; TA=Therapeutic Alternative; Source: "Medicare Drug Price Negotiation Program: Final Guidance" (Oct 2024); Inflation Reduction Act of 2022 (H.R.5376 – 117th Congress); Putnam Analysis 2025.

Negotiations proceed to account for three factors:

1. Identification of Therapeutic Alternatives

The starting price for negotiations is determined based on the net price of therapeutic alternatives (TAs), weighted by their relative utilization. The Act defines TAs as "clinically comparable" products, and CMS has flexibility to interpret this across chemical class, therapeutic class, or mechanism of action[4]. Although CMS prefers within-class alternatives whenever possible, it may expand outside of the class if no direct analog exists.

TAs are identified through review of clinical guidelines, payer policies, manufacturer-submitted data, and input from clinicians and patient groups. However, CMS does not publish a detailed rationale for TA selection, limiting transparency into this aspect of negotiation dynamics.

2. Clinical Efficacy Comparison

After identifying TAs, CMS refines the starting price by adjusting for comparative clinical data. This includes[3]:

- Randomized controlled trial (RCT) data with priority given to head-to-head trials between the selected drug and TAs
- Real-world evidence (RWE), especially within the Medicare dominant populations (e.g., adults 65 years of age or older) and groups with high disease burden and unmet need
- Clinical outcomes, including quality of life (QoL) and patient-reported outcomes (PROs)

- Direct and indirect cost offsets, such as reductions in hospitalizations, medical interventions, or other downstream healthcare costs
- Cost effectiveness analyses (e.g., ICER values), though certain methodologies are excluded from consideration under the IRA (i.e., Cost per Life Year Saved may be used, Cost per Quality-Adjusted Life Year Saved may not be used)

While CMS has emphasized that it prioritizes head-to-head RCTs, most round one products lacked direct head-to-head trials. As a result, CMS likely relied on cross-trial comparisons, RWE from retrospective studies, and comparative effectiveness data from meta-analyses.

Given the frequent reliance on indirect comparisons, manufacturers should focus on development of RWE for Medicare-relevant patient populations that can support positive clinical and health economic differentiation from competitors.

3. Non-clinical Factor Adjustment

In addition to clinical evidence, CMS may incorporate manufacturer-specific data, including[3]:

- Research & development (R&D) costs and the extent of cost recoupment
- Costs of goods sold (COGS), particularly for complex biologics or high-cost manufacturing processes
- Prior federal financial support received in developing the selected drug
- Patent protections and exclusivity, including pending or approved patents that may impact future pricing dynamics
- Market data, including historical revenue, sales volume, and prior discounting practices

However, CMS has provided little guidance on how it weighs these inputs. MFP explanations offer minimal transparency into how non-clinical data affected final pricing decisions, leaving uncertainty for manufacturers on how to best prepare these submissions.

Relevant Considerations for MFP Negotiations

Our analysis suggests CMS considered two key questions when determining final MFPs:

- Have market forces brought down net prices?
- How clearly has the product differentiated itself from therapeutic alternatives based on clinical outcomes, safety, and unmet need?

1. Have market forces brought down net prices?

Drugs with prolonged exclusivity or limited pre-negotiation rebates were more likely to face steeper price reductions. These were cases where CMS likely saw an opportunity to enforce price reductions that market dynamics had not yet delivered.

Imbruvica is a clear example. Despite being on the market since 2013, Imbruvica maintained high net prices relative to its list price by maintaining a dominant position in the BTKi class and offering limited commercial rebates. While newer BTKis like Brukinsa and Calquence have gained share, net pricing for Imbruvica remained steady[5], likely due to CMS restrictions on payer management within Protected Classes (including oncology) obviating the need for BTKi manufacturers to offer payer rebates for favorable Medicare Part D formulary access.

Figure 5 shows estimated pre-IRA manufacturer rebates derived from a Brookings analysis of MedPac data and CBO reports on the relationship between WAC and Medicare Part D gross sales[2], supplemented with insights from Putnam's extensive experience in these therapeutic areas. Imbruvica experienced an estimated 25% increase in net discounts due to IRA negotiations, resulting in a net price far below the defined price ceiling.

Takeaway: CMS may be more aggressive when it perceives that market forces have not adequately constrained net price. Products with long market tenure and minimal prior discounting are likely to face deeper cuts.

2. Is the product clearly differentiated?

Where market forces have already driven net prices down, CMS appears to have placed greater emphasis on clinical differentiation, including unmet need, comparative efficacy, and safety relative to therapeutic alternatives.

CMS took a broad approach to defining TAs, often including drugs with different MoAs (Mechanisms of Actions) within the same therapeutic class (Figure 6A and 6B). For example, Eliquis was benchmarked against Xarelto (both factor Xa inhibitors) and dabigatran, a direct thrombin inhibitor. This approach was consistent across multiple drug classes and highlights the importance of shaping the therapeutic alternative set through clinical guidelines, formularies, and real-world usage patterns.

The Eliquis vs. Xarelto example also underscores how CMS evaluated differentiation within therapeutic classes.

Both drugs have demonstrated clinical superiority over warfarin in RCT data, but lack head-to-head comparisons. In the absence of direct trial data, CMS likely relied on real-world evidence (RWE) to assess relative performance. Publicly available observational studies suggest Eliquis has lower rates of all-cause and stroke-related hospitalizations, as well as lower medical costs compared to other direct oral anti-coagulants[6].

Safety also may have played a significant role in negotiations. BMS submitted RCT data showing Eliquis reduced stroke and all-cause mortality without increasing GI bleeding, a key concern among Medicare's older adult population. Janssen submitted RWE for Xarelto, which pointed to higher GI and extracranial bleeding risk, despite a mortality and stroke benefit. CMS awarded Eliquis an MFP $34 greater than Xarelto, despite its higher lifetime cost, signaling that comparative clinical benefit was prioritized in price negotiations.

Fig. 4

MFP VS. CEILING PRICE FOR FIRST ROUND PICKS

Medicare Part D Drugs Negotiated for Price Applicability Year 2026							
Brand Name	Manufacturer	Disease Area	Part D Gross Drug Costs, 2023	IRA Price Ceiling Category (Monopoly)	% of non-FAMP Calculation	MFP (30 day)	Deviation from Ceiling Price
Farxiga	AstraZeneca	Cardiovascular / Metabolic	$4.3B	short monopoly	$408.66	$178.50	-56%
Jardiance	Boehringer-Ingelheim	Cardiovascular / Metabolic	$8.8B	short monopoly	$421.16	$197.00	-53%
Xarelto	Janssen	Cardiovascular / Hematologic	$6.3B	short monopoly	$380.00	$197.00	-48%
Januvia	Merck	Endocrine	$4.1B	long monopoly	$206.58	$113.00	-45%
Eliquis	BMS	Cardiovascular / Hematologic	$18.3B	short monopoly	$382.94	$231.00	-40%
Novolog/Fiasp	Novo Nordisk	Endocrine	$2.6B	long monopoly	$194.04	$119.00	-39%
Entresto	Novartis	Cardiovascular	$3.4B	short monopoly	$461.58	$295.00	-36%
Enbrel	Amgen	Immunology / Inflammatory	$3B	long monopoly	$2,785.55	$2,355.00	-15%
Imbruvica	Janssen and Pharmacyclics LLC	Oncology	$2.4B	short monopoly	$10,976.49	$9,319.00	-15%
Stelara	Janssen	Immunology / Inflammatory	$3B	long monopoly	$5,423.71	$4,695.00	-13%

Note:
After initial price applicable year 2030, extended monopoly categorization will be included in price ceiling determination;
Source: Medicare Part D Drug Spending Dashboard | CMS Data (Accessed Feb 3 2025); Brookings: Impact of Federal Negotiation of Prescription Drug Prices (Aug 19 2024); Inflation Reduction Act of 2022 (H.R.5376 – 117th Congress).

Fig. 5

NET CHANGE IN MANUFACTURER CONCESSIONS

Medicare Part D Drugs Negotiated for Price Applicability Year 2026						
Brand Name	Manufacturer	Disease Area	Part D Gross Drug Costs, 2023	Pre-IRA Manufacturer Rebates[a]	Post-IRA Manufacturer Rebates	Net Change in Manufacturer Concessions
Entresto	Novartis	Cardiovascular	$3.4B	25%	51%	-26%
Imbruvica	Janssen and Pharmacyclics LLC	Oncology	$2.4B	10%	35%	-25%
Stelara	Janssen	Immunology / Inflammatory	$3B	40%	64%	-24%
Enbrel	Amgen	Immunology / Inflammatory	$3B	45%	65%	-20%
Januvia	Merck	Endocrine	$4.1B	60%	78%	-18%
Xarelto	Janssen	Cardiovascular / Hematologic	$6.3B	45%	60%	-15%
Eliquis	BMS	Cardiovascular / Hematologic	$18.3B	40%	54%	-14%
Novolog/Fiasp	Novo Nordisk	Endocrine	$2.6B	65%	75%	-10%
Jardiance	Boehringer-Ingelheim	Cardiovascular/ Metabolic	$8.8B	55%	64%	-9%
Farxiga	AstraZeneca	Cardiovascular / Metabolic	$4.3B	65%	66%	-1%

Note:
[a]Pre-IRA manufacturer rebates based on analyses from Brookings and Hernandez et al., (2024), supplemented with insights from Putnam Associates; Source: Medicare Part D Drug Spending Dashboard | CMS Data (Accessed Feb 3 2025); Brookings: Impact of Federal Negotiation of Prescription Drug Prices (Aug 19 2024); Price Benchmarks of Drugs Selected for Medicare Price Negotiation and Their Therapeutic Alternatives (June 21 2024); Inflation Reduction Act of 2022 (H.R.5376 – 117th Congress).

Fig. 6a

DRUGS SELECTED FOR FIRST ROUND OF PRICE NEGOTIATION

Drug	MoA	Indications	TAs with Same MoA	TAs with Different MoA
Xarelto *(rivaroxaban)*	Factor Xa inhibitor	• NVAF • VTE prophylaxis (following surgery / acutely ill) • Active / recurrent VTE • CAD • PAD • Post-Fontan Procedure	• apixaban	• Direct thrombin inhibitor *(dabigatran)* • P2Y12 inhibitor *(ticagrelor; clopidogrel)* • LMWH *(enoxaparin)* • Vitamin K antagonist *(warfarin)*
Eliquis *(apixaban)*	Factor Xa inhibitor	• NVAF • VTE prophylaxis following surgery • Active / recurrent VTE	• rivaroxaban	• Direct thrombin inhibitor *(dabigatran)*
Farxiga *(dapagliflozin)*	SGLT2 inhibitor	• CKD • HF • T2DM & CVD/CV risk factors • T2DM Glycemic Control	• empagliflozin • canagliflozin	• GLP-1 receptor antagonist *(dulaglutide; liraglutide; semaglutide)* • Sulfonylurea *(glimepiride; glipizide)* • AMPK activator *(metformin)* • PPAR agonist *(pioglitazone)* • DPP-4 inhibitor *(sitagliptin)*
Jardiance *(empagliflozin)*	SGLT2 inhibitor	• CKD • HF • T2DM with CVD • T2DM Glycemic Control	• dapagliflozin • canagliflozin	
Januvia (*sitagliptin)*	DPP-4 inhibitor	• T2DM	• linagliptin	• SGLT2 inhibitor *(dapagliflozin; empagliflozin)* • GLP-1 receptor antagonist *(dulaglutide; semaglutide)* • Sulfonylurea *(glimepiride; glipizide)* • AMPK Activator *(metformin)* • PPAR Agonist *(pioglitazone)*
Entresto *(sacubitril/valsartan)*	ARNI	• HF	*No TAs with the same MoA*	• ACE inhibitor *(enalapril; lisinopril)* • ARB *(losartan; valsartan)* • Aldosterone antagonist *(spironolactone)*
NovoLog/Fiasp *(insulin aspart)*	Insulin	• Diabetes Mellitus	• insulin lispro	*No TAs with different MoA*

Abbreviations:
ACE=Angiotensin-Converting Enzyme; AMPK=AMP-Activated Protein Kinase; ARB=Angiotensin II Receptor Blocker; ARNI=Angiotensin Receptor-Neprilysin Inhibitor; CAD=Coronary Artery Disease; CKD=Chronic Kidney Disease; CV=Cardiovascular; CVD=Cardiovascular Disease; DPP-4=Dipeptidyl Peptidase-4; HF=Heart Failure; LMWH=Low Molecular Weight Heparin; MoA=Mechanism Of Action; NVAF=Non-Valvular Atrial Fibrillation; PAD=Peripheral Artery Disease; PPAR=Peroxisome Proliferator-Activated Receptor; TA=Therapeutic Alternative; T2DM=Type 2 Diabetes Mellitus; VTE=Venous Thromboembolism.

Fig. 6b

THERAPEUTIC ALTERNATIVES FOR FIRST ROUND PICKS

Drug	MoA	Indications	TAs with Same MoA	TAs with Different MoA
Enbrel (etanercept)	TNF inhibitor	• PS • PA • RA • pJIA • AS	• adalimumab • infliximab	• IL-23 inhibitor (risankizumab • IL-17A inhibitor (secukinumab) • IL-12/IL-23 inhibitor (ustekinumab)
Stelara (ustekinumab)	Il-23/IL-12 inhibitor	• PS • PA • CD • UC	No TAs with the same MoA	• TNF inhibitor (adalimumab; etanercept; infliximab) • IL-23 inhibitor (guselkumab; risankizumab; tildrakizumab) • IL-17A inhibitor (ixekizumab; secukinumab) • Integrin inhibitor (vedolizumab)
Imbruvica (ibrutinib)	BTK inhibitor	• CLL/SLL • WM • cGVHD	• acalabrutinib • zanubrutinib	• Combination chemotherapy regimens (venetoclax with obinutuzumab/rituximab; bendamustine with rituximab; dexamethasone, rituximab, and cyclophosphamide) • ROCK2 inhibitor (belumosudil) • JAK1/2 inhibitor (ruxolitinib)

Abbreviations:
BTK=Bruton's Tyrosine Kinase; CD=Crohn's Disease; CLL=Chronic Lymphocytic Leukemia; cGVHD=Chronic Graft-Versus-Host Disease; IL-12=Interleukin-12; IL-17A=Interleukin-17A; IL-23=Interleukin-23; MoA=Mechanism Of Action; PA=Psoriatic Arthritis; pJIA=Polyarticular Juvenile Idiopathic Arthritis; PS=Plaque Psoriasis; RA=Rheumatoid Arthritis; SLL=Small Lymphocytic Lymphoma; TA=Therapeutic Alternative; UC=Ulcerative Colitis; WM=Waldenström's Macroglobulinemia

Strategic Considerations

The first round of IRA negotiations offers critical insight into CMS' approach, highlighting both the levers manufacturers can use to influence the negotiation and the key CMS priorities. We highlight three areas of focus to strengthen positioning ahead of future negotiations:

1. Proactively Shape Therapeutic Alternatives

TAs play a significant role in determining the magnitude of IRA price reductions, yet the methodology for identifying them is opaque. While guidelines, compendia, formulary data, and manufacturer submitted evidence appear to inform TA selection, the process is not formally defined.

Manufacturers should take early, active steps to shape the treatment landscape and influence the set of alternatives against which their products may be defined. Beyond formulary and guideline inclusion, investment in robust RWE which further substantiates meaningful areas of clinical and economic benefit can facilitate favorable comparison against competitive alternatives.

2. Strengthening Medicare-Relevant Evidence Generation

Head-to-head RCTs remain the gold standard for negotiations under the IRA, but in their absence, CMS has demonstrated willingness to rely on RWE, especially when focused on outcomes relevant to the Medicare population.

To support clinical differentiation, manufacturers should initiate RWE studies, which measure patient-relevant outcomes (e.g., hospitalization, mortality, functional decline) among older adults and high-risk subgroups.

Availability at time of negotiation is critical to maximize impact, so studies should be initiated early in the product's lifecycle.

3. Anticipate the Impact of Market Factors

Negotiated discounts appear to be informed not just by clinical value, but also by length of exclusivity and magnitude of pre-negotiated rebates. Products with extended exclusivity and limited rebating were subject to larger reductions.

To prepare, manufacturers should evaluate historical market positioning and pricing history to assess risk. To defend against negotiation pressures, demonstration of real-world clinical and economic advantages, particularly those tied to Medicare costs may also help to defend against steeper reductions.

Conclusion

Manufacturers that align their evidence strategy, access planning, and competitive positioning with CMS' evolving approach will be best positioned to navigate Medicare price negotiations. Proactively shaping TA selection, generating Medicare-relevant clinical evidence, and anticipating where CMS may impose pricing pressure are critical components of negotiation strategy.

Looking ahead, factors considered in CMS negotiations may evolve with policy shifts, including the prospect of Most Favored Nation pricing[7]. The Trump Administration's Executive Order on May 12, 2025, threatens to undertake rulemaking to "impose most-favored-nation pricing" if manufacturers do not adequately respond to price targets to be communicated by CMS. While no details on how such a policy would be implemented – including affected drugs, eligible populations, and enforcement mechanisms – have been formally communicated, one potential scenario is the incorporation of international reference pricing benchmarks into the IRA negotiation process. Manufacturers should prepare for a broader set of pricing benchmarks, including international reference prices, and remain agile in response to changing political and regulatory environments.

Sources

1. Centers for Medicare & Medicaid Services (CMS). Medicare Drug Price Negotiation Program: Negotiated Prices for Initial Price Applicability Year 2026. March 14, 2024. Available at: https://www.cms.gov/newsroom/fact-sheets/medicare-drug-price-negotiation-program-negotiated-prices-initial-price-applicability-year-2026
2. Kanavos, P., & Sood, N. Impact of Federal Negotiation of Prescription Drug Prices. Brookings Institution. August 29, 2023. Available at: https://www.brookings.edu/articles/impact-of-federal-negotiation-of-prescription-drug-prices/
3. Centers for Medicare & Medicaid Services (CMS). Medicare Drug Price Negotiation Program: Final Guidance for Initial Price Applicability Year 2027 and Manufacturer Effectuation of the Maximum Fair Price for 2026 and 2027. May 3, 2024.
4. Shih, C., & Wilensky, G. R. Incorporating Information on Therapeutic Alternatives into the IRA Prescription Drug Negotiations. Brookings Institution. April 10, 2024.
5. Chambers, J. D., Thorat, T., Ponce, S., Wilkinson, C. L., & Neumann, P. J. Estimated Effects of Drug Price Negotiation on Medicare Part D Spending on Top-Selling Brand-name Drugs. JAMA Network Open. 2023;6(3):e237467.
6. Institute for Clinical and Economic Review (ICER). Assessment of Eliquis®, Pradaxa®, and Xarelto® for the Treatment of Nonvalvular Atrial Fibrillation in Medicare Patients. October 2, 2023.
7. Centers for Medicare & Medicaid Services (CMS). Fact Sheet: President Donald J. Trump Announces Actions to Put American Patients First by Lowering Drug Prices and Stopping Foreign Free-riding on American Pharmaceutical Innovation. May 12, 2025.

Putnam
Inizio Advisory

About Putnam

Putnam, an Inizio Advisory company, is a leading scientific and strategic consulting partner that helps the global life science community make confident decisions, build value, and bring life-changing innovations to clinicians and patients. For more than 30 years, our rigorous, bespoke approach and globally diverse team have delivered unrivaled depth across therapeutic areas, business functions, geographic markets, healthcare sectors, and technology platforms to maximize the human impact and commercial success of client innovations.