Evaluating Therapeutic Alternative Selection in Medicare's Initial Drug Price Negotiation Explanations

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Fewer than 1 in 5 therapeutic alternatives fully aligned with their corresponding DPNP-selected medications, when evaluated on mechanism of action, US Pharmacopeia classification, and route of administration.

BACKGROUND & OBJECTIVE

- The Inflation Reduction Act (IRA) directs the Centers for Medicare and Medicaid Services (CMS) to compare each drug selected for the IRA's Drug Price Negotiation Program (DPNP) to therapeutic alternatives (TA) in its determination of offers and counteroffers.[1]
- CMS defines a TA as a pharmaceutical product that is clinically comparable to the selected drug.[1]
- In December 2024, CMS released the "maximum fair price" (MFP) explanations for the first round of drugs selected for the DPNP (Initial Price Applicability Year [IPAY] 2026).[2]
- This study aims to characterize the TAs identified in CMS's MFP explanations for the first ten drugs selected for the DPNP.

METHODS

- Therapeutic alternatives identified in the MFP explanations (Table 1) were compared to their corresponding selected drugs on **three characteristics** based on the Agency for Healthcare Research and Quality's guidance[3] on comparator selection in comparative effectiveness research:
  - Mechanism of action
  - Class, defined here by the US Pharmacopeia (USP)
  - Treatment modality, narrowly defined here as route of administration.
- Descriptive statistics summarized TA alignment with their corresponding IPAY 2026 drugs on these three characteristics. (Table 2).

RESULTS

- Across the 10 DPNP-selected drugs, the number of TAs identified by CMS ranged from 1 to 10 unique options per drug (median: 7; IQR: 5-9).
- CMS identified the highest number of TAs for selected diabetes and immunologic drugs (medians: 9 and 7, respectively).
- Across 33 unique drug-indication pairs, the median number of TAs selected by CMS was 2 (range: 1-9; IQR: 1-5).

RESULTS

Table 1. IPAY 2026 Selected Drugs and CMS-Identified Therapeutic Alternatives

IPAY 2026 Drug	MOA	USP Class	Route of Administration	Number of Unique TAs	TAs Listed Across All Indications
Eliquis (apixaban)	Direct Xa Inhibitor	Anticoagulants	Oral	2	Dabigatran, rivaroxaban
Enbrel (etanercept)	TNF Inhibitor	Immunosuppressants	SC Injection	5	Adalimumab, infliximab, risankizumab, secukinumab, ustekinumab
Entresto (sacubitril/valsartan)	Neprilysin Inhibitor/ARB	Cardiovascular Agents, Combination	Oral	5	Enalapril, lisinopril, losartan, spironolactone, valsartan
Farxiga (dapagliflozin)	SGLT2 Inhibitor	Antidiabetic Agents	Oral	10	Canagliflozin, dulaglutide, empagliflozin, glimepiride, glipizide, liraglutide, metformin, pioglitazone, semaglutide, sitagliptin
Imbruvica (ibrutinib)	BTK Inhibitor	Molecular Target Inhibitors	Oral	8	Acalabrutinib, belumosudil, ruxolitinib, zanubrutinib, venetoclax + obinutuzumab (combo), venetoclax + rituximab (combo), bendamustine + rituximab (combo), dexamethasone + rituximab + cyclophosphamide (combo)
Januvia (sitagliptin)	DPP-4 Inhibitor	Antidiabetic Agents	Oral	9	Dapagliflozin, dulaglutide, empagliflozin, glimepiride, glipizide, linagliptin, metformin, pioglitazone, semaglutide
Jardiance (empagliflozin)	SGLT2 Inhibitor	Antidiabetic Agents	Oral	10	Canagliflozin, dapagliflozin, dulaglutide, glimepiride, glipizide, liraglutide, metformin, pioglitazone, semaglutide, sitagliptin
NovoLog and Fiasp (insulin aspart)	Rapid-Acting Insulin	Insulins	SC Injection	1	Insulin lispro
Stelara (ustekinumab)	IL-12/IL-23 Inhibitor	Immunological Agents, Other	SC Injection	9	Adalimumab, etanercept, guselkumab, infliximab, ixekizumab, risankizumab, secukinumab, tildrakizumab, vedolizumab
Xarelto (rivaroxaban)	Direct Xa Inhibitor	Anticoagulants	Oral	6	Apixaban, clopidogrel, dabigatran, enoxaparin, ticagrelor, warfarin

IPAY: Initial Price Applicability Year; TA: Therapeutic Alternative; MOA: Mechanism of Action; USP: US Pharmacopeia; SC: Subcutaneous

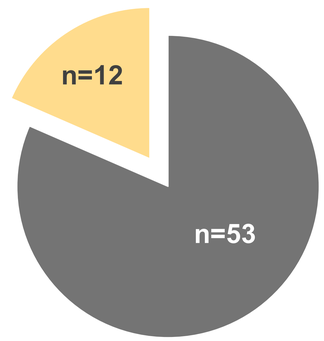
Table 2. Assessment of Therapeutic Alternatives with IRA Drug Price Negotiation Program-Selected Drugs

IPAY 2026 Drug	# of TAs	Same MOA (%)	Same USP Class (%)	Same Route (%)	All Three Criteria (%)
Eliquis	2	50%	100%	100%	50%
Enbrel	5	40%	40%	80%	40%
Entresto	5	0%	0%	100%	0%
Farxiga	10	20%	100%	80%	20%
Imbruvica	8	25%	38%	50%	25%
Januvia	9	11%	100%	89%	11%
Jardiance	10	20%	100%	80%	20%
NovoLog/Fiasp	1	100%	100%	100%	100%
Stelara	9	0%	67%	67%	0%
Xarelto	6	17%	67%	83%	17%
Overall	**65**	**18%**	**72%**	**78%**	**18%**

IPAY: Initial Price Applicability Year; TA: Therapeutic Alternative; MOA: Mechanism of Action; USP: US Pharmacopeia

0-19% 20-39% 40-59% 60-79% 80-100%

Across 65 TAs, only **18.5% aligned with the DPNP-selected drug on all three characteristics** studied.



DISCUSSION & CONCLUSIONS

- CMS-identified TAs differed from DPNP-selected drugs on key characteristics, including mechanism of action, USP class, and route of administration.
- CMS's process is not transparent and may not be scientifically rigorous.
  - Uncertainty remains regarding how or why TAs were selected, how CMS weighted the evidence they reviewed, and how CMS incorporated patient and public input.
- CMS's choices of TAs are of particular interest as TAs drive the outcomes and potential validity of assessments of a drug's relative clinical or economic benefits. Our findings **further amplify** concerns surrounding the appropriateness of TA selection during the MFP determination process.

REFERENCES

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