Formulary Inclusion for Oncologic Indications: Comparing FDA-Approved Indications and Off-Label Compendia Support

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OBJECTIVES

To assess how FDA-approved indications versus off-label compendia support (e.g., NCCN guideline recommendations) influence formulary coverage and prior authorization requirements for oncology therapies. This analysis aims to clarify how evidence source impacts payer decisions and implications for patient access across major U.S. health plans

METHODS

We conducted a comparative policy review across five major U.S. commercial payers (Aetna, Anthem, Cigna, Humana, and UnitedHealthcare) to evaluate formulary inclusion and access requirements for three oncology therapy pairs. Each pair consisted of:

- A therapy with an FDA-approved indication in a specified cancer type
- A therapy used off-label in the same indication but supported by NCCN or Micromedex compendia

For each therapy, we assessed:

- Formulary tiering and inclusion status
- Prior authorization requirements
- Monthly WAC pricing (April 2025)

This mixed-methods analysis focused on coverage differentials to better understand the weight payers place on regulatory vs. compendia-based evidence in oncology access decisions

ONCOLOGY THERAPIES ASSESSED

PRODUCT	LAUNCH YEAR	FDA INDICATIONS (HIGH LEVEL)	RELEVANT OFF-LABEL RECOMMENDATION
Voranigo (vorasidenib)	2024	Adults and pediatric patients 12+ with IDH1/2 susceptible astrocytomas or oligodendroglioma following surgery	Not Applicable to Analysis
Tibsovo (ivosidenib)	2018	Adults with newly diagnosed AML, relapsed or refractory AML, relapsed or refractory MDS, locally advanced or metastatic cholangiocarcinoma	IDH1-positive Stage 2 oligodendrogliomas and astrocytomas
Pemazyre (pemigatinib)	2020	Adults with previously treated, locally advanced or metastatic cholangiocarcinoma with FGFR2 fusion or rearrangement	Not Applicable to Analysis
Balversa (erdafitinib)	2019	Adults with locally advanced or metastatic metastatic urothelial cancer with FGFR3 genetic alteration	Subsequent treatment if disease progression for unresectable or metastatic cholangiocarcinoma with FGFR2 fusions or rearrangements
Tabrecta (capmatinib)	2020	Adults with metastatic NSCLC whose tumors have a mutation that leads to METex14 skipping	Not Applicable to Analysis
Xalkori (crizotinib)	2011	Adults with metastatic NSCLC whose tumors are ALK+ or ROS-1+, pediatric and young adults with ALK+ relapsed or refractory systemic ALCL	METex14 skipping NSCLC

Table 1. Summary of oncology therapies included in analysis
Products selected may have off-label recommendations in other indications, however, were not included in analysis

RESULTS

Coverage and access varied substantially between therapies with FDA-approved indications and those relying solely on compendia support:

- Formulary Access & Prior Authorization:
  Therapies with FDA-approved indications (e.g., Voranigo, Pemazyre, Balversa) had higher rates of favorable coverage. Across the five reviewed payers:
  - Therapies with FDA-approved indications were on formulary with standard PA in 80–100% of cases
  - Therapies with only compendia support (e.g., Tibsovo, Tarceva, Xalkori) showed more restrictive access, with at least one plan listing them as non-formulary and more frequent use of step therapy or indication-specific restrictions
- Pricing Comparison:
  Monthly WAC prices did not consistently correlate with access:
  - Voranigo, the most expensive therapy assessed (~$39.8K/month), had favorable formulary positioning across all five plans due to its on-label status.
  - Tibsovo (~$34.1K/month), used off-label for the same indication (LGG), saw less consistent coverage despite being less expensive.
  - Similarly, other therapy pairs (e.g., Balversa vs. Tarceva) showed better access for the FDA-approved option, even when price differences were minimal.

These findings suggest that FDA label status plays a more decisive role in payer management than compendia support alone, even in the context of similar clinical use and cost.

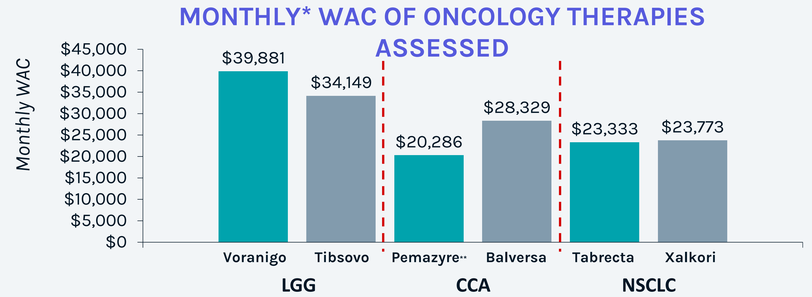

*Figure 1. *Monthly (28-30 days) maintenance cost of assessed oncology therapies, price as of April 21st, 2025*
*Note: WAC for adult dosing; **Pemazyre is administered once daily for 14 days followed by 7 days off therapy, price shown is for 21-day cycle*

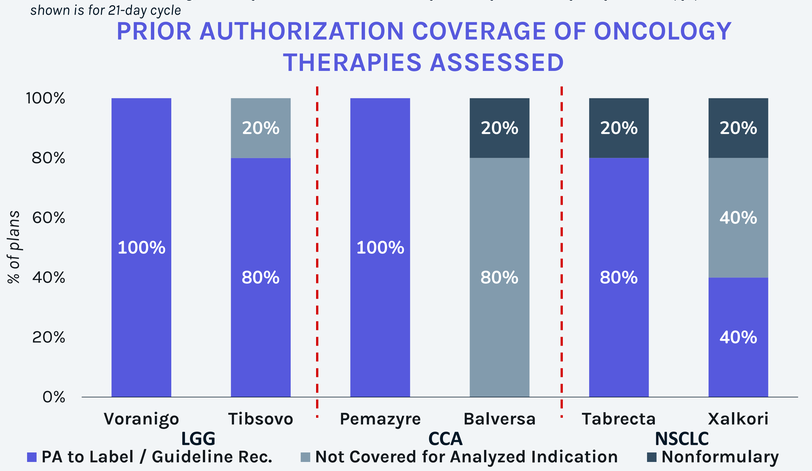

Figure 2. Commercial coverage for oncology therapies assessed at five of the largest plans by count of lives
Public commercial plans analyzed: Anthem, Aetna, United Healthcare, Cigna, Humana Analysis conducted on 04/21/2025, updates to coverage may have occurred since initial analysis

CONCLUSIONS & LIMITATIONS

CONCLUSIONS

- This analysis reinforces the central role that FDA-approved labeling and compendia support (e.g., NCCN guidelines) play in driving formulary inclusion and access for oncology therapies. Across five major U.S. commercial payers, therapies with on-label indications generally experienced broader formulary coverage and less burdensome prior authorization requirements than therapies used off-label—even when off-label use was supported by reputable clinical guidelines.
- That said, exceptions to this pattern highlight the importance of broader market context. For instance, Xalkori, though used off-label in our analysis, was covered by all payers reviewed. However, this likely reflects its long-standing presence on the market and broad familiarity among payers rather than a pure endorsement of NCCN support alone. Such examples suggest that time on market, provider comfort, and historical precedent also play important roles in access decisions.
- Additionally, the data suggest that formulary decision-making is shaped by multiple overlapping factors beyond regulatory or guideline status:
  - Pricing: While FDA-labeled therapies had more favorable access even at higher prices (e.g., Voranigo vs. Tibsovo), price remains an important consideration—especially in more competitive settings.
  - Competitive Landscape: Therapies in crowded classes may face higher scrutiny regardless of labeling or guideline support.
  - Disease Burden and Rarity: In rare oncology indications with fewer treatment options, some off-label therapies still secured meaningful access based on perceived clinical need or limited alternatives.

LIMITATIONS

- This analysis included only three therapy comparisons and five national payers, limiting generalizability
- Formulary and PA data reflect a single point in time (April 2025) and may change with contracting, new clinical evidence, or pricing shifts
- We did not quantify or stratify strength of compendia support (e.g., NCCN category), which may further explain variability in access
- We also did not assess real-world uptake as coverage may appear restrictive on paper but not materially limit use in practice

FUTURE IMPLICATIONS

Manufacturers should prioritize early engagement strategies that account not only for regulatory and guideline alignment but also broader payer considerations such as price positioning, competitive context, and real-world usage trends. As payers increasingly apply nuanced frameworks to oncology access decisions, a singular focus on FDA approval or NCCN inclusion may be insufficient to secure optimal coverage.

REFERENCES

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2. https://www.microdexsolutions.com

Coverage Policies

1. Anthem: https://www.anthem.com/
2. Aetna: https://www.aetna.com/
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5. UHC: https://www.uhc.com/

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