Analysis of Pharmacy Benefit Manager Formulary Exclusions in Oncology

Kyle A. Noonan, PharmD[1]; Zade Hikmat, PharmD[1]; Alex Kilgore, PharmD, MS[2]; Jennifer Snow, MPH[2]; Scott Shields, MBA[1]
1. Xcenda, Carrollton, TX, USA; 2. AmerisourceBergen, Inc., Conshohocken, PA, USA

Background and objective

- The practice of formulary exclusions is relatively new, being first adopted by CVS Caremark in 2011. Since then, formulary exclusions have gradually increased by the top 3 pharmacy benefit managers (PBMs): **CVS Caremark, Express Scripts, and OptumRx**
- Further, the PBM market has become highly consolidated with these 3 PBMs handling 80% of all prescriptions within the United States[1]
- Only recently have formulary exclusions for oncology drugs become common.[2] Therefore, the objective of this research was to evaluate oncology drug formulary exclusions and assess whether such exclusions were warranted based on publicly available clinical evidence and market factors

Methods

- The Xcenda formulary exclusions database was used to analyze oncology drugs from the 3 largest national PBMs (Express Scripts, CVS Caremark, and OptumRx) for 2022
- The database was developed by a team of PharmDs who standardized therapeutic categories and classes to facilitate comparison across the 3 PBMs
- Oncology medications were appraised on a case-by-case basis for clinical evidence to understand potential justification for the formulary exclusion

Results

Table 1. List of drugs excluded from at least 1 formulary that were included in analysis (N=43)

Afinitor (everolimus)	**Kisqali Femara Co-Pack** (ribociclib and letrozole)	**Tazverik** (tazemetostat)
Aliqopa (copanlisib)	**Kyprolis** (carfilzomib)	**Tepmetko** (tepotinib)
Avastin (bevacizumab)	**Nilandron** (nilutamide)	**Treanda** (bendamustine HCl)
Belrapzo (bendamustine)	**Ogivri** (trastuzumab-dkst)	**Trelstar** (triptorelin)
Bendamustine (generic)	**Ontruzant** (trastuzumab-dttb)	**Truseltiq** (infigratinib)
Blenrep (belantamab mafodotin-blmf)	**Onureg** (azacitidine)	**Truxima** (rituximab-abbs)
Darzalex Faspro (daratumumab and hyaluronidase-fihj)	**Phesgo** (pertuzumab, trastuzumab and hyaluronidase-zzxf)	**Velcade** (bortezomib)
Erleada (apalutamide)	**Piqray** (alpelisib)	**Xalkori** (crizotinib)
Fotivda (tivozanib)	**Qinlock** (ripretinib)	**Xatmep** (methotrexate)
Gavreto (pralsetinib)	**Riabni** (rituximab-arrx)	**Xpovio** (selinexor)
Herceptin (trastuzumab)	**Rituxan** (rituximab)	**Yonsa** (abiraterone acetate)
Herceptin Hylecta (trastuzumab and hyaluronidase-oysk)	**Rituxan Hycela** (rituximab and hyaluronidase human)	**Zydelig** (idelalisib)
Herzuma (trastuzumab-pkrb)	**Scemblix** (asciminib)	**Zytiga** (abiraterone acetate)
Inqovi (decitabine and cedazuridine)	**Targretin** (bexarotene)	
Kisqali (ribociclib)	**Tasigna** (nilotinib)	

Results (cont.)

- A total of 43 medications were reviewed, with 39 (91%) being potentially justified for formulary exclusion and 4 (9%) that were determined to have a reasonable objection to formulary exclusion (**Figure 1**)
- There were 2 primary categories for excluded products (**Table 2**), with 30 (77%) therapies likely being excluded due to market-related factors and 9 (23%) therapies likely being excluded due to clinical factors

Figure 1. Adjudication of formulary exclusions based on clinical evidence and market factors (N=43)

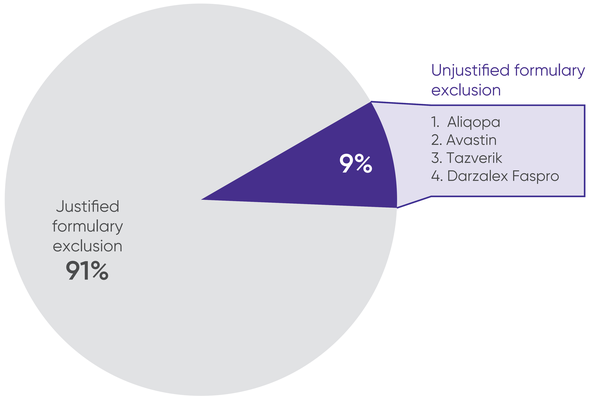


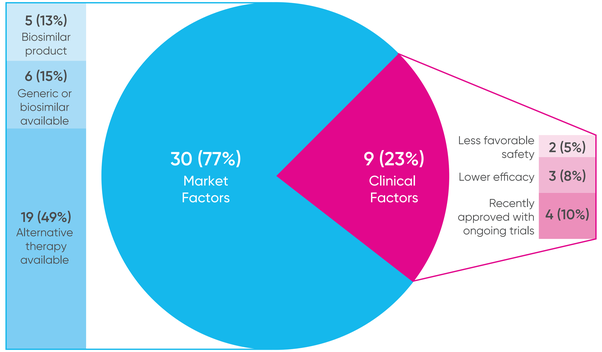
Table 2. Criteria for justified formulary exclusions

Exclusion from formulary likely due to:	
Market-related factors for exclusion	Availability of a therapeutic alternative (ie, different class of medication for same indication)
	Product itself being a biosimilar
	Branded innovator product with the availability of generic or biosimilar
Clinical-based factors for exclusion	Product recently being FDA approved (2020 or later) with required or ongoing confirmatory trial
	Lower efficacy than direct competitors
	Less favorable side effect profile than direct competitors

Key: FDA – Food and Drug Administration.

- Of the 30 (77%) therapies likely excluded due to market factors (**Figure 2**):
  - 19 (49%) were justified due to availability of therapeutic alternative
  - 6 (15%) were branded products with a generic or biosimilar available
  - 5 (13%) were excluded biosimilars
- Of the 9 (23%) therapies likely excluded due to clinical factors (**Figure 2**):
  - 4 (10%) were recently approved products with ongoing confirmatory trials
  - 3 (8%) were stated to be less effective than the alternatives
  - 2 (5%) were stated to have a less favorable safety profile than the alternatives

Figure 2. Detailed results of excluded therapies adjudicated as a justified formulary exclusion (N=39)



- Four medications (9%), **Aliqopa, Avastin, Tazverik, and Darzalex Faspro**, were deemed to be unjustified formulary exclusions based on publicly available evidence
- Reasonable objections to these exclusions included (**Table 3**):
  - **Aliqopa** having a unique mechanism of action that affords it a greater range of activity than direct competitors
  - **Avastin** being excluded despite biosimilars lacking the full spectrum of indications
  - **Tazverik** is the first and only FDA-approved therapy for epithelioid sarcoma
  - **Darzalex Faspro** is a subcutaneous formulation that has shown significantly fewer infusion reactions and offers a significant advantage in administration time compared to the intravenous product

Table 3. Detailed findings of therapies adjudicated as unjustified formulary exclusions

Excluded therapy	Objection to formulary exclusion
Aliqopa (copanlisib)	• Despite many competing drugs for R/R FL, Aliqopa has a unique MOA that affords it a larger range of activity compared to other PI3K inhibitors[3,4] • In a clinical trial, the overall response rate for the combination of copanlisib and rituximab was 80.8% vs 47.7% for rituximab and placebo, and Aliqopa is the only guideline-recommended PI3K inhibitor[4]
Avastin (bevacizumab)	• Some indications (ie, breast cancer) are not indicated by the biosimilar; therefore, there could be some ineligible patient populations if the biosimilar is not being used off-label[5] • For example, Express Scripts and CVS cover Zirabev and Mvasi, but these drugs are not indicated for breast cancer and thus it is unknown whether they may receive the biosimilar for this indication[6,7]
Tazverik (tazemetostat)	• Tazverik is a targeted therapy for epithelioid sarcoma and a preferred treatment per NCCN guidelines; Tazverik may also be used for R/R FL with an EZH2 mutation[8,9] • Treatment options for epithelioid sarcoma are extremely limited with few alternatives;[9] therefore, excluding this product may negatively impact patients with this form of cancer
Darzalex Faspro (daratumumab and hyaluronidase-fihj)	• Darzalex Faspro is the SC version of an IV drug, but the SC version has shown significantly fewer infusion reactions (12.7% vs 34.5%) and offers a significant advantage in the administration time (IV given over several hours vs SC given over 3-5 mins)[10,11] • Since there is a noticeable difference in infusion reactions between the IV and SC formulations,[10,11] convenience of SC dosing was not the only factor to consider

Key: FL = follicular lymphoma; IV = intravenous; MOA = mechanism of action; NCCN = National Comprehensive Cancer Network; PI3K = phosphoinositide 3-kinase; R/R = relapsed or refractory; SC = subcutaneous.

Limitations

- Due to this research being based solely on public information and interpretation of clinical data or market factors, many assumptions were made regarding the hypothesized reason for formulary exclusion, and we acknowledge there are numerous considerations at play when making these decisions
- While specific criteria were used to evaluate these therapies, final adjudication of therapies was ultimately based on subjective interpretation of public information
- Exercise caution when generalizing these results since no information on pricing, contracting, or reimbursement was evaluated in this analysis
- For medications excluded from the formulary, the analysis does not take into consideration any medical exemptions/appeals

Conclusions

- A vast majority of oncology medications were found to have some merit for exclusion. However, there was a small minority of therapies with a reasonable objection to their excluded status
- Findings of this analysis should be taken with caution as these results were meant to identify clinical- and market-related factors to justify formulary exclusions, rather than dispute the decision itself
- Formulary exclusions can be based on numerous factors, but the practice of formulary exclusions is new in oncology; therefore, further research should be considered to understand PBM exclusions for oncology products and their implication on patient outcomes

References: 1. Fein A. The top pharmacy benefit managers of 2021: the big get even bigger. April 5, 2022. Accessed January 26, 2023. https://www.drugchannels.net/2022/04/the-top-pharmacy-benefit-managers-of.html **2.** AmerisourceBergen Xcenda. Skyrocketing growth in PBM formulary exclusions continues to raise concerns about patient access. May 24, 2022. Accessed January 26, 2023. https://www.xcenda.com/~/media/assets/xcenda/english/content-assets/white-papers-issue-briefs-studies-pdf/xcenda_pbm_exclusion_may_2022.pdf **3.** Datamonitor Healthcare. Disease analysis: follicular lymphoma. November 17, 2022. Accessed January 26, 2023. https://service.datamonitorhealthcare.com/hkc/disease/oncology/lymphoma/follicular-lymphoma/disease-analysis/article225371.ece **4.** National Comprehensive Cancer Network. B-cell lymphomas (Version 1.2023). Accessed January 26, 2023. https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf **5.** Avastin prescribing information. Genentech, Inc.; 2022. **6.** Zirabev prescribing information. Pfizer, Inc.; 2021. **7.** Mvasi prescribing information. Amgen, Inc.; 2021. **8.** Datamonitor Healthcare. Market spotlight: sarcoma. November 10, 2022. Accessed January 26, 2023. https://service.datamonitorhealthcare.com/hkc/disease/oncology/other-solid-cancers/sarcoma/market-spotlight/article185528.ece **9.** National Comprehensive Cancer Network. Soft tissue sarcoma (Version 2.2022). Accessed January 26, 2023. https://www.nccn.org/professionals/physician_gls/pdf/sarcoma.pdf **10.** Darzalex Faspro prescribing information. Janssen Biotech, Inc.; 2022. **11.** Darzalex prescribing information. Janssen Biotech, Inc.; 2022.

Presented at:
AMCP 2023 Annual Meeting, March 21-24, 2023; San Antonio, Texas.
Please direct all questions to Kyle Noonan at Kyle.Noonan@xcenda.com or Zade Hikmat at Zade.Hikmat@xcenda.com
Funded by Xcenda.

AmerisourceBergen