White Paper

Controlling Cancer Care: The Emergence of Formulary Exclusions in Oncology

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Introduction

Formulary exclusions were once rare among cancer medicines. This was, in part, driven by the lack of brand and generic alternatives within a specific tumor type and oncology's protected class status.

As more oncology treatments with similar clinical profiles have launched, formulary exclusions are becoming increasingly more common. Major pharmacy benefit managers (PBMs) and national insurers first started placing oncology medicines with generic alternatives on their formulary exclusion lists in 2017[1], and by 2019 these lists showed the beginning of competitive contracting as the use of exclusions was continuing to expand. Because there is not the same precedent of payer control in anti-cancer medicines as there may be in other therapy areas, manufacturers could be unprepared for the ways in which exclusions can influence physician treatment preference and patient access, and support program demand. Understanding how cancer patients navigate payer control is critical for the biopharmaceutical companies operating in the oncology space as well as public health.

Using published national formularies and longitudinal claims data, this paper demonstrates the growing challenge of payer exclusions in oncology. Case studies in metastatic breast cancer further evaluate the impact these exclusions have on treatment initiation, demonstrating the need for action, measurement, and strategy across tumor types.

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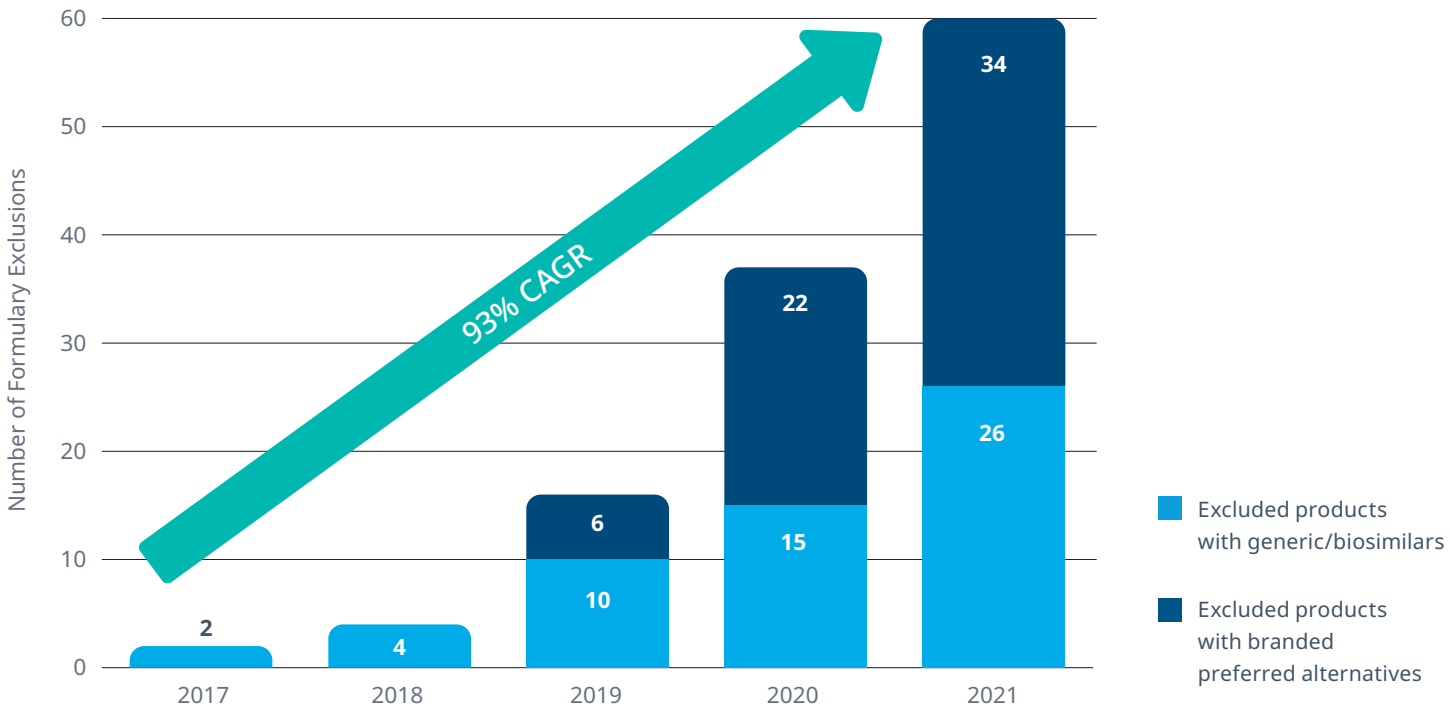
Rising use of exclusions in oncology

When evaluating payer control, both payer willingness and ability must be considered. Willingness is often defined as whether a payer will restrict patient access through the formulary, whereas ability looks at the impact these controls have on new patient starts, share, and other performance measures. In a market like oncology where it has been long been common belief that payers are unwilling to exert control, today their published formularies tell a different story. Every year, major PBMs and national insurers publish their formularies - annual lists of excluded products and their preferred alternatives. These formularies are one way in which industry stakeholders can measure and track which therapeutic areas face payer control by way of formulary blocks.

TYPES OF EXCLUSIONS

In order to analyze exclusion trends, public, historical formularies provide a snapshot that is exemplary of broader controls in the market. Among the six commercial payers evaluated, the first formulary exclusions against cancer treatments were in 2017 where the brands had a generic alternative. As generic and biosimilar versions of existing treatments continued to become available, so came more exclusions. In time, continued development in oncology created more treatment options and competition, facilitating the expansion of formulary blocks into tumor types without generic/biosimilar options (for example, Kisqali was blocked in favor of Ibrance and Verzenio at Express Scripts in 2019). In 2021, more than half of the oncology exclusions are against cancer treatments where only brand competitors are listed as preferred alternatives, not generics or biosimilars. In some instances, brands are even favored over the generic or biosimilar. Payers

Figure 1 - Number of national formulary exclusions (top national payers, commercial insurance, oncology)



Note: Top National Payers include Aetna, CVS Caremark, Cigna, Express Scripts (the PBM subsidiary of Cigna), OptumRx (the PBM subsidiary of UnitedHealthcare), and Prime Therapeutics. **Source:** Published national formularies, US Market Access Strategy Consulting analysis, IQVIA

have thus demonstrated their willingness to leverage mechanisms that are proven to be effective in other therapeutic classes to tighten the control for the oncology space.

BROAD TUMOR TYPE IMPACT

Though limited initially, oncology exclusions quickly expanded to multiple tumor types (Appendix 1). As of 2021, twelve tumor types have at least one exclusion. As new treatment development continues, payers will have even greater willingness to grant select brands preferred access and block others. That said, tumor type markets with fewer treatment options have also shown an increase in control. Launch and established brands alike may encounter more control than originally expected and may have to re-evaluate their forecasts and strategies in light of rising exclusions. Open access in oncology is no longer a safe assumption.

As well as applying to multiple tumor types, these exclusions can affect therapies across all modes of administration. It may not come as a surprise that formulary exclusions affect oral and self-administered treatments (medicines that are easy to control through PBMs' utilization management tools), because they are dispensed through pharmacies. Yet cross-benefit management[3], white-bagging[4] and other practices have enabled payers to apply their formulary tools to physician-administered medicines, as well. Becoming increasingly more common in exclusions, physician-administered treatments account for nearly half of excluded products to date in 2021. For providers and manufacturers that may have thought certain oncology treatments were immune to control due to their administration, recent trends in payer exclusions suggest otherwise (Appendix 2).

Although not all plans within a payer will necessarily opt into these national formularies, the published formulary demonstrates the payer's willingness to control the market. Beyond willingness, however, the payer's ability to exert control and shift demand must also be taken into account.

Impact of oncology formulary exclusions

For years, brands in traditional, retail therapies have analyzed payer ability by measuring the effect of control – particularly formulary exclusions – on new patient behavior and prescription demand. Yet, this approach is still novel to many in the oncology space. Nevertheless, it is crucial for brands that are expecting an exclusion to further contextualize payer willingness to control with their ability to do so. It has been historically accepted that oncology treatments, even if subject to an exclusion, are easily obtained with the proper paperwork and patient history given the necessity of treatment among cancer patients. Yet, analysis of the data suggests that in at least some markets, the impact to patient access is substantial.

Furthermore, there are market-specific considerations that can alter the risk a given treatment might face when an exclusion is implemented. These include:

- **Patient mix** –Treatments with high volumes of new patient starts are more vulnerable to formulary exclusions given that patients already established on treatment are not likely to see their therapy disrupted by an exclusion.
- **Line of therapy** – Treatments focused on second- or third-line patients are likely to be eligible for medical exceptions, thus reducing the rate of rejections.
- **Treatment differentiation** – Some treatments are more easily managed when they are considered therapeutically equivalent to other therapies, making it easier for payers to consider and implement formulary restrictions.

TREATMENT INITIATION – A CASE STUDY IN METASTATIC BREAST CANCER

An oral metastatic breast cancer medication had been excluded from a payer's national formulary in 2020. Among plans that appear to follow the national

formulary, only 40% of new patient attempts were approved for treatment, 14 percentage points less than before the exclusion. While the brand had been restricted by prior authorizations and step therapies at this payer before the exclusion was implemented, most restrictions shifted to coverage blocks after the formulary change. In all other commercial payers, new patient approval rates for the excluded brand remained stable once the formulary exclusion was implemented.

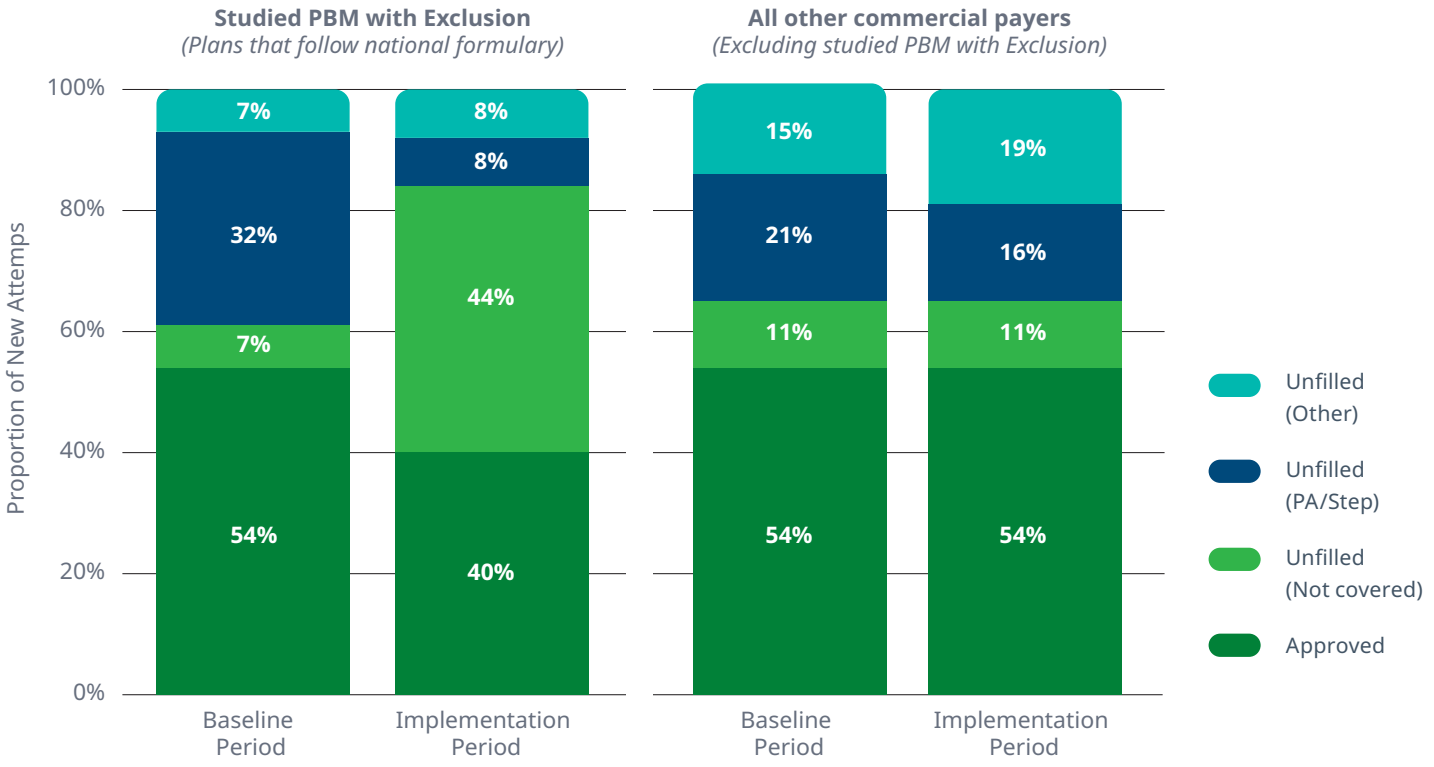
In this case, the payer's formulary exclusion resulted in a 14-percentage point reduction in new patient approvals for the blocked product. Though approval rates are also low – just barely over 50% – among other commercial payers, the plans following the national formulary exclusion have a 40% approval rate for the excluded product. In addition, a substantial proportion of new patient attempts were affected by NDC blocks after the exclusion, which would previously have been prior authorizations and step edits in the baseline period.

TREATMENT PROGRESSION - A CASE STUDY IN METASTATIC BREAST CANCER

Though formulary exclusions against medicines do not ban patients from treatment altogether, they still disrupt treatment adjudication. Moreover, not all patients move directly to the preferred alternatives, which is made evident by the disproportionate changes to demand following an exclusion. While this has been understood within retail markets for nearly a decade, these same patterns now appear in Oncology.

Of the patients that encountered a formulary exclusion and were unable to initiate treatment in the example above, very few proceeded to start therapy with the excluded brand after being rejected. The remaining patients were diverted to other treatments – mostly the excluded brand's preferred alternatives. Yet 17%

Figure 2 - Impact of formulary exclusion on therapy initiation (oral metastatic breast cancer brand, commercial, 2019-2020)

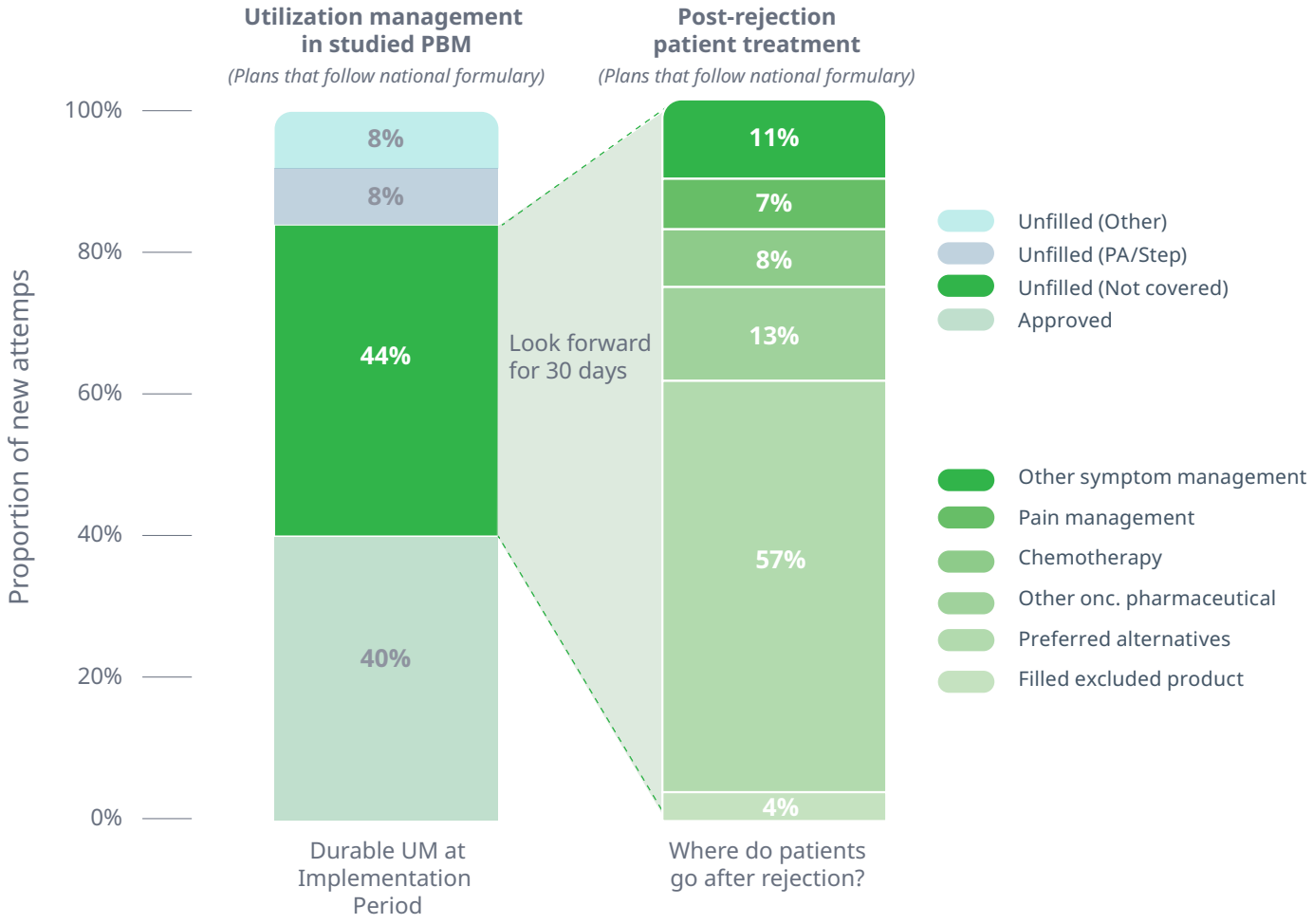


Note: Analysis is limited to new-to-brand prescriptions (NBRx) only. A 30-day look-forward period is applied after new attempts to account for rejection durability. Baseline period precedes January 2020 exclusion: Q1 2019 through Q3 2019. Implementation period follows January 2020 exclusion: Q1 2020 through Q2 2020. PA = Prior Authorization. Step = Step Therapy Restriction. **Source:** IQVIA LAAD Pharmacy Data, US Market Access Strategy Consulting Analysis, IQVIA

switched to a different, non-preferred pharmacy product altogether or pursued chemotherapy, instead. Another 13% filled only symptom and pain management prescriptions.

The impact of a not-covered rejection on patient treatment journeys will vary. Nevertheless, it is important for stakeholders to consider not only the impact an exclusion has on drug utilization, but also the impact on patient lives. Anti-cancer medications are essential treatments that may influence a patient's chance of survival. Even if a patient can switch to other suitable treatments, the disruption to therapy, especially if prolonged, may be impactful. Due to the nature of oncology prescriptions, key stakeholders must think of the potentially greater consequences a formulary exclusion in this sphere may have.

Figure 3 - Impact of formulary exclusion on therapy initiation (oral metastatic breast cancer brand, commercial, 2019-2020)



Note: Analysis is limited to new-to-brand prescriptions (NBRx) only. A 30-day look-forward period is applied after new attempts to account for rejection durability. Baseline period precedes January 2020 exclusion: Q1 2019 through Q3 2019. Implementation period follows January 2020 exclusion: Q1 2020 through Q2 2020. PA = Prior Authorization. Step = Step Therapy Restriction. **Source:** IQVIA LAAD Pharmacy Data, US Market Access Strategy Consulting Analysis, IQVIA

Discussion

As oncology product exclusions become more prevalent, key stakeholders need to understand and account for the effects that payer control may have on treatments that often play a life-or-death role for patients. It is increasingly common that physicians are unable to successfully write for their first-line treatment choice as payer control in oncology grows. As such, the industry as a whole must consider the potential impacts of these exclusions, including:

- **Impact on physician demand:** Providers may change their treatment recommendations in anticipation of control barriers
  - + Decreased provider prescribing of excluded oncology products
  - + Increased provider prescribing of preferred brand alternatives
  - + Less patient-centered approach to treatment selection
  - + Unwillingness to adopt new, more innovative, treatments
- **Impact on treatment initiation and progression:** Patients that encounter a formulary exclusion or other control may not end up with the originally intended treatment
  - + Decreased approval rates and increased rejection rates of excluded oncology products
  - + Delayed treatment initiation as control barriers are worked through
  - + Rejected patients switching to other, second choice, cancer treatments
  - + A subset of patients discontinuing cancer treatments altogether and turning to symptom management, instead

It is likely that payer control of oncology products will continue to grow. Current oncology exclusions are driven by payers, including the negotiated prices and therapeutic equivalence of the brands they contract with. It remains to be seen how ICER evaluations of anti-cancer drugs, as well as guidelines from the National Comprehensive Cancer Network (NCCN), may further encourage payers to utilize formulary exclusions. Additionally, continued vertical integration within the healthcare industry may spur organizations to focus on overall cost effectiveness and vertical integration between PBMs and payers that further facilitates control.

Formulary exclusions are one of several types of payer control that may become more prevalent for oncology products. Payers may directly influence access/reimbursement through Step Therapy/Prior Authorization requirements or in-network dispensing. Indirectly, payers may also influence treatment through clinical pathways and provider reimbursement. It will be important for key stakeholders to monitor the impact as payer control on oncology products continues to expand and change.

Manufacturers, specifically, should consider how their forecasts and strategies will need to adapt as payer controls expand. For oncology brands, this could require completely new business practices, particularly for tumor types that were uncontrolled until recently. Longitudinal patient studies to quantify and monitor payer control effectiveness is the necessary analytic foundation for ongoing strategy assessments that might include adjustments to payer contracting, pricing, and rebating, as well as patient support programs. As control continues to evolve across cancer treatments, manufacturers must be prepared to respond when these access challenges arise.

Appendix

Appendix 1: Number of national formulary exclusions by tumor type (top national payers, commercial insurance, oncology)

	2017	2018	2019	2020	2021
Chronic lymphocytic leukemia	2	2	3	5	5
Acute lymphoblastic leukemia	1	2	3	4	4
Acute myeloid leukemia					1
Multiple myeloma			2	3	8
Non-small cell lung cancer				2	3
Follicular lymphoma					6
Non-Hodgkin lymphoma				1	5
Gastrointestinal stromal tumor					1
Prostate cancer		1	4	10	9
Breast cancer			4	13	18
Myelofibrosis			1	1	1
Brain cancer			1		
Myelodysplastic syndrome					1

Note: One excluded product may count towards multiple tumor types if it has more than one indication. Top National Payers include Aetna, CVS Caremark, Cigna, Express Scripts (the PBM subsidiary of Cigna), OptumRx (the PBM subsidiary of UnitedHealthcare), and Prime Therapeutics. **Source:** Published national formularies; US Market Access Strategy Consulting Analysis, IQVIA

Appendix 2: Number of national formulary exclusions by mode of administration (top national payers, commercial insurance, oncology)

	2017	2018	2019	2020	2021
Oral	2	4	15	28	31
Subcutaneous				1	6
Intramuscular			1	2	2
Intravenous				6	23

Note: One excluded product may count towards multiple tumor types if it has more than one indication. Top National Payers include Aetna, CVS Caremark, Cigna, Express Scripts (the PBM subsidiary of Cigna), OptumRx (the PBM subsidiary of UnitedHealthcare), and Prime Therapeutics. **Source:** Published national formularies; US Market Access Strategy Consulting Analysis, IQVIA

References

1. In 2017, Gleevec and Tasigna were excluded in favor of generic treatments. By 2019, Verzenio, Ibrance, and Kisqali were excluded with competing brands preferred.

2. Aetna, CVS Caremark, Cigna, Express Scripts (the PBM subsidiary of Cigna), OptumRx (the PBM subsidiary of UnitedHealthcare), and Prime Therapeutics have consistently published their national formularies and also maintain historical records of their lists, facilitating the trend analysis of this paper.

3. Cross-benefit management refers to the integration of pharmacy and medical coverage such as sharing a deductible or treatment protocol.

4. White bagging is the process by which healthcare providers acquire physician-administered medicines through a specialty pharmacy that distributes and processes the drug portion of the claim as part of the pharmacy benefit. This is an alternative to the buy-and-bill model, in which providers purchase medicines and then bill the medical insurance benefit for the drug.

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Jing has more than six years of life science and biotechnology experience advising clients on market access insights and analytics. In the past few years, she has worked closely with clients to develop oncology market access specific tactics for pipeline, launch, and mature products across multiple tumor types, including supporting the development of extensive launch readiness strategies for a recent oral oncolytic launch. Jing holds a B.A. in Biology from Peking University, and a Master of Public Health in Epidemiology and Regulatory Affairs from Yale School of Public Health.

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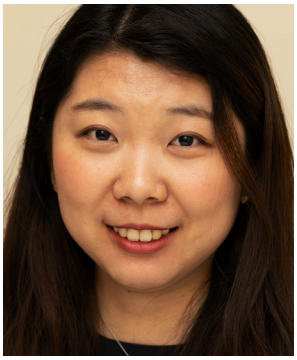

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