Provider Perspectives on Clinical and Non-Clinical Considerations in BTKi Selection

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Introduction

Bruton tyrosine kinase inhibitors (BTKis) have reshaped the management of B-cell malignancies such as chronic lymphocytic leukemia (CLL) and mantle cell lymphoma (MCL). While ibrutinib established the class, second-generation agents acalabrutinib, zanubrutinib, and pirtobrutinib have demonstrated improved selectivity and tolerability, prompting providers to evaluate BTKis through a more refined balance of efficacy, safety, and comorbidity considerations.[1]

However, BTKi use in practice is influenced by far more than clinical evidence alone. Providers operate within an increasingly complex environment shaped by payer restrictions, administrative burden, workflow limitations, specialty pharmacy disruptions, patient anxiety, and evolving federal policies such as the Inflation Reduction Act (IRA) and Maximum Fair Price (MFP).[2,3,4] These factors affect not only which BTKi is prescribed but how efficiently therapy can be initiated, monitored, and sustained.[5]

This white paper synthesizes findings from a national provider survey (n=96) to characterize the clinical and non-clinical considerations currently driving BTKi selection. It further illuminates the real-world dynamics shaping treatment choice and identifies opportunities to strengthen patient support, streamline operations, and anticipate policy changes that will influence access and prescribing in the years ahead.

Survey Overview

A comprehensive survey was conducted among oncology professionals working in community-based and medically integrated practice settings to better understand how BTKis are selected, managed, and supported throughout the patient treatment journey. Respondents included both physicians and pharmacists, representing the two clinical roles most directly involved in BTKi prescribing, patient counseling, toxicity management, and medication access navigation. Together, these professionals provide a broad, multidimensional view of how BTKis are used in real-world practice.

Participants practice within environments that routinely manage oral oncolytics internally, offering a valuable perspective on the clinical and operational realities associated with BTKi therapy. These settings also provide insight into how payer policies, workflow design, and patient experience influence therapeutic decision-making. Since physicians and pharmacists contribute to different stages of the care continuum and frequently collaborate on initiation, monitoring, and with class switching decisions, the survey was structured to reflect the nuances inherent to each role.

The survey consisted of thirty-five questions exploring a wide range of factors that shape BTKi decision-making. These included clinical considerations such as efficacy, tolerability, and comorbidity risk; patient-centered issues such as hesitancy, misunderstanding, and counseling needs; operational influences including prior authorization burden, documentation demands, and workflow disruption; and external pressures stemming from payer steering, limited distribution networks, and emerging federal pricing poli-

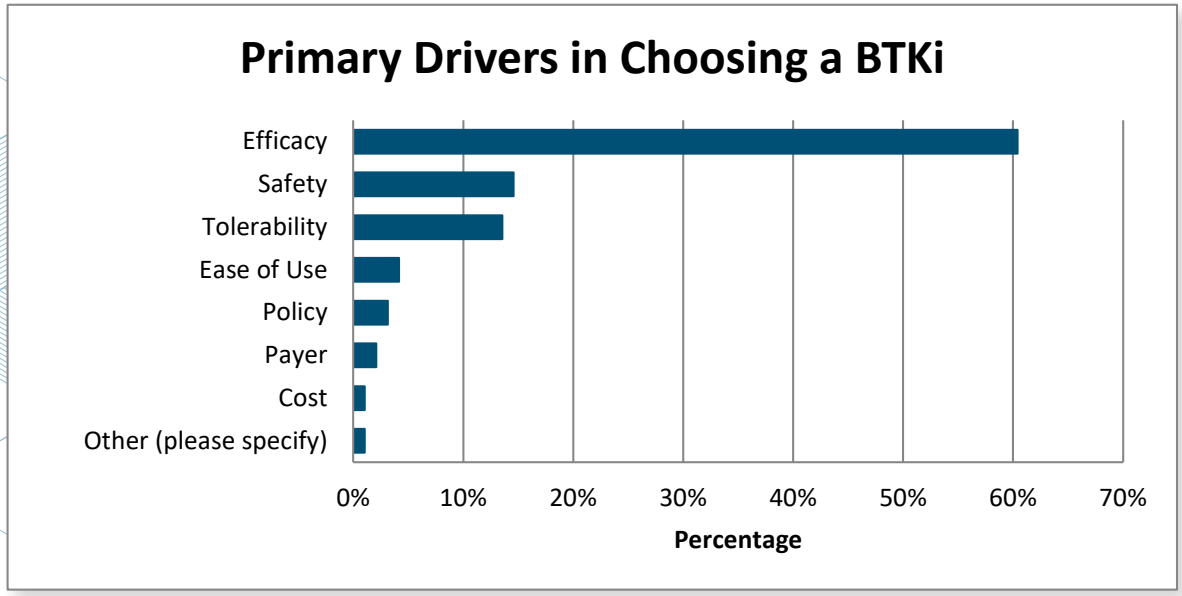


Figure 1. Providers most frequently identified efficacy as the leading determinant of BTKi choice, outweighing tolerability and safety considerations.

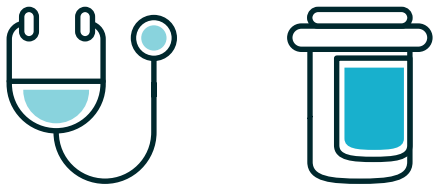
cies. The survey also examined how prepared physicians and pharmacists are to navigate anticipated changes in coverage requirements and formulary alignment as the reimbursement landscape evolves.

By analyzing physician and pharmacist responses separately, the survey offers a clear view of how these roles differ in their assessment of clinical risk, patient concerns, and access challenges. Physicians, who drive treatment initiation and switching decisions, often focus on clinical rationale and long-term outcomes. Pharmacists, who manage patient access, financial navigation, adherence monitoring, and toxicity reinforcement, bring a complementary perspective grounded in day-to-day patient interaction. Understanding these distinctions is key to appreciating how BTKi decisions are made collaboratively within practice settings.

Key Points:

- **96 oncology providers (60 MD/DO, 36 PharmD) surveyed across community-based and medically integrated practices.**
- **Survey included 35 questions covering clinical drivers, workflows, counseling, payer issues, and policy awareness.**
- **Role-based analysis highlights alignment and differences between physicians and pharmacists in BTKi decision-making.**

This paper includes survey insights from 96 respondents



60
Physicians

36
Pharmacists

Provider Demographics

The survey included 96 respondents, comprised of 60 physicians (62.5%) and 36 pharmacists (37.5%), all working within community oncology or medically integrated practices. More than 85% of participants reported practicing in settings with medically-integrated dispensing, enabling direct management of BTKis and reducing dependency on external specialty pharmacies. Over 70% indicated their practice structure supports rapid access to oral oncolytics, typically facilitated through coordinated workflows involving clinicians, pharmacists, and patient access teams.

Across professional roles, respondents described extensive hands-on involvement with BTKi therapy. Approximately 82% reported direct participation in treatment selection, including evaluating the need for initiation, switching due to intolerance, and adjusting therapy based on comorbidity profiles. Nearly 90% indicated routine responsibility for

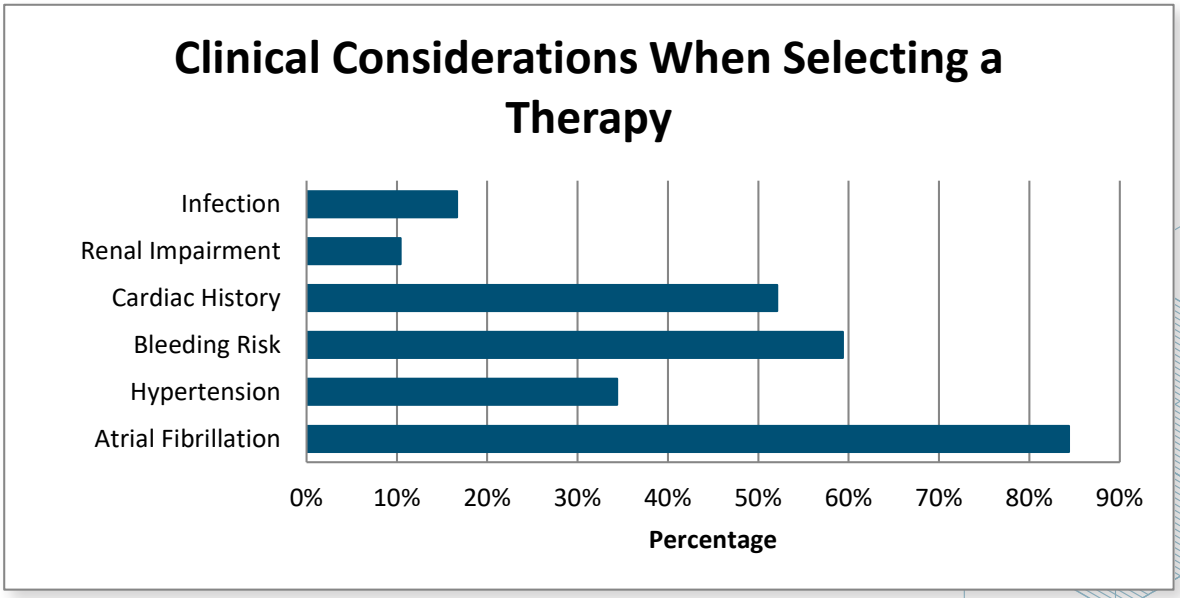


Figure 2. Cardiovascular-related risks were the most commonly cited comorbidities affecting BTKi selection, reflecting known toxicity differences across agents.

Provider Demographics *Cont.*

medication counseling, providing guidance on dosing, safety expectations, and management of early adverse events.

Adverse event monitoring was a common responsibility, with over 75% of physicians reporting frequent patient interactions related to cardiovascular symptoms, bleeding concerns, and blood pressure management. This aligns closely with the known toxicity risks of first- and second-generation BTKis. Monitoring was not limited to scheduled follow-ups; many respondents indicated involvement in between-visit triage and symptom escalation pathways.

Operational and access-related tasks were also widely reported. Roughly three-quarters of all respondents indicated direct involvement in prior authorizations, benefit investigations, appeals, or other payer navigation activities tied to BTKi prescribing. Moreover, over 60% highlighted challenges associated with insurance-driven dispensing restrictions, requiring additional coordination to maintain continuity of care.

Overall, the demographic profile reflects a respondent group with broad, high-intensity exposure to all facets of BTKi management from clinical decision-making to operational navigation.

Key Points:

- **Majority of respondents practice in community oncology settings with high engagement in BTKi initiation, monitoring, and access coordination.**
- **Over 80% reported direct involvement in treatment selection, counseling, and AE monitoring.**
- **~75% participate in prior authorizations, appeals, and payer navigation.**

Clinical Considerations in BTKi Selection

Clinical factors remain the dominant force shaping physician decisions around BTKi selection, and the survey data reinforce how strongly efficacy and tolerability define real-world practice patterns. A majority of both physicians and pharmacists identified efficacy as the primary driver of BTKi selection, with 68% of physicians and 69% of pharmacists ranking it as their top consideration. This alignment underscores the clinical focus on achieving durable disease control and minimizing progression risk.

Across the dataset, 47% of all respondents reported that they believe one BTKi offers a meaningful clinical advantage over others, while 27% were unsure. Among those who did identify a superior agent, zanubrutinib was most frequently selected, endorsed by 84% of respondents, followed by acalabrutinib (34%), pirtobrutinib (17%), and ibrutinib (10%). Role-stratified data mirrored this trend: among respondents who felt one agent was superior, 82% of physicians and 89% of pharmacists selected zanubrutinib as their clinically preferred BTKi.

Comorbidity risk strongly influenced BTKi selection. Physicians consistently identified cardiovascular-related concerns as the most influential comorbidity domains with hypertension selected by 55–56%, atrial fibrillation by 33–41%, and bleeding risk by approximately 7–10% of respondents across roles.

These patterns closely align with the known off-target toxicities of earlier BTKis and help explain the preference shift toward more selective next-generation inhibitors.

Tolerability represented a second major driver, particularly among pharmacists. While tolerability was ranked primary by 19% of pharmacists versus 12% of physicians, nearly all respondents emphasized minimizing adverse events as critically important when choosing between BTKis. Additionally, most participants (76%) reported that they "always" or "sometimes" consider switching to an alternative BTKi when a patient is intolerant but not progressing. These findings align with survey data showing that 73% of physicians and 83% of pharmacists would switch a clinically stable patient due to tolerability issues.

Physicians also showed increasing comfort with the concept that switching between BTKis can restore tolerability without compromising disease control. The broader survey results reinforce this, indicating that second-generation agents are favored when toxicity emerges, and that physicians view agent selectivity and cardiovascular risk reduction as core components of clinical decision-making.

Overall, the survey demonstrates that BTKi selection is shaped by a combination of high-priority clinical drivers, including efficacy, safety, and comorbidity risk, along with practical experience related to patient tolerance and sustained treatment adherence. Both physicians and pharmacists rely on comparative real-world outcomes, evolving trial evidence, and firsthand observations of treatment interruptions to guide clinical decisions, ultimately prioritizing therapies that balance strong disease control with manageable side-effect profiles.

Key Points:

- **Efficacy was the top driver for 68% of physicians and 69% of pharmacists; zanubrutinib most often viewed as superior.**
- **Tolerability and comorbidity risks (AFib, bleeding, hypertension) strongly shape agent choice.**
- **73% of physicians and 83% of pharmacists would switch stable patients to another BTKi for tolerability concerns, reflecting real-world experience.**

Patient Perspectives and Counseling in BTKi Selection

Patient perspectives play a decisive role in whether BTKi therapy is initiated or successfully transitioned. Findings from the NCODA Member Insights Survey highlight that patient hesitation driven by fear, uncertainty, cost concerns, and limited understanding often shapes real-world treatment pathways as strongly as clinical evidence or payer policy. Physicians across roles emphasized that even when a BTKi switch is clinically warranted, patients frequently approach the decision with ambivalence or anxiety, requiring substantial education, reassurance, and multidisciplinary support.

Patient Hesitancy and Emotional Barriers

Survey responses showed that hesitancy is a widespread and consistent challenge. When asked to identify the most common patient barriers to BTKi initiation or switching, both physicians and pharmacists overwhelmingly cited fear of leaving a therapy perceived as "working." This sentiment was reported by 67% of physicians and 75% of pharmacists, reflecting the deep psychological connection many patients develop to their current regimen. In chronic conditions such as CLL, patients often equate treatment stability with disease control, even when tolerability concerns suggest a safer or more effective alternative is available.

Anxiety about unknown or anticipated side effects further contributes to reluctance. More than 52% of pharmacists reported that patients frequently express fears about cardiovascular events, bleeding, fatigue, or general intolerance with a new BTKi. Physicians noted that this fear can delay treatment changes, even in cases where continuing the current therapy poses ongoing risk.

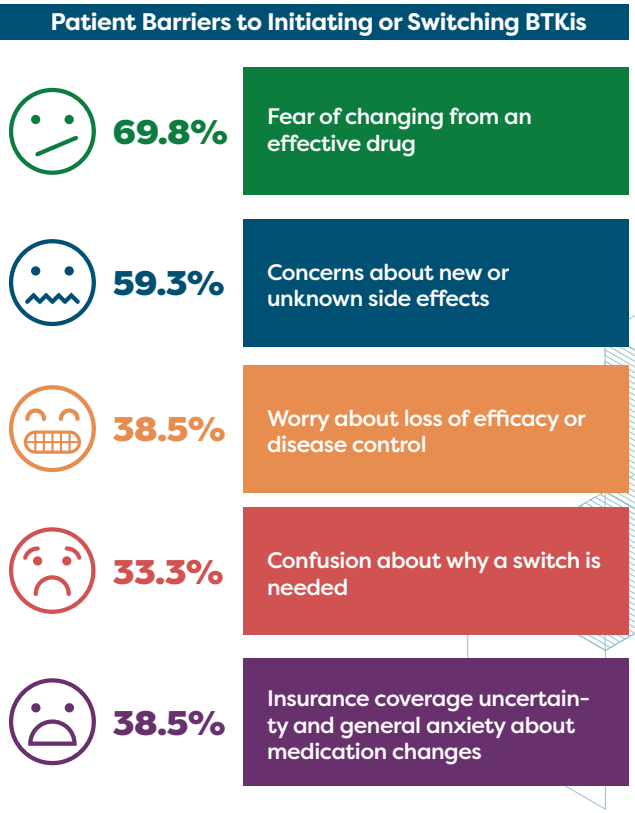
Confusion surrounding the rationale for switching is also common. According to the survey, 30% of physicians and 39% of pharmacists indicated that patients struggle to understand why a switch is clinically recommended. Patients may misinterpret a change in therapy as an indication of disease progression rather than a proactive measure to address toxicity or reduce future complications. Without clear explanation, this misunderstanding can create mistrust or resistance, particularly in patients who have lived with long-term stability.

Figure 3. Fear of leaving a stable therapy, anticipated adverse events, and uncertainty about treatment rationale were the most frequently reported patient obstacles.

Financial Concerns and Insurance-Driven Anxiety

Financial uncertainty emerged as another significant barrier, especially among pharmacists who are often responsible for coordination of benefits, prior authorizations, and patient financial assistance. Survey responses indicated that 44% of pharmacists encountered frequent patient concerns about copay increases, formulary changes, or disruptions associated with payer steering. Even when coverage remains stable, patients often anticipate higher costs or administrative hurdles when transitioning to a different medication.

These financial worries compound emotional reluctance. Patients who previously experienced difficulty obtaining oral oncolytics, whether due to limited distribution restrictions, PBM specialty pharmacy delays, or inconsistent copays, may assume that switching therapy will recreate these burdens. Importantly, physicians emphasized that a change in therapy does not necessarily translate to higher patient costs, as many second-generation BTKis have comparable copay structures, robust financial-assistance programs, and, in some cases, more predictable insurance coverage than older agents. Also, physicians reported that these perceptions sometimes overshadow the clinical advantages of alternative BTKis, making financial navigation support essential to successful treatment transitions.



Emotional Impact and Perceived Threat to Stability

Physicians emphasized that BTKi switching discussions often trigger a broader emotional response beyond clinical or financial concerns. Patients may fear losing control, worsening disease, or destabilizing a routine that has become psychologically comforting. Physicians described instances in which patients interpreted a recommended switch as a sign that their cancer was "getting worse," even when switching was motivated solely by avoidable toxicity.

This emotional dimension is rarely captured in clinical trial endpoints but is central to real-world acceptance and adherence. Physicians reported that these reactions often emerge gradually across multiple encounters and require consistent messaging from both physicians and pharmacists to build confidence.

Counseling Demands and the Need for Enhanced Education

The survey revealed a substantial need for expanded patient education resources. 70% of physicians and 61% of pharmacists indicated they require moderate to extensive tools to support BTKi counseling. These resources are essential not only to correct misconceptions but also to help patients navigate the emotional, financial, and logistical aspects of therapy initiation or transition.

Physicians typically prefer materials that support efficient, evidence-based communication. They expressed the greatest need for concise talking points, simple explanations of comparative toxicity, and clear risk–benefit framing to help patients understand the clinical rationale behind switching. Physicians noted that patients respond best when information is direct, digestible, and tied to long-term health outcomes.

Pharmacists, who interact with patients at numerous touchpoints throughout the treatment journey, emphasized the need for structured, repeatable, and visually oriented materials. They requested handouts, charts, dosing calendars, symptom-tracking tools, and medication summaries that can be used in initial education and follow-up adherence calls. Pharmacists highlighted that many patient concerns resurface days or weeks after the initial conversation, and consistent materials reinforce comprehension and build confidence over time.

Impact of Counseling on Adherence and Persistence

67% of physicians and 81% of pharmacists described BTKi counseling as moderately challenging. These findings suggest that the difficulty arises from more than clinical complexity; it reflects a convergence of emotional distress, financial uncertainty, and anxiety surrounding treatment. Physicians underscored that early follow-up during the first weeks of BTKi therapy is critical: patients who receive proactive, coordinated outreach from physicians, pharmacists, and nursing teams show improved adherence and reduced anxiety.

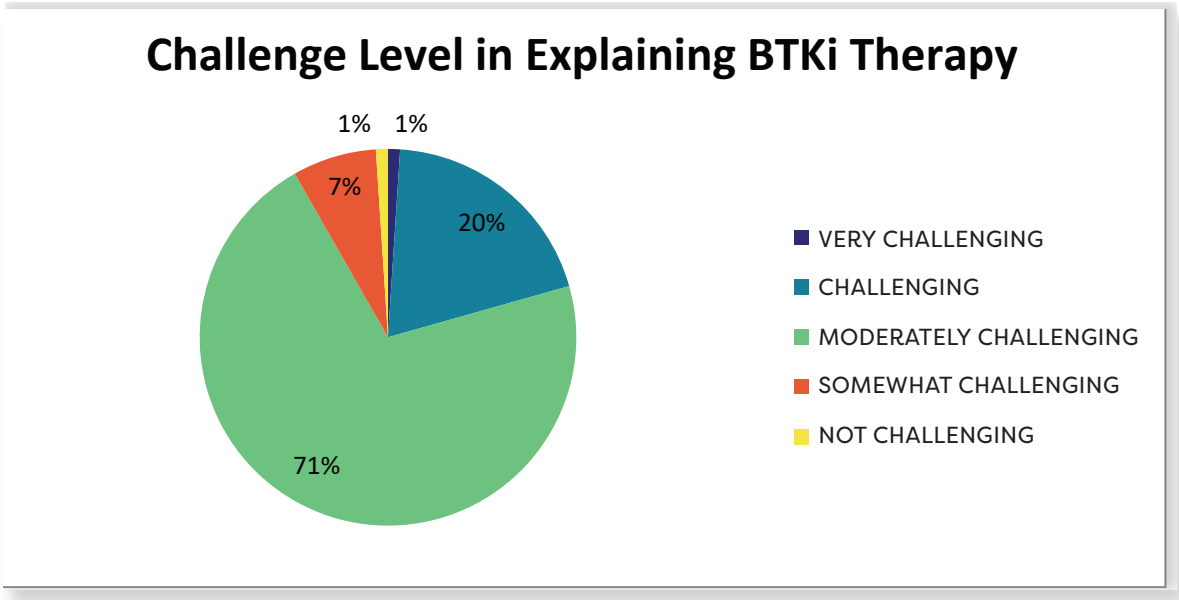


Figure 4. Most providers described BTKi counseling as moderately challenging due to therapeutic complexity and patient anxiety.

The Role of Multidisciplinary Reinforcement

The collective insights from the survey underscore the necessity of a multidisciplinary approach to BTKi education. Physicians anchor discussions in clinical evidence, while pharmacists reinforce practical considerations including access, financial support, and toxicity management. Cooperative reinforcement of key messages was repeatedly identified as essential for building trust and promoting adherence. Physicians emphasized that without unified communication, patients may perceive conflicting information and become more hesitant.

The survey findings reveal that patient counseling is not an isolated task but a longitudinal process requiring repeated engagement, clarity, and empathy. Through coordinated physician–pharmacist communication, consistent educational materials, and structured follow-up, medically integrated oncology practices are well positioned to support successful BTKi initiation and long-term persistence.

Key Points:

- **Fear of switching, anxiety about toxicity, and confusion about rationale are key barriers to BTKi acceptance.**
- **70% of physicians and 61% of pharmacists need additional patient education tools to support adherence.**
- **Patient understanding strongly influences adherence, early tolerance, and successful therapy switching.**

Non-Clinical Factors Shaping BTKi Selection

Beyond clinical considerations, non-clinical influences emerged as a powerful driver of BTKi selection in real-world practice. Survey results indicate that physicians are increasingly attentive to the evolving policy and payer environment, particularly as new federal pricing reforms and commercial payer trends create uncertainty around future access. These external pressures are reshaping the operational landscape for both physicians and pharmacists and are expected to exert growing influence on BTKi decision-making.

A notable finding from the survey was the difference in awareness of federal pricing reforms, including the Inflation Reduction Act (IRA) and Maximum Fair Price (MFP) provisions. Pharmacists demonstrated higher familiarity, with 14% reporting they were extremely familiar with IRA/MFP policy changes, compared with 7% of physicians who indicated the same level of knowledge. Under the IRA, ibrutinib is one of the first oncology drugs scheduled to receive a Maximum Fair Price in 2026, placing it under federal negotiation and altering Medicare reimbursement. As MFP pricing begins to influence commercial payer behavior, both physicians and pharmacists anticipate shifts in formulary design, preferred product status, and potential restrictions on BTKi selection. Physicians expressed concern that these reforms may ultimately narrow therapeutic options, particularly for patients requiring specific agents based on comorbidities or intolerance.[4]

The survey also underscored growing apprehension regarding commercial payer behavior. Across respondents, there was broad expectation that commercial insurers will even-

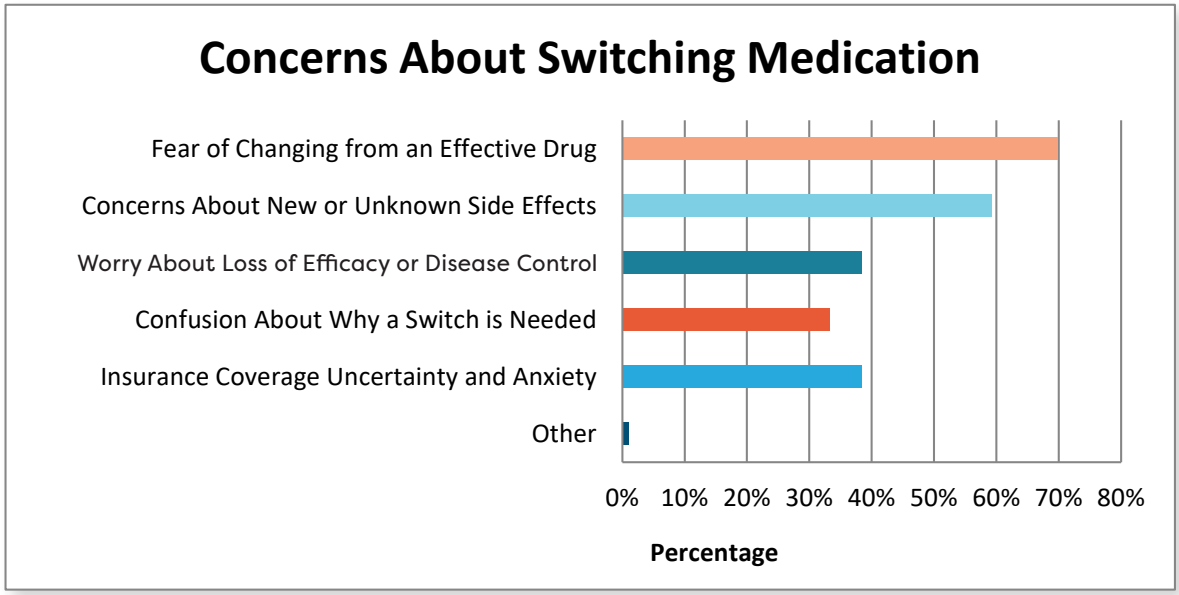


Figure 5. Side-effect worry, perceived loss of disease control, and coverage concerns were the dominant themes driving patient reluctance to switch BTKi therapy.

tually align with Medicare once MFP pricing takes effect. This expectation was more pronounced among physicians, 70% of whom anticipated commercial alignment, compared with 50% of pharmacists. Physicians reported that such alignment could have substantial downstream consequences, including narrowing of BTKi formularies, increased step-therapy requirements, and heightened justification for continued use of specific agents. These dynamics may create a treatment environment where payer preference, rather than clinical reasoning, increasingly dictates which BTKi a patient receives.

Operational strain represents an even more universally acknowledged non-clinical factor. Survey data show that nearly all respondents expect administrative burden to increase, with 90% of physicians and 86% of pharmacists anticipating rising documentation requirements and access hurdles. Physicians cited multiple drivers of this increased workload: expanded prior authorization processes, more complex step-therapy protocols, an uptick in appeals and resubmissions, and frequent modifications to EMR order sets to reflect shifting payer mandates. Many respondents noted that these operational pressures divert time and attention away from direct patient care and may delay therapy initiation, particularly for patients requiring rapid access to treatment.

Physicians also emphasized that administrative burden disproportionately affects pharmacists, who manage the majority of access-related communications. Pharmacists described encountering frequent interruptions to workflow as they navigate payer steering, reconcile conflicting formulary rules, and resolve repeated documentation requests. Physicians, while closely involved in clinical justification, rely on pharmacists and access specialists to coordinate the substantial administrative lift required to secure and maintain BTKi therapy.

Collectively, these non-clinical factors illustrate a treatment environment that is becoming increasingly shaped by external forces rather than purely clinical considerations. Awareness of federal pricing reform, anticipation of commercial payer alignment, and concern over growing administrative workload all contribute to a sense that BTKi selection will become more constrained and documentation-heavy in the years ahead. Physicians across roles recognize that future BTKi decisions will require not only clinical judgment but also a deep understanding of payer expectations, policy shifts, and workflow implications.

Key Points:

- **Pharmacists showed greater familiarity with IRA/MFP policy changes; Physicians expressed more concern about access restrictions.**
- **70% of physicians vs 50% of pharmacists anticipate commercial payers aligning with Medicare pricing rules.**
- **Nearly all providers expect increased administrative burden due to prior authorization expansion, step therapy, and documentation demands.**

Conclusion

BTKi selection occurs at the intersection of clinical data, patient experience, operational realities, and payer pressures. Physicians contribute deep therapeutic insight, while pharmacists bring expertise in safety, access, and adherence. Together, their combined perspectives shape a comprehensive, patient-centered approach to BTKi decision-making.

As the marketplace evolves, practices must prepare for increasing administrative complexity, payer-driven restrictions, and heightened patient anxieties. Medically integrated practices are uniquely positioned to lead through education, workflow innovation, and advocacy to protect access to optimal BTKi therapy.

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