ORIGINAL RESEARCH

Realized and Projected Cost-Savings from the Introduction of Generic Imatinib Through Formulary Management in Patients with Chronic Myelogenous Leukemia

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BACKGROUND: Imatinib, a first-generation tyrosine kinase inhibitor (TKI), and the newer second-generation TKIs have dramatically improved outcomes for patients with chronic myelogenous leukemia (CML). A previous model estimated the potential cost-savings over the next 2 years after the loss of patent exclusivity for imatinib in the United States in 2016 and its availability in a generic form. Payers have indeed realized meaningful savings, but it took 2 years for the prices of generic imatinib to decline substantially.

OBJECTIVE: To quantify the cost-savings for a US health plan from the passive substitution of generic imatinib and the impact of step-edit therapy with the use of generic imatinib before coverage of a second-generation TKI.

METHODS: We updated the previously published model utilizing hypothetical 1-million-member commercial and Medicare plans to include current TKI use and pricing combined with recent epidemiologic data. Regression models were used to project utilization to 5 years after the loss of imatinib’s patent exclusivity. We compared generic imatinib costs with a scenario in which generic imatinib was not available. The impact of a step-edit therapy restriction was explored for patients with incident CML. The analyses were repeated for the entire US population based on national census data.

RESULTS: The 1-million-member commercial plan saved $0.5 million (3%) from pharmacy spending on TKIs in year 1 and $3.9 million (19%) in year 2 after the loss of patent exclusivity. The projected savings significantly increased to $7.8 million (37%), $8.3 million (39%), and $8.6 million (40%) in years 3, 4, and 5, respectively. Step-edits were projected to result in small incremental savings of $0.3 million (1.5%) annually in years 3 to 5. The 1-million-member Medicare plan saved $1.7 million (3%) in year 1 and $14.1 million (19%) in year 2. The projected savings were $27.8 million (37%), $29.5 million (39%), and $30.8 million (40%), with step-edit estimated to add only $0.9 million (1.2%) annually in years 3 to 5. Generic imatinib saved US payers $2.5 billion (13% of the total spending on TKIs) in years 1 and 2. In years 3 to 5, the cumulative projected savings totaled $12.2 billion, and the savings were expected to grow to 39% as a result of passive generic imatinib substitution, with only 1.7% additional savings from step-edit restriction.

CONCLUSIONS: As a result of a lower price for generic imatinib relative to the brand-name version of the drug, substantial cost-savings to US payers over the next 3 years are expected without step-edit formulary management restrictions. Cost-saving strategies, including formulary management restrictions, should adhere to evidence-based guidelines to ensure the appropriate use of generic imatinib and all available TKIs, with the objective to maintain positive outcomes and, in turn, increase the value of patient care.

KEY WORDS: chronic myelogenous leukemia (CML), cost-savings, formulary management, generic imatinib, pharmacy spending, prior authorization, step-edits, tyrosine kinase inhibitors (TKIs)
KEY POINTS

➤ The availability of first- and second-generation TKIs improved outcomes for patients with chronic myelogenous leukemia (CML).
➤ This study updated a previous model with hypothetical 1-million-member commercial and Medicare plans to quantify savings after imatinib’s loss of patent exclusivity.
➤ The commercial plan saved $0.5 million (3%) of the pharmacy spending on TKIs in year 1 and $3.9 million (19%) in year 2 after the loss of patent exclusivity.
➤ These savings were projected to increase to $7.8 million (37%), $8.3 million (39%), and $8.6 million (40%) in years 3, 4, and 5 of generic imatinib on the market.
➤ The use of step-edit therapy was estimated to result in incremental cost-savings of $0.3 million (1.5%) annually in years 3, 4, and 5.
➤ The use of generic imatinib saved payers $2.5 billion in years 1 and 2 and was projected to lead to $12.2 billion in cumulative savings in years 3 to 5.
➤ In the next 3 years, the estimated savings are expected to grow to 38.5% as a result of passive generic imatinib substitution, with only 1.7% additional savings from step-edit restriction.
➤ Cost-saving strategies initiated by payers should adhere to evidence-based guidelines to ensure that TKIs are used properly and increase value-based care.
➤ Initiatives that improve medication adherence, meet guideline recommendations, and optimize treatment selection could lower the costs of care and improve patient outcomes.

C hronic myelogenous leukemia (CML) is a hematologic malignancy occurring primarily in adults, with a median age of 65 years at diagnosis.1 The overall age-adjusted incidence rate of CML was approximately 2.04 per 100,000 individuals in 2016, and it is estimated that 8990 new cases of CML will be diagnosed in 2019 in the United States.1 CML is caused by a translocation of the breakpoint cluster region (BCR) gene on chromosome 22 and the Abelson (ABL) oncogene on chromosome 9, creating a shortened chromosome 22 known as the Philadelphia chromosome (Ph).2 This forms the BCR-ABL fusion gene that produces a tyrosine kinase protein (BCR-ABL oncoprotein), which causes abnormal proliferation of myeloid cells.3

The US Food and Drug Administration (FDA) approval of imatinib, the first-generation tyrosine kinase inhibitor (TKI) targeting the BCR-ABL fusion gene, dramatically changed the treatment landscape for CML and significantly improved survival outcomes for patients with this disease. Patient care has further advanced with the FDA approval of second-generation TKIs, which, along with imatinib, have prolonged survival in patients with chronic-phase CML to approach that of age-matched controls.4

Currently, 4 TKIs are FDA approved for front-line therapy of chronic-phase CML, including imatinib, dasatinib, nilotinib, and bosutinib.4-8 Ponatinib is indicated for patients with refractory disease and for a small subset of patients with T151-positive CML.9 Although imatinib is the most prescribed agent in the front-line setting, several factors must be considered when selecting the proper TKI therapy for patients with CML, including disease risk level, CML mutation type, individual TKI toxicity profile and the potential interaction with the patient’s comorbidities, speed to cytogenetic response targets, and ease of administration.10

The current National Comprehensive Cancer Network (NCCN) CML guidelines recommend that the choice of a TKI for first-line therapy be based on the patient’s risk disease level in concert with these additional factors, with all approved agents as Category 1 recommendations (indicating the highest level of evidence) for patients with low-risk disease and second-generation TKIs (ie, dasatinib, nilotinib, and bosutinib) retaining Category 1 recommendation status for intermediate- and high-risk disease.1 Notably, in the absence of treatment initiation within the chronic phase, the natural course of CML follows a triphasic progression from the indolent chronic phase to an accelerated phase, in which the disease takes on aggressive features, such as cytogenetic abnormalities, and ultimately on to a terminal blast crisis, in which blast cells proliferate uncontrollably.1 Patients in the terminal blast crisis phase of CML may require advanced high-cost care, including stem-cell transplant for eligible patients.4

Since the loss of patent exclusivity and the entry of a generic version of imatinib in the United States in February 2016, US payers have started realizing cost-savings; however, generic prices have taken 2 years to decline substantially. A previous study estimated the projected impact of the entry of generic imatinib in the first 2 years from the perspective of a US payer based on projected prices using an Excel-based model.11 This model, which used market share and pricing projections before imatinib’s loss of exclusivity, estimated that the 2-year cost-savings would be $6.8 million (28.8%) in a commercial plan and $22.9 million (28.8%) in a Medicare plan. The adoption of step-therapy formulary manage-
ment was expected to lower incremental TKI spending nominally, by 1.1% and 2.2% for the commercial and Medicare plans, respectively.

In the 2 years since imatinib’s loss of patent exclusivity, real-world market share and pricing information have become available, and modeling assumptions should be updated to reflect this reality. In the present analysis, we updated the model to evaluate the realized and projected impact of generic imatinib and the impact of step-edit formulary management on cost-savings over a 5-year period from imatinib’s loss of exclusivity.

Furthermore, we examined and quantified, from a US health plan perspective, the cost-savings from the substitution of brand-name imatinib with generic imatinib relative to the potential savings from requiring step therapy through generic imatinib before a second-generation TKI. We assessed these savings for a hypothetical 1-millon-member commercial plan and a 1-million-member Medicare plan and at a US national level for all commercially and Medicare-insured patients.

**Methods**

We updated the previously published model exploring the impact of brand-name imatinib’s loss of patent exclusivity and the formulary management of TKIs to reflect the current real-world use and pricing of TKIs. The Excel-based model represented the pharmacy budget of hypothetical 1-million-member commercial and Medicare plans for the TKIs that are indicated for the treatment of CML (ie, imatinib, dasatinib, and nilotinib).

The cost-savings were calculated over a 5-year period as the realized savings accrued by payers since imatinib’s loss of patent exclusivity to the most recent data available at that time (February 2016-September 2018) and the projected future savings (2018-2021). Using the same methods, we repeated the analyses for the entire commercially and Medicare-covered population in the United States to estimate the overall pharmacy cost-savings for TKIs at a national level.

**Market Share**

We fitted logarithmic regression models to historical market share data to project the use of brand-name TKIs and generic imatinib up to 5 years after imatinib’s loss of patent exclusivity (Figure 1). Similar to the original model, TKIs with <5% market share were not considered, which included ponatinib and bosutinib. Market share was calculated based on observed trends and did not include the potential changes among second-generation TKIs that might have occurred in the absence of generic imatinib’s entry into the market after the loss of exclusivity of brand-name imatinib.

**Costs**

We used historical wholesale acquisition cost pricing for the period between January 2016 and September 2018. The daily drug costs in September 2018 for brand-name imatinib, generic imatinib, dasatinib, and nilotinib were $337, $12, $430, and $455, respectively. The daily drug costs assume standard first-line CML starting doses per the respective drug’s prescribing information. Future drug prices were assumed to remain constant from September 2018 to the end of the model’s time horizon (ie, February 2021); the lowest price among generic imatinib manufacturers for the 400-mg dose was used.

The default patient copay values were based on the average patient out-of-pocket costs for dispensed claims for commercial and Medicare members. The default co-
Table

<table>
<thead>
<tr>
<th>Health plan type</th>
<th>Patients aged 18-64 years</th>
<th>Patients aged ≥65 years</th>
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<td>Estimate (N)</td>
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<td>Prevalence of TKI use for CML</td>
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<td>Age distribution</td>
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<td>Prevalence of TKI use for CML</td>
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CML indicates chronic myelogenous leukemia; TKI, tyrosine kinase inhibitor.

Results

Commercial Plan of 1 Million Members

In our new analysis, a commercial plan with 1 million members was estimated to save $0.5 million (3%) of the TKI pharmacy budget for CML in the first year and $3.9 million (19%) in the second year after imatinib’s loss of patent exclusivity (Figure 2).

The projected savings from generic imatinib entry alone (ie, without step-edit formulary management) increased significantly to $7.8 million (37%), $8.3 million (39%), and $8.6 million (40%) in the third, fourth, and fifth years, respectively, after the loss of patent exclusivity (Figure 2), and continued to result in significantly greater projected savings than the initiation of step-edit therapy during that same time period (Figure 3). Initiating a step-edit therapy for treatment-naïve patients with CML in the commercial plan was associated with limited projected incremental savings of $0.3 million (1.5%) annually over the next 3 years (years 3, 4, and 5).

Medicare Plan of 1 Million Members

We estimated that a Medicare plan with 1 million members saved $1.7 million (2.5%) of the TKI pharma-

Model Population

Commercial and Medicare plan analyses assumed a hypothetical 1-million-member population each. The population of the US national level analyses included 216,203,000 commercial insurance enrollees and 53,372,000 Medicare enrollees (US census data). We analyzed the prevalence based on claims data in the Truven MarketScan database and estimated the size of the patient population who received a TKI by applying these age-stratified (18-64 years; ≥65 years) prevalence rates to the hypothetical plan. Data on the incidence and prevalence of CML were taken from surveillance, epidemiology, and end results cancer statistics review, and all incident cases of CML were assumed to be managed with a TKI.

In our hypothetical commercial and Medicare 1-million-member plans, the numbers of patients with CML receiving treatment with TKIs were estimated to be 96 and 289, respectively, with 11 (11.6%) patients in the commercial plan and 74 (25.5%) patients in the Medicare plan estimated to have newly diagnosed CML.

We assumed the prevalence of CML to be constant over time, and the standard TKI dose and frequency were based on the prescribing information for the treatment of newly diagnosed patients with Ph-positive chronic-phase CML. Patients were assumed to continue using therapy and to be fully adherent to the therapy during the entire year. The prevalence of TKI treatment that is indicated for use in patients with CML was consistent with the previously published model (Table).
Figure 2 Incremental Cost-Savings on TKI Spending with Step-Edit Therapy in a 1-Million-Member Plan Before and After Loss of Patent Exclusivity for Brand-Name Imatinib

<table>
<thead>
<tr>
<th>Year</th>
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<th>Medicare plan</th>
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<td>Year 1</td>
<td>19.7</td>
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<td>Year 4</td>
<td>16.5</td>
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<td>Year 5</td>
<td>21.3</td>
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**NOTE:** The slight increase in the scenario without imatinib LOE can be attributed to the market share trends that are expected to occur between 2018 and 2021. During that time, the combined market share of dasatinib plus nilotinib is expected to increase from 41.9% to 43.9%.

Commercial and Medicare health plans.

The results presented here have been rounded to the nearest hundred thousand dollars.

LOE indicates loss of exclusivity; TKI, tyrosine kinase inhibitor.

Figure 3 Trends in Total Costs of TKI Treatment with and without the Generic Imatinib Entry and Step-Edit Formulary Management in a 1-Million-Member Commercial Plan

<table>
<thead>
<tr>
<th>Year</th>
<th>Commercial plan</th>
<th>Medicare plan</th>
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<td>Jan 2016</td>
<td>1,000,000</td>
<td>1,000,000</td>
</tr>
<tr>
<td>Apr 2016</td>
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<td>Jul 2016</td>
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<tr>
<td>Oct 2016</td>
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<td>1,600,000</td>
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<td>Jan 2017</td>
<td>1,800,000</td>
<td>1,800,000</td>
</tr>
<tr>
<td>Apr 2017</td>
<td>2,000,000</td>
<td>2,000,000</td>
</tr>
<tr>
<td>Jul 2017</td>
<td>1,800,000</td>
<td>1,800,000</td>
</tr>
<tr>
<td>Oct 2017</td>
<td>1,600,000</td>
<td>1,600,000</td>
</tr>
<tr>
<td>Jan 2018</td>
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<td>Apr 2018</td>
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<tr>
<td>Jul 2018</td>
<td>1,000,000</td>
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<tr>
<td>Oct 2018</td>
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<td>800,000</td>
</tr>
<tr>
<td>Jan 2019</td>
<td>600,000</td>
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<td>Apr 2019</td>
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<td>Jan 2020</td>
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**A**The monthly costs of the commercial plan only are presented here. The overall monthly costs trends of the Medicare plan were similar to the commercial plan but had a different magnitude, reflecting the difference in the size of the population with chronic myelogenous leukemia.

TKI indicates tyrosine kinase inhibitor.
cy budget for CML in the first year and $14.1 million (19%) in the second year after imatinib’s loss of patent exclusivity (Figure 2). The projected cost-savings from generic imatinib entry alone (without step-edit formulary management) significantly increased to $27.8 million (37%), $29.5 million (39%), and $30.8 million (40%) in the third, fourth, and fifth years, respectively, after the loss of exclusivity (Figure 2).

Initiating a step-edit therapy for newly diagnosed patients with CML in the Medicare plan was again associated with projected small incremental savings of $0.9 million (1.2%) annually over the next 3 years (years 3, 4, and 5).

Overall Spending and Savings
We calculated that in the first 2 years of generic imatinib’s entry, US payers saved $2.5 billion—12.6% of the total spending on this drug class. In the next 3 years, the estimated savings with generic imatinib entry and without formulary management strategies are expected to grow to 38.5%, resulting in additional savings of $3.8 billion, $4.1 billion, and $4.2 billion in years 3, 4, and 5, respectively, for a cumulative savings of $12.2 billion (rounded numbers).

Furthermore, over the 5-year period, the estimated savings are expected to total $15 billion in the absence of step-edit formulary management. In fact, nearly all potential savings for this drug class over the next 3 years (years 3, 4, and 5 from imatinib’s loss of exclusivity) come from generic imatinib’s market entry alone, with limited additional savings from step-therapy formulary management estimated to be 1.7% (or $176 million) annually.

Discussion
In 2015, a hypothetical model that estimated the economic impact of the availability of generic imatinib for payers in the United States forecasted that the loss of patent exclusivity would result in >$6 million in savings for a 1-million-member commercial plan during a 2-year period, or 28.8% of the total pharmacy spending on TKIs for the treatment of CML.10 The forecasted savings were even greater in the 1-million-member Medicare plan ($22.9 million, or 28.8%) as a result of higher TKI utilization rates.10 This current update to the original model, using real-world market share and pricing data, reveals that the savings for commercial and Medicare plans were slower to accumulate within the first 2 years after loss of patent exclusivity than was originally forecasted (a total of $4.4 million and $15.8 million, respectively).

The reduction in plan savings during the first 2 years is attributed to higher-than-anticipated pricing for generic imatinib, but its price has steadily decreased and continues to decline. Furthermore, continued price reductions for generic imatinib resulting from competition from additional market entrants have progressed to a 96% price discount from the brand-name drug at the time of this current analysis. This large discount is expected to result in substantial cost-savings to US payers that are expected to materialize over the next 3 years, independent of step-edit formulary management strategies.

Based on the current projections for a 1-million-member commercial plan, savings from generic imatinib’s entry (and without step-edit formulary management) are estimated to significantly increase to $7.8 million (37%), $8.3 million (39%), and $8.6 million (40%) in the third, fourth, and fifth years, respectively, after the loss of patent exclusivity. For a 1-million-member Medicare plan, the projected savings from generic imatinib’s entry (and without step-edit formulary management) are now estimated to significantly increase to $27.8 million (37%), $29.5 million (39%), and $30.8 million (40%), respectively, in the third, fourth, and fifth years after the loss of patent exclusivity. Similar to the initial analysis by Bloudek and colleagues,11 the projected incremental savings through the use of step-therapy formulary management restrictions is associated with a limited incremental savings of $0.3 million (1.2%) for commercial and $0.9 million (1.5%) for Medicare plans annually over the next 3 years (years 3, 4, and 5).

Of note, the limited savings projected from step-therapy formulary management included a conservative $20 administrative cost per prior authorization for health plans. The actual savings may be less when considering that the time and resource burdens for prescriber practices and patients are also substantial. To complete prior authorizations for necessary therapies, it is estimated that prescriber practices average almost 20 hours weekly between physician, nursing, and clerical hours.19 This prior authorization administrative burden equates to $2161 to $3430 annually per physician in a primary care setting.20

Compared with step-therapy formulary management, there may be greater opportunities to manage the treatment costs for CML and to make patient outcomes better through initiatives that aim to improve patient adherence; meet guideline recommendations for molecular monitoring; identify at-risk populations, pediatric patients, and elderly patients who are not eligible for stem-cell transplant; and ultimately, to support optimal treatment selection.

In fact, overly restrictive formularies may be associated with unintended prescribing patterns that do not align with NCCN recommendations, which note that based on individual TKI toxicity profiles, second-generation TKIs dasatinib or bosutinib may be preferred for patients with heart disease, arrhythmias, pancreatitis,
and/or hyperglycemia, whereas nilotinib or bosutinib may be preferred for patients with a history of lung disease or those who are at risk for pleural effusion.12,21 Notably, in a recent, large retrospective analysis of 1120 patients with CML utilizing 2 US claims databases, up to 57% of patients had comorbidities relevant to the selection of TKI for the treatment of CML.21

Furthermore, regular molecular monitoring for disease response to treatment (or lack thereof) has been associated with reduced disease progression, presumably by assisting in the timely detection of primary or secondary resistance to first-line TKI therapy in patients with chronic-phase CML.22 The NCCN guidelines recommend that molecular testing (ie, a qualitative reverse transcription polymerase chain reaction) be performed every 3 months in patients who start TKI therapy to evaluate potential resistance to their current TKI therapy, and, if confirmed, a switch in TKI therapy can be initiated to prevent disease progression to an accelerated phase of CML or to blast crisis.3

However, a retrospective review of more than 1200 patients with CML across 2 insurance databases showed that less than 30% of patients had molecular monitoring at least 3 times during the first year after diagnosis.23 Furthermore, in an insurance database review, patients with CML who did not have the recommended monitoring had poor outcomes, increased hospitalizations, and greater total treatment costs than patients who received recommended monitoring.23,24

In addition, in an economic model, the total healthcare costs (including those associated with detected progression and molecular monitoring at 3 tests annually) were $1142 per patient per year (PPPY) for patients with monitoring and $6982 for patients without monitoring.21 This equates to a total cost-savings of $584,005 with full adherence to monitoring versus no monitoring in a 100-patient hypothetical cohort.21 In addition, the ability to detect resistance to a TKI early, before disease progression, facilitates switching to second-line therapy within the chronic phase and potentially avoids the costly sequelae and the poor patient outcomes that occur with more advanced CML disease.

As previously noted, without effective treatment in the chronic phase of CML, the disease will progress to the more aggressive accelerated phase and finally to blast crisis. Poor adherence to TKI therapy in the chronic phase has been noted as one of the main drivers for loss of response to treatment and subsequent progression to the more costly and potentially fatal accelerated phase and blast crisis in CML.25-27

The progression of CML from the chronic phase is associated with a significant cost increase. In a claims analysis of 587 patients with CML that included Medicare beneficiaries, the annual per-patient total healthcare cost was more than 6 times higher in patients with disease progression from chronic-phase CML than in patients without disease progression ($320,635 PPPY vs $49,710 PPPY; P < .001) after adjusting for patient age, sex, geographic region, health plan type, comorbidities, and follow-up duration.22

Limitations

Our updated model was developed for illustrative purposes to explore the impact of generic imatinib and step-edit formulary management on pharmacy spending for the most frequently used TKIs for the treatment of CML in patients with commercial or Medicare plans. The limitations of this study are inherent in any economic modeling analysis in that a variety of assumptions regarding the model population, treatment patterns, and costs (as previously noted) were involved. Furthermore, only TKI treatments for CML with ≥5% market share were included in this model, and market share projections using a logarithmic regression model may differ from the actual future market shares.

It took 2 years for the price of generic imatinib to decline substantially; the lower generic drug prices in year 3 may have a relatively larger impact on the market share than anticipated. However, our model aligned well with the observed trends, and because the realized cost-savings from generic imatinib entry have already materialized, our model projects a stabilizing shift in market share in the future.

All drug pricing data included in the model were based on published sources and did not represent actual pricing to any party; the model did not consider potential price increases among brand-name drugs that might have happened in the absence of generic imatinib entry into the market. Patients were assumed to continue therapy and to be fully adherent to the prescribed therapy during the entire year; actual adherence rates of less than 100% would result in pharmacy savings for the plan.

Finally, guidelines do not imply comparable efficacy, safety, or interchangeability among the TKIs. Comparisons of costs under different scenarios are beyond the scope of this study.

Conclusions

In the United States, payers have realized considerable savings in the first 2 years since brand-name imatinib’s loss of patent exclusivity. Because the price of generic imatinib has steadily declined, it is estimated that the cost-savings to US payers will increase substantially over the next 3 years, independent of formulary management consisting of step-edit therapy with the use of generic imatinib.
Formulary management restricting access to second-generation TKIs may result in minimal additional savings. Initiatives that aim to improve patient adherence, meet guideline recommendations for molecular monitoring, and support optimal treatment selection would afford all stakeholders the opportunity to manage the costs of patient care by also improving patient outcomes.

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References
5. Gleevec (imatinib mesylate) tablets, for oral use [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2018.
The approval of imatinib (Gleevec) in May 2001 was a clinical breakthrough and provided an opportunity for patients with chronic myelogenous leukemia (CML) who responded to the drug to achieve a cure. Managed care plans then looked at this cancer type as a chronic disease that required the long-term management of patients. The $26,000 annual price tag for the branded imatinib was concerning at the time, because it represented a very high-cost oral therapy in the oncology space that had a significant budget impact on health plans.

Despite its high cost, all health plans covered Gleevec, with utilization management targeting the US Food and Drug Administration (FDA)’s approved indication for CML, and additional indications were added per the National Comprehensive Cancer Network guidelines or as approved by the FDA.

**DRUGMAKERS:** The launch of the generic version of imatinib on February 1, 2016, was also met with great excitement, because the cost of the branded version had risen to approximately $120,000 annually by then. Sun Pharmaceuticals, the manufacturer of genetic imatinib, priced the generic agent within 10% of the brand-name drug’s price, and imatinib became the first generic drug to launch with a 6-month exclusivity period per the FDA’s rules. This pricing was consistent with typical generic drug pricing in the market; a first-to-launch company recoups the largest share of its drug development and marketing costs in the first 6 to 12 months after a drug’s launch.

In their article, Campbell and colleagues have highlighted the challenges in budgeting potential savings with the launch of generic drugs to the market. Several factors contribute to the speed of decline in the price of generics, including the size of the market, number of generic drug competitors after the initial exclusivity period, brand-name drug company contracting after the generic drug launch, and the willingness of patients and providers to accept the switch to a generic option.

**PATIENTS/PHYSICIANS:** The use of closed formularies and mandatory generic substitution in many states helps to drive generic drug uptake, as well as lower out-of-pocket costs for patients; however, physicians can overrule the switch by requiring the branded version for a patient. In some benefit designs, the patient pays the cost difference between the brand-name drug and the generic, and in others, the patients may pay the full price for the drug, if the plan no longer covers the brand-name agent. If a patient cannot tolerate the generic version of a drug, an appeal can be filed to gain access to the brand-name version. If the appeal is granted, the brand-name drug is usually covered at the highest copay or coinsurance tier.

Some confusion in the market can occur at the pharmacy level, because existing prescriptions may continue to be filled with the brand-name agent until a new prescription is written after a generic drug launch. Again, this is typically covered by state interchange laws regarding the use of generic drugs. Many of these drugs were also dispensed through specialty pharmacies that might have contracted with Novartis, the manufacturer of brand-name imatinib, to provide the brand-name drug in lieu of the generic drug, provided that the cost was comparable with the generic drug on the market, and that health plans were not mandating the conversion of patients to the generic drug option.

**PAYERS:** As discussed in the article by Campbell and colleagues, the step edit for treatment-naïve patients with CML makes sense for health plans; however, some clinicians will argue that the second-generation tyrosine kinase inhibitors (TKIs) may be better choices for this patient population. I agree with the assumption that plans would not attempt to forcibly switch existing patients with CML who are receiving other TKIs to imatinib.

The administrative cost of the prior authorization process is low and immaterial in comparison to the potential cost-savings with generic imatinib. The bulk of the savings with generics is achieved through the declining cost of the generic drugs, as more competitors launch drugs into the market, which currently stands at 11 drug companies with approved ANDAs (Abbreviated New Drug Applications) for imatinib per the FDA’s website.
The most concerning finding of this research is the very low rate of molecular monitoring of only 30% in a sample of more than 1200 patients.\(^2\) As expected, patients who were not monitored had worse outcomes. Cytogenetic testing identifies patients who are resistant to or are simply not responding to the current TKI treatment and affords the provider the opportunity to change the medication. The progression to the accelerated phase or blast crisis of CML can be fatal and is associated with a significant cost burden to the patient and the health plans.

My personal experience in this area consists of a contract with Bristol-Myers Squibb that focused on promoting routine cytogenetic testing of patients every 3 months to detect disease progression in patients with CML. A cooperative effort led to much higher rates (60%-80%) of testing in a commercial patient population.

Generic drugs routinely provide significant savings to health plans if competition is present in the market. Plans need to model the impact of significant generic drug launches, because this may influence their budgets and potential premium rates for subsequent annual insurance filings. Utilization management can be a useful tool in driving the uptake of generic drugs; however, clinical differences among drugs may limit a drug’s success in the market. Plans are encouraged to promote routine molecular testing of patients to promote best-in-class care and improved outcomes in the patient population with CML.
