An Economic Model to Evaluate the Impact of Formulary Tier Increases for Apixaban on the Incidence and Cost of Clinical Events in Patients with Non-Valvular Atrial Fibrillation in the United States

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#EE510

Introduction

- Atrial fibrillation (AF) places considerable burden on patients and healthcare systems; AF prevalence is estimated to exceed 12 million by 2030 in the US.[1]
- Medicare plans regulate spending by categorizing treatments into "formulary tiers", which determine the level of insurance coverage and patients' out-of-pocket (OOP) costs.[2]
- Formulary tier increases are associated with higher OOP costs for patients with AF. A nationwide claims data analysis from Deitelzweig et al.[3] found that 57.5% of patients with AF facing a formulary tier increase for apixaban continued treatment, while 12.4% of patients switched to another DOAC and 30.1% discontinued treatment, as a result of higher OOP costs.
- Non-medically indicated treatment switching or discontinuation, driven by formulary tier increases that raise patients' OOP costs,[3] may increase the risk of downstream adverse health outcomes in patients with AF.[4-6]
- Understanding the clinical and economic implications of formulary tier increases among Medicare patients with AF can provide payers with important insights into the effectiveness of these utilization strategies.

Objective

- This study aimed to evaluate the potential impact of a formulary tier increase for apixaban (a direct oral anticoagulant [DOAC] to reduce the risk of stroke and systemic embolism [SE]) on the incidence and cost of clinical events in patients with non-valvular AF (NVAF) from the US Medicare perspective.

Methods

- A decision model was built in Microsoft Excel® to evaluate the incidence and cost of clinical events in adults with NVAF in two cohorts (patients experiencing a tier increase versus no tier increase) from the US Medicare perspective.
- The target population was derived based on a hypothetical cohort of 1,000,000 US Medicare Fee-For-Service plan members; epidemiology data and market share estimates were applied to derive the treatment eligible population (i.e., adult patients diagnosed with NVAF who initiated apixaban treatment) entering the model (N = 47,036).[7-9]
- To capture the potential impact of tier increases on treatment utilization, patients with no tier increase were assumed to continue apixaban, while patients with a tier increase were assumed to continue apixaban, switch (to any DOAC [base-case 1] or rivaroxaban [base-case 2]), or discontinue treatment at rates of 57.5%, 12.4%, and 30.1%, respectively, based on Deitelzweig et al.[3]
- The incidence and cost (acute and long-term) of stroke (composite of ischemic stroke, hemorrhagic stroke and SE), major bleeding (MB; composite of gastrointestinal bleeding, intracranial hemorrhage and other MB) and event-driven mortality were modelled over a one-year time horizon.
- Clinical inputs for base-case 1 and 2 were sourced from real-world evidence studies assessing clinical event rates among continuers, switchers and discontinuers of different DOACs (**Table 1**).[4-6,10]
- Acute (one-off) and long-term (monthly) event management cost inputs were sourced from a published cost-consequence analysis[11] based on Medicare-specific databases in the US (CMS.gov and AHRQ) and were inflated to 2024 US dollars.[12-14]
- Severity distributions derived from randomized controlled trials[15,16] were used to calculate weighted average costs for ischemic stroke, hemorrhagic stroke and event-driven mortality in base-case 1 and 2.
- Model outcomes included the number of clinical events, cost of clinical events, and cost per member or patient per month/year.
- The following scenario analyses were conducted to test the impact of alternative input values and assumptions:

  SCENARIO 1 | Time horizon of three years

  SCENARIO 2 | US commercial perspective (based on US commercial costs)

  SCENARIO 3 | Lower bound 95% CI for "discontinuer" vs. "continuer" HRs

  SCENARIO 4 | Lower bound 95% CI for "switcher" vs. "continuer" HRs

  SCENARIO 5 | Upper bound 95% CI for "discontinuer" vs. "continuer" HRs

  SCENARIO 6 | Upper bound 95% CI for "switcher" vs. "continuer" HRs

  SCENARIO 7 | Reduced (- 20%) proportion of patients eligible for OAC

Methods (continued)

Table 1. Summary of clinical event inputs

Parameter	CONTINUERS Incidence rate per 100 PY	SWITCHERS HR (95% CIs)	DISCONTINUERS HR (95% CIs)
BASE-CASE 1‡			
Ischemic stroke	**0.77**	**1.36** (0.89–2.06)	**3.85** (2.70–5.56)
Hemorrhagic stroke	**0.18**	**1.36** (0.89 –2.06)	**0.53** (0.15–1.56)^
Systemic embolism	**0.03**	**1.36** (0.89–2.06)	**3.85** (2.70–5.56)
Gastrointestinal bleeding	**1. 75**	**2.00** (1.52–2.64)	**0.81** (0.44–1.43)†
Intracranial hemorrhage	**0.35**	**2.00** (1.52–2.64)	**0.53** (0.15–1.56)
Other major bleeding	**0.25**	**2.00** (1.52–2.64)	**0.81** (0.44–1.43)†
Source	*Ray et al.*[10]	*Dhamane et al.*[5]	*Tawfik et al.*[6]
BASE-CASE 2§			
Ischemic stroke	**0.53**	**1.89** (1.21–2.94)	**3.85** (2.7 0–5.56)
Hemorrhagic stroke	**0.19**	**2.12** (1.03–4.35)	**0.53** (0.15–1.56)^
Systemic embolism	**0.03**	**3.38** (0.60–18.89)	**3.85** (2.70–5.56)
Gastrointestinal bleeding	**1.13**	**2.15** (1.61–2.88)	**0.81** (0.44–1.43)†
Intracranial hemorrhage	**0.57**	**1.36** (0.83–2.24)	**0.53** (0.15–1.56)
Other major bleeding	**0.87**	**1.50** (1.03–2.19)	**0.81** (0.44–1.43)†
Source	*Deitelzweig et al.*[4]	*Deitelzweig et al.*[4]	*Tawfik et al.*[6]

Abbreviations: CI, confidence interval, HR, hazard ratio, PY, person-years
‡Patients with a tier increase were assumed to continue apixaban (57.5%), switch to **any DOAC** (12.4%), or discontinue treatment (30.1%)
§Patients with a tier increase were assumed to continue apixaban (57.5%), switch to **rivaroxaban** (12.4%) or discontinue treatment (30.1%)
^Assumed to be the same as intracranial hemorrhage
†Assumed to be the same as major bleeding (Tawfik et al.[6] did not provide breakdown HRs for each component [gastrointestinal bleeding and other major bleeding])

Results

BASE-CASE 1

(Patients with a tier increase were assumed to continue apixaban, switch to any DOAC, or discontinue treatment)

- Over a one-year time horizon, a tier increase for apixaban resulted in an additional 330 stroke/SEs, 58 MBs and 32 event-driven mortalities versus the "no tier increase" cohort across the treatment eligible population (N = 47,036) (**Figure 1A**).
- The higher clinical event rates associated with a tier increase for apixaban translated into increased event management costs of $6,542,373 per year ($11.59 per eligible patient/month [N = 47,036]; $0.55 per plan member/month [N = 1,000,000]) for US Medicare payers versus the "no tier increase" cohort (**Figure 1B**). These findings were largely driven by the increased stroke risk in the "tier increase" cohort, due to higher rates of treatment switching and discontinuation in these patients.

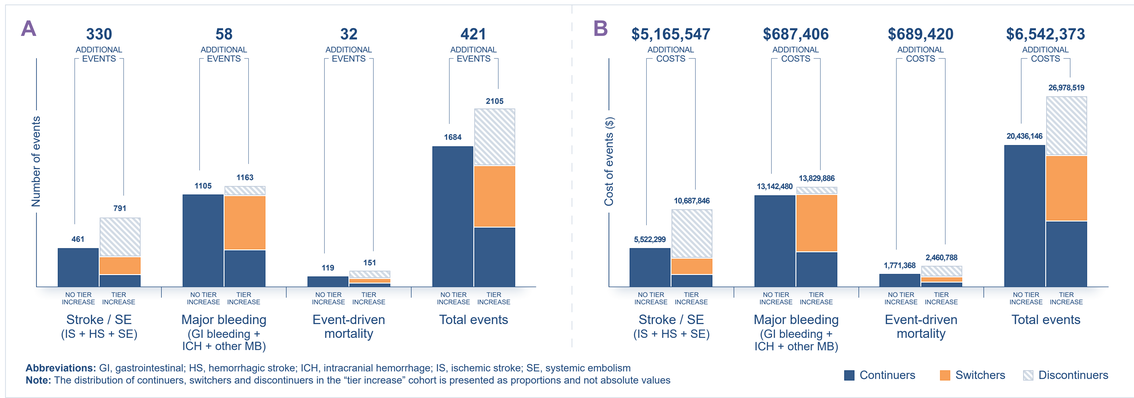
BASE-CASE 2

(Patients with a tier increase were assumed to continue apixaban, switch to rivaroxaban, or discontinue treatment)

- Over a one-year time horizon, a tier increase for apixaban resulted in an additional 257 stroke/ SEs, 20 MBs and 25 event-driven mortalities versus the "no tier increase" cohort across the treatment eligible population (N = 47,036) (**Figure 2A**).
- The higher clinical event rates associated with a tier increase for apixaban translated into increased event management costs of $4,656,305 per year ($8.25 per eligible patient/month [N = 47,036]; $0.39 per plan member/month [N = 1,000,000]) for US Medicare payers versus the "no tier increase" cohort (**Figure 2B**). These findings were mainly driven by the higher stroke risk in the "tier increase" cohort, as a result of increased treatment switching and discontinuation.

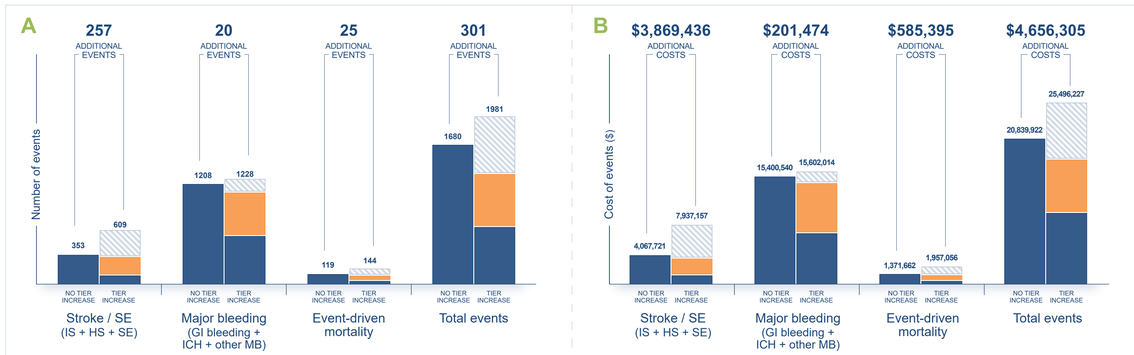
Results (continued)

Figure 1. Incidence (A) and costs (B) of clinical events for "no tier increase" and "tier increase" cohorts over a one-year time horizon from the US Medicare perspective (Base-case 1: patients with a tier increase were assumed to continue apixaban, switch to any DOAC, or discontinue treatment)



Abbreviations: GI, gastrointestinal; HS, hemorrhagic stroke; ICH, intracranial hemorrhage; IS, ischemic stroke; SE, systemic embolism
Note: The distribution of continuers, switchers and discontinuers in the "tier increase" cohort is presented as proportions and not absolute values

Figure 2. Incidence (A) and costs (B) of clinical events for "no tier increase" and "tier increase" cohorts over a one-year time horizon from the US Medicare perspective (Base-case 2: patients with a tier increase were assumed to continue apixaban, switch to rivaroxaban, or discontinue treatment)



Abbreviations: GI, gastrointestinal; HS, hemorrhagic stroke; ICH, intracranial hemorrhage; IS, ischemic stroke; SE, systemic embolism
Note: The distribution of continuers, switchers and discontinuers in the "tier increase" cohort is presented as proportions and not absolute values

Scenario analyses

- Results of scenario analyses were consistent with the findings of both base-case analyses (**Table 2**), suggesting robustness of the model inputs and outcomes.

Table 2. Scenario analyses results (Incremental cost per member per month)

	Base-case	Scenario 1	Scenario 2	Scenario 3	Scenario 4	Scenario 5	Scenario 6	Scenario 7
BASE-CASE 1	**$0.55**	**$0.67**	**$0.06**	**$0.23**	**$0.44**	**$1.08**	**$0.68**	**$0.44**
BASE-CASE 2	**$0.39**	**$0.47**	**$0.04**	**$0.11**	**$0.26**	**$0.89**	**$0.60**	**$0.31**

Limitations

- This cost-consequence analysis only considered clinical event-management costs and did not account for impacts and implications of formulary tier increases.
- It was assumed that clinical event rates were consistent over the entirety of the time horizon.

Conclusion

- A formulary tier increase for apixaban was projected to increase the risk of stroke/SE, major bleeding and event-driven mortality as a result of treatment switching and discontinuation, leading to **higher event-related costs** for US Medicare payers versus the "no tier increase" cohort.
- Results of scenario analyses were consistent with base-case analyses, suggesting **robustness of findings**.

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Disclosures

This study was sponsored by Pfizer and Bristol Myers Squibb.

RS, EV, and SD are employees and shareholders of Pfizer. CD and ES are employees of Health Economics and Outcomes Research Ltd., who received consulting fees from Pfizer in relation to the conduct of this study

Poster presented at: ISPOR 2025, May 13-16; Montreal, QC, Canada