EE355

The Budgetary Consequences of Increasing Utilization of Dronedarone Relative to Other Antiarrhythmic Drugs to a Hypothetical U.S. Payer

Ken-Opurum J[1], Vadagam P[1], Faith L[1], Srinivas SSS[1], Park S[2], Charland S[2], Revel A[2]

[1]Axtria, Berkeley Heights, NJ, USA, [2]Sanofi, Bridgewater, NJ, USA

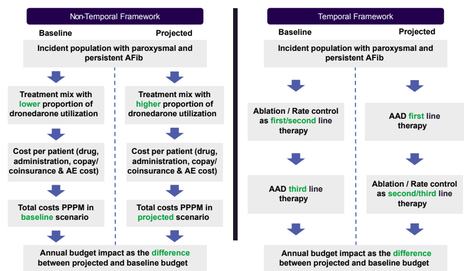
BACKGROUND AND OBJECTIVES

- Atrial Fibrillation (AFib), characterized by arrhythmia, tachycardia, and/or bradycardia, can symptomatically include heart palpitations, shortness of breath, and weakness. AFib is associated with an increased risk for heart-related complications which may include stroke, heart failure (HF), and death.[1]
- AFib is the most common sustained cardiac arrhythmia. In 2010 AFib affected approximately 5.1 million Americans and is projected to double by 2030.[2]
- Management of AFib broadly includes rhythm and rate control therapies, and stroke thromboprophylaxis through anticoagulation. Catheter ablation has also emerged as a suitable alternative for selected patients when rhythm or rate control therapies are ineffective.[3] Guidelines recommend antiarrhythmic drugs (AADs) to address AFib symptoms; however, limitations remain in the accessibility of effective AADs with a low risk of adverse events (AEs).[4,5]
- Recent research has demonstrated the efficacy of early use of AADs vs standard of care.[6]
- Dronedarone is an AAD indicated to reduce the risk of hospitalization for AFib in patients in sinus rhythm with a history of paroxysmal or persistent AFib.[7]
- A budget impact model (BIM) was developed from the U.S. payer perspective:
  - To evaluate the replacement of other AADs with dronedarone
  - To assess the value of dronedarone vs. ablation or rate control
  - To investigate placing AADs earlier in the treatment sequence for AFib.

METHODS

- The economic impact of dronedarone was calculated using a BIM developed in Microsoft Excel 2010 (Microsoft Corp, Redmond, WA). The impact was calculated by comparing annual healthcare costs with an assumption of lower market utilization of dronedarone in the baseline scenario versus higher market uptake of dronedarone in projected scenarios.
- The expected budget impact of dronedarone was calculated as the difference in costs between these two scenarios (**Figure 1**).
- The base-case scenario was a comparison of dronedarone versus other AADs (amiodarone, sotalol, flecainide, dofetilide, and propafenone). The BIM included both non-temporal scenarios (the order of treatments [AADs, ablation, or rate control] is not considered) and temporal scenarios (in which the order of treatments is considered).
- An incident-based modeling approach was employed, in which patients were only included in the study if they were not previously using AADs (i.e., incident patients).
- In each scenario analysis, total healthcare costs were calculated on an annual basis for all incident patients in the target population during each year of the projection period.
- The analysis was conducted from a US payer perspective over a time horizon of 5 years. The BIM considered direct medical costs to the payer including medication costs, inpatient and outpatient administration costs, and AE costs, reported in 2021 USD. Monitoring costs associated with AAD use were not considered. Discount rates over time were not included in the budget impact calculations.

Figure 1. Framework of Budget Impact Model



Abbreviations: AEs: Adverse Events; AFib: Atrial Fibrillation; PPPM: Total cost per patient in target population, per-month

Model Assumptions and Other Considerations

- Annual growth rate for incident AFib cases was considered as 4.6% and assumed to be the same across the time horizon.[2]
- Utilization mix proportions were based on RWE.[8]
- Baseline market share for dronedarone was based on RWE[8] and estimated at 8.4% (Feb 2019 – Jan 2021).
- The default scenario assumed market share for dronedarone to be 10%, 12%, 15%, 18%, and 20% in projected years 1-5, respectively.
- Default AAD drug costs were estimated using the minimum per-unit price of product form and strength to arrive at a singular cost for each product (2021).[9]
- Copay and coinsurance were taken from Kaiser's employer health benefits - 2021 annual survey.[10]
- It is assumed that patient cost-sharing (copay/coinsurance) is paid once per refill frequency.
- Proportion of treatment received in the inpatient setting for dofetilide and sotalol is 100%, in dronedarone is 0%, and for other AADs is 50%. Remaining treatment is assumed to be received in the outpatient setting (based on clinical opinion) (**Figure 2**).
- AEs included in the model were (1) Withdrawals due to AEs, (2) Proarrhythmia, (3) Stroke, and (4) AFib recurrence.
- For dofetilide and sotalol, the cost of inpatient administration is taken directly from literature.[11] For the rest of the AADs, inpatient administration cost is assumed to be the average of the inpatient administration costs of dofetilide and sotalol.
- Wholesale Acquisition Costs (WAC) were obtained from drugs.com in October 2021. Cost per dosage: Dronedarone (400mg): $12.19; Amiodarone (200mg): $0.31; Sotalol (120mg): $0.26; Flecainide (100mg): $0.57; Propafenone (225mg): $0.77; and Dofetilide (125mg): $3.99.
- All risk ratios for the AEs were obtained from published results of RCTs (**Table 1**).[12,13]
- For the non-temporal scenario for comparison of AADs, the treated risk is calculated from the formula given below, which is equivalent to the standard epidemiological calculation for risk ratio.[14] Risk ratios are from a Cochrane Review of AADs; risk in the comparison group (i.e., general population) is from RWE.

*Treatment group risk = Risk ratio * Risk in comparison group*

- Due to limited availability of data, there was no distinction between different AADs in the temporal scenarios.

Table 1. Risk Ratios for AEs and Cost of AEs

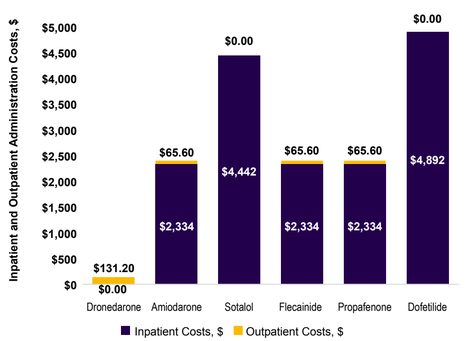
		Withdrawal due to AE	Proarrhythmia	Stroke	AFib Recurrence
Risk Ratios for AEs	Dronedarone	0.118	0.356	0.039	0.464
	Amiodarone	0.502	0.405	0.068	0.278
	Sotalol	0.146	0.648	0.087	0.443
	Flecainide	1.154	0.876	0.120	0.347
	Propafenone	0.121	0.241	0.020	0.358
	Dofetilide	0.133	1.004	0.064	0.384
Cost of AE		$6,389[15]	$10,952[16]	$28,008[17]	$10,288[18]

Abbreviations: AEs: Adverse Events; AFib: Atrial Fibrillation

Sensitivity Analysis

- A one-way sensitivity analysis (OWSA) evaluated the impact of individual parameters on model results. The variables included in the OWSA were target population, utilization mix, and cost (including cost of different treatments [AADs, ablation, and rate control], cost of managing AEs, and discounts applied), which were varied by ±20% from baseline.

Figure 2. Administrative Costs of Dronedarone Versus Other AADs

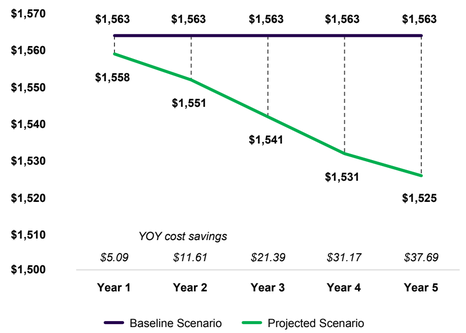


RESULTS

Non-Temporal Base-Case Scenario: Dronedarone Versus Other AADs

- In the base-case scenario, replacement of other AADs with dronedarone resulted in increased PPPM cost savings of ~$38 over 5 years' time horizon with a projected utilization of 20% (**Figure 3**). This translates to annual budget reduction of -$452.30 when dronedarone replaces other AADs.
- Although the drug acquisition cost of dronedarone is higher than other AADs, cost reductions in projected scenarios were driven by lower AE and administration costs.

Figure 3. Base-Case Analysis – Difference from Baseline, PPPM Results



PPPM: Total cost per patient in target population, per-month; YoY: Year-on-Year

Non-Temporal Scenario: Dronedarone Versus Non-AADs

- Due to lower AE costs associated with dronedarone and higher cost of ablation treatment, dronedarone yielded higher cost savings over ablation alone and rate control therapies in conjunction with ablation (**Table 2**).
- AE cost of dronedarone was comparable to the AE cost associated with other AADs and rate control therapies. Dronedarone is a better performing treatment from a patient perspective.

Table 2. Non-Temporal Scenario Analysis

Treatment Comparison	Utilization Mix/ Cost Savings	1st year	2nd year	3rd year	4th year	5th year
Dronedarone vs. Ablation	Projected utilization	30%	39%	51%	66%	86%
	Savings (in PPPM)	-$113.67	-$261.43	-$458.45	-$704.73	-$1033.10
Dronedarone vs. Rate Control + Ablation	Projected utilization	37%	48%	62%	81%	105%
	Savings (in PPPM)	-$147.94	-$336.30	-$576.02	-$901.37	-$1312.33

Abbreviation: PPPM: Total cost per patient in the target population, per-month

Temporal Scenario Analysis

- Inclusion of AADs as first-line therapy followed by ablation as second-line and rate control as third-line demonstrated cost savings in the majority of temporal scenarios.
- A marginal cost difference was observed when AADs and ablation were compared in the temporal analysis, i.e., AADs coming before or after ablation had minimal impact on the overall cost (**Table 3**).
- A large cost difference was observed which favors AADs preceding rate control therapies in the treatment sequence.

Table 3. Temporal Base-Case Scenario Analysis

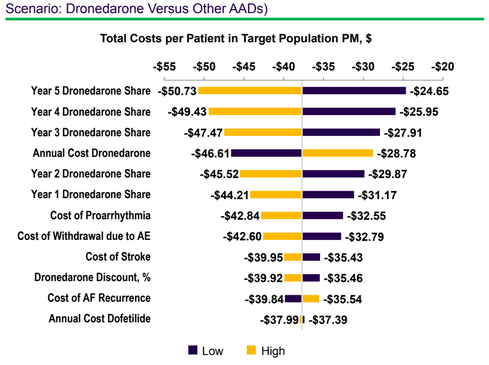
Reference Scenario (1st line → 2nd line → 3rd line treatment)	Projected Scenario (1st line → 2nd line → 3rd line treatment)	Cost Savings for Reference Scenario (PPPM), $ *
AAD → Ablation → Rate control	Rate Control → Ablation → AAD	$0.24
	Rate Control → AAD → Ablation	$0.24
	AAD → Rate Control → Ablation	$0.18
	Ablation → Rate Control → AAD	$0.04
	Ablation → AAD → Rate control	-$0.04
AAD → Rate Control → Ablation	Ablation → Rate Control → AAD	-$0.14
	AAD → Ablation → Rate control	-$0.18
	Ablation → AAD → Rate control	-$0.22
	Rate Control → Ablation → AAD	$0.07
	Rate Control → AAD → Ablation	$0.07
AAD → Ablation	Ablation → AAD	-$0.08
Ablation → AAD	AAD → Ablation	$0.08
AAD → Rate Control	Rate Control → AAD	$0.09
Rate Control → AAD	AAD → Rate Control	-$0.09

Abbreviations: AAD: Antiarrhythmic Drug; PPPM: Total cost per patient in the target population, per-month
*Positive cost results favor the reference scenario and negative cost results favor the projected scenario

Sensitivity Analysis (Non-Temporal Scenario)

- Market shares and the annual cost of dronedarone had the greatest influence on OWSA results.
- A 20% increase in the market share of dronedarone at year 5 over other AADs increased PPPM savings by $13.04 from its base-case value ($37.69).
- Other key variables influencing OWSA results are depicted in **Figure 4**.

Figure 4. Tornado Diagram - Sensitivity Analysis Results (Non-Temporal Scenario: Dronedarone Versus Other AADs)

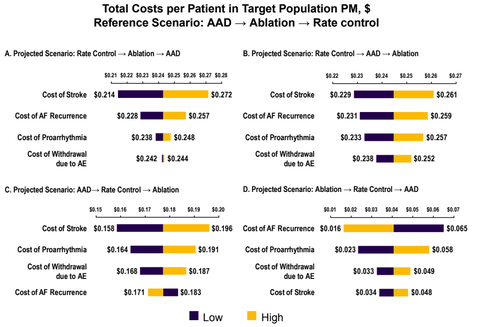


Abbreviations: AAD: Antiarrhythmic Drug; AE: Adverse Events; AF: Atrial Fibrillation; PM: Per-Month

Sensitivity Analysis (Temporal Scenario)

- A temporal sensitivity analysis was conducted to test the impact of factors influencing the temporal analysis results (**Figure 5**).
- Population and utilization did not differ in projected years for temporal scenarios, so only costs associated with AEs are considered (**Figure 5**).

Figure 5. Tornado Diagram - Sensitivity Analysis Results (Temporal Scenario)



Abbreviations: AAD: Antiarrhythmic Drug; AE: Adverse Event; AF: Atrial Fibrillation; PM: Per-Month

CONCLUSIONS

- **Increasing use of dronedarone demonstrated incremental cost reductions over time.**
- **Placement of AADs as first-line treatment followed by ablation and rate control medications resulted in cost savings compared to when AADs were placed as third-line treatment after ablation and rate control medications.**
- **Findings from this BIM can be used to help guide decision-makers in terms of formulary placement and utilization controls.**

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DISCLOSURES:

JKO, LF, and SSSS are employees of Axtria, which received funding from Sanofi for this analysis. PV was an employee of Axtria during the conduct of this study. SP, SC and AR are employees of Sanofi and are stockholders of Sanofi stock.

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