Cost-minimization analysis of rivaroxaban in comparison to enoxaparin plus warfarin for the treatment of Venous Thromboembolism (VTE) under the private Healthcare system perspective

Piedade A¹, Paladini L¹, Tobarrella F², Nakada C²
¹Evidências - Kantar Health, Campinas, Brazil, ²Bayer Healthcare, São Paulo, Brazil

ABSTRACT

Objective: Venous thromboembolism (VTE) which comprises deep vein thrombosis (DVT) and pulmonary embolism (PE) is associated with a significant healthcare burden. Currently, the standard of care is parenteral low molecular weight heparin (enoxaparin) plus warfarin. Rivaroxaban is an oral anticoagulant that does not require dose adjustment or routine coagulation monitoring, bringing an important advantage for the treatment of VTE. The EINSTEIN clinical program of rivaroxaban showed that, overall, hospitalized patients who received initial treatment with rivaroxaban for DVT and PE stayed in the hospital fewer days compared with patients who received enoxaparin/vitamin K antagonist (VKA). Therefore, the objective of this study is to compare the direct costs of treatment with rivaroxaban versus enoxaparin/warfarin.

Methods: A cost-minimization analysis (CMA) was chosen once the EINSTEIN program showed that rivaroxaban is non-inferior to enoxaparin/VKA regarding efficacy for treatment of VTE, being possible to consider that there is no difference in outcomes. The study was conducted under the Brazilian private healthcare system and the time horizon was one year. Costs related to hospitalization, outpatient management and adverse events were obtained by micro-costing approach and resource use was captured from literature and expert panel. Costs were expressed in 2015 prices and exchange rate used was 1.00USD = 4.00BRL.

Results: Rivaroxaban use was less expensive than enoxaparin + warfarin in the treatment of VTE. Estimated total cost of treatment for one patient with VTE is $1,559 with rivaroxaban and $2,007 with enoxaparin + warfarin. The greater difference in costs was for PE treatment, which was $481.05 less for rivaroxaban. For DVT treatment, estimated savings for rivaroxaban was $399.45. Robustness of the model was tested in a deterministic univariate sensitivity analysis in which all results remained cost saving.

Conclusions: Rivaroxaban is a cost-saving alternative compared to the current practice for VTE treatment under the Brazilian private healthcare system perspective.

INTRODUCTION

• Venous thromboembolism (VTE) is a major cause of morbidity and mortality worldwide and its treatment costs are considerable and increasing1.
• According to EINSTEIN trials, rivaroxaban is non-inferior to enoxaparin followed by vitamin K antagonist (VKA) regarding recurrent VTE in patients with deep vein thrombosis (DVT)2 and in patients with pulmonary embolism (PE)3. Current American College of Physicians (ACP) guidelines recommend either parenteral anticoagulant therapy or anticoagulation with rivaroxaban for acute VTE treatment4.
• In EINSTEIN randomized trials, rivaroxaban led to fewer days hospitalized compared with enoxaparin/VKA5.
• There are scarce data on the costs related to VTE patients in Brazil. The purpose of this research is to provide a cost-minimization analysis (CMA) of rivaroxaban in comparison to enoxaparin/VKA for the treatment of VTE under the Brazilian private healthcare system perspective.

METHODS

Economic model
• CMA was chosen once the EINSTEIN program showed that rivaroxaban is non-inferior to enoxaparin/VKA regarding efficacy for treatment of VTE, being possible to consider that there is no difference in recurrent VTE primary outcome.
• The EINSTEIN program also showed that patients in treatment with rivaroxaban had a mean length of stay lower than with enoxaparin + VKA as well as lower risk of major bleeding in patients with PE. Costs considered in the model are represented in Figure 1.
• Perspective was from the Brazilian private healthcare system and the time horizon was one year.

Resource use and costing
• Costs considered in the model were those reimbursed by private payers in Brazil, and included: hospitalization costs (including drugs and tests used in index and in recurrent events and costs related to the management of complications) and monitoring costs (including post-discharge visits and tests).
• Inputs were obtained from literature and expert panel.
• It was assumed the same treatment duration distribution in 3, 6 and 12 months for both groups (rivaroxaban or enoxaparin + warfarin), in accordance to EINSTEIN program findings.
• Main inputs in the model were based on EINSTEIN program results, which were adverse events rates, need for hospitalization due the index event, recurrence rate, mean length of stay in the hospital, and treatment and follow up duration.
• An expert's panel with seven specialists was conducted to obtain resource utilization. Experts were asked about their practice in hospitalization and outpatient management of VTE.
• Based on the consensus of resource utilization, costs were obtained by a micro-costing approach.
• Cost sources were publicly available reference tables such as CBHPM and SIMPRO.
• Costs were expressed in 2015 prices and exchange rate used was 1.00USD=4.00BRL.

Sensitivity Analysis
• A deterministic univariate sensitivity analysis was developed to test the robustness of the model.
• Parameters tested were 100% increase in surgeries cost, cost of enoxaparin (±14.3%), days hospitalized in both groups (±20%), rivaroxaban cost (±7%) and hospitalization and outpatient costs (±15%).
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RESULTS

Base case results
- Rivaroxaban use was cost saving in comparison with enoxaparin + warfarin in the treatment of VTE.
- Estimated total cost of treatment for one patient with VTE is $1,559 with rivaroxaban and $2,007 with enoxaparin + warfarin (Figure 2).
- The use of rivaroxaban would cause a cost reduction of 22% in VTE treatment, 32.5% in DVT treatment and 19% in PE treatment.

Cost composition
- Hospitalization costs for both DVT and PE represents the greatest portion of the total cost. Table 1 shows model mean costs, weighted by the percentage of hospitalization/outpatient treatment, recurrence and adverse events.

SENSITIVITY ANALYSIS
- All results obtained with the sensitivity analysis remained cost saving (Figure 3).

Table 1: Model costs weighted by rates of occurrence

<table>
<thead>
<tr>
<th></th>
<th>DVT</th>
<th>PE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rivaroxaban</td>
<td>Enoxaparin + warfarin</td>
<td>Rivaroxaban</td>
</tr>
<tr>
<td>Treatment</td>
<td>USD</td>
<td>USD</td>
</tr>
<tr>
<td>Hospitalizations</td>
<td>$ 566.7</td>
<td>$ 854.7</td>
</tr>
<tr>
<td>Outpatient follow up</td>
<td>$ 124.5</td>
<td>$ 220.5</td>
</tr>
<tr>
<td>Outpatient treatmet</td>
<td>$ 75.0</td>
<td>$ 80.7</td>
</tr>
<tr>
<td>Recurrence</td>
<td>$ 19.3</td>
<td>$ 29.1</td>
</tr>
<tr>
<td>Adverse Events</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major bleeding</td>
<td>$ 2.7</td>
<td>$ 2.7</td>
</tr>
<tr>
<td>Bleeding clinically relevant &quot;non-major&quot;</td>
<td>$ 1.1</td>
<td>$ 1.1</td>
</tr>
<tr>
<td>Intracranial bleeding</td>
<td>$ 0.0</td>
<td>$ 0.0</td>
</tr>
<tr>
<td>Retropertioneal bleeding</td>
<td>$ 0.0</td>
<td>$ 0.0</td>
</tr>
<tr>
<td>Post thrombotic syndrome</td>
<td>$ 38.7</td>
<td>$ 38.7</td>
</tr>
<tr>
<td>Total</td>
<td>$ 828.1</td>
<td>$ 1,227.5</td>
</tr>
</tbody>
</table>

Figure 2: Total costs and cost differences of the treatment of VTE

Figure 3: Univariate sensitivity analysis: yearly cost difference of patients

LIMITATIONS
- We assumed 100% adherence to therapy and to monitoring of patients.
- Length of stay, which was responsible for a significant proportion of costs, was extrapolated from a controlled trial (although it was left to the judgment of the attending physician).

REFERENCES

CONCLUSIONS
- Hospitalization costs represent the greatest share of the total cost in acute VTE patients.
- Rivaroxaban constitutes a single-drug oral regimen that can lead to reduction in VTE treatment costs in comparison with enoxaparin/VKA under the Brazilian private healthcare system perspective.