A health economic evaluation of a new vaccine for the prevention of herpes zoster (HZ) and post-herpetic neuralgia (PHN) in Belgium

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Presentation outline

1. Background
2. Objective
3. Methods
4. Results
5. Discussion and conclusion
Background

- Herpes zoster (HZ) or “shingles” results from the reactivation of the varicella zoster virus (VZV)
  - Symptoms: rash and pain, often severe

- 25% cumulative risk of developing HZ over lifetime
  - HZ annual risk increases with age, roughly doubling every decade after 50 years

- Post-herpetic neuralgia (PHN) is the most common and debilitating consequence of HZ
  - Pain persisting or occurring at least (1 or ) 3 months after the HZ rash onset

- 20% of HZ patients develop PHN
  - PHN occurs approximately 15 times more often after 50 years

Objective

- New vaccine - Zostavax® - is indicated for prevention of herpes zoster ("zoster" or shingles) and herpes zoster-related post-herpetic neuralgia (PHN).
  - for immunization of individuals 50 years of age or older.
  - a single dose administered subcutaneously
  - The Shingles Prevention Study (SPS) trial\(^3\), a double-blind, placebo-controlled RCT of 38,546 adults aged 60 years and above
    - Incidence of HZ reduced by 51.3%
    - HZ cases with severe and long lasting pain reduced by 73%
    - Incidence of PHN reduced by 66.5%

- Objective:
  - Cost-effectiveness analysis that compares a vaccination strategy of older adults (60+) against HZ and PHN to the current situation of no vaccination

### Analytical framework

- **Study population**
  - Base case: 60+
  - Subgroup analyses: 50+, 60-64, 65-69, 60-69, 65+

- **Comparative strategies**
  - Vaccination strategy
  - No vaccination

- **Perspectives**
  - Third-party payer (TPP), *i.e.* NIHDI
  - Healthcare perspective = TPP + patient copayments
  - Societal perspective = TPP + patient copayments + productivity losses

- **Time horizon**
  - Lifetime

- **Cost-effectiveness threshold**
  - Unofficial threshold of €30,000 per QALY
Model development

- Markov
- Lifetime divided into cycles of 1 month
- Health states divided into pain severity levels
Input parameters - Epidemiology

- HZ incidence
  - Provided by Scientific Institute of Public Health (Belgian Sentinel Network of General Practitioners)\(^4\)

- PHN proportion & gender split
  - General Practice Research Database (GPRD) study (UK) \(^5\)

- Average HZ duration: 1 month, based on SPS trial\(^3\)

- Average PHN duration: 9 months, based on SPS trial\(^3\)

- Pain split from SPS trial\(^3\)

- HZ/PHN mortality: no associated mortality assumed

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VZV Vaccination-Belgium

Input parameters - Vaccination and other data: the SPS trial\(^3\)

- **Vaccine efficacy on HZ and PHN cases**
  - Direct effect: reduction of HZ, PHN cases
  - Indirect effect: further reduction of PHN cases through reduction of HZ cases

<table>
<thead>
<tr>
<th>Vaccine efficacy</th>
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<tbody>
<tr>
<td>Age group</td>
<td>HZ - direct</td>
<td>PHN - direct</td>
</tr>
<tr>
<td>50-69</td>
<td>63.90%</td>
<td>4.80%</td>
</tr>
<tr>
<td>70+</td>
<td>37.60%</td>
<td>30.00%</td>
</tr>
</tbody>
</table>

- **Vaccine efficacy on PHN duration**

<table>
<thead>
<tr>
<th>Pain duration PHN (months)</th>
<th>Vac</th>
<th>No Vac</th>
</tr>
</thead>
<tbody>
<tr>
<td>60-69</td>
<td>6.1</td>
<td>8.3</td>
</tr>
<tr>
<td>70+</td>
<td>7.6</td>
<td>10.9</td>
</tr>
</tbody>
</table>

- **Vaccine efficacy duration: lifetime**

- **Vaccination costs:** 141.18€ (including administration costs)

Input parameters – HCRU: IMS burden of illness study

- Burden of illness of HZ and PHN among adults aged 50+ in Belgium

- Expert panel of 19 physicians:
  - 3 dermatologists, 4 ophthalmologists, 4 neurologists, 4 pain specialists, 4 GPs

- Medical resource use and cost data on:
  - Primary & secondary care
  - Pharmacological treatment
  - Non-pharmacological treatment
  - Diagnostic tests
  - Hospitalisation
  - Work absenteeism

Other input parameters

- Utilities
  - Belgian age-specific utilities by EuroQol Group\textsuperscript{7}
  - Disease-specific utilities for mild, moderate and severe pain by Oster \textit{et al.}\textsuperscript{8} based on US PHN population.
    - A utility of 1 assumed for “no pain” states.

<table>
<thead>
<tr>
<th>Pain severity</th>
<th>Utility</th>
<th>Utility decrement</th>
</tr>
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<tbody>
<tr>
<td>No pain</td>
<td>1.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Mild pain</td>
<td>0.69</td>
<td>0.31</td>
</tr>
<tr>
<td>Moderate pain</td>
<td>0.58</td>
<td>0.42</td>
</tr>
<tr>
<td>Severe pain</td>
<td>0.25</td>
<td>0.75</td>
</tr>
</tbody>
</table>

- Discount rates from KCE\textsuperscript{9}: 3% for costs, 1.5% for benefits

- Population & employment data: Belgian national statistics\textsuperscript{10}

Base case results: 60+ population

- 2.3 M people, 20% coverage rate

### Effectiveness

<table>
<thead>
<tr>
<th>Effectiveness</th>
<th>Vac Policy</th>
<th>No Vac Policy</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>QALYs</td>
<td>26,326,269</td>
<td>26,318,674</td>
<td>7,595</td>
</tr>
<tr>
<td>HZ Cases</td>
<td>373,251</td>
<td>412,732</td>
<td>39,480</td>
</tr>
<tr>
<td>PHN Cases</td>
<td>84,171</td>
<td>97,613</td>
<td>13,442</td>
</tr>
</tbody>
</table>

### Number needed to vaccinate to avoid one case of HZ/PHN

<table>
<thead>
<tr>
<th>NNV</th>
<th>60+ population</th>
</tr>
</thead>
<tbody>
<tr>
<td>HZ</td>
<td>12</td>
</tr>
<tr>
<td>PHN</td>
<td>35</td>
</tr>
</tbody>
</table>
Base case results: 60+ population

- Incremental cost-effectiveness ratios (ICERs)

<table>
<thead>
<tr>
<th>ICERs</th>
<th>TPP</th>
<th>Healthcare</th>
<th>Societal</th>
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</thead>
<tbody>
<tr>
<td>Cost per QALY gained</td>
<td>€ 6,799</td>
<td>€ 7,166</td>
<td>€ 7,137</td>
</tr>
<tr>
<td>Cost per HZ Case Avoided</td>
<td>€ 1,308</td>
<td>€ 1,379</td>
<td>€ 1,373</td>
</tr>
<tr>
<td>Cost per PHN Case Avoided</td>
<td>€ 3,842</td>
<td>€ 4,050</td>
<td>€ 4,033</td>
</tr>
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- ICERs per 5-year age group (TPP perspective)
Deterministic sensitivity analysis

- Tornado diagram: TPP perspective

Base case: €6,799/QALY

- Vaccine price: €100.38
- 0% Discount Rate
- Vaccine Efficacy: Upper limit of 95% CI
- HZ/PHN Resource 75%
- HZ Related Mortality
- Bala/Oster QALYs
- Vaccine Efficacy: Lower limit of 95% CI
- Vaccine price: €160.38
- Vaccine duration 20 years
- QALYs - Multiplicative method
- SPS QALYs
- Vac Dur Waning 8.3%
- 5.0% Discount Rate
- Opstelten HZ&PHN rates & Gender Proportion
- Repeat dose vaccine - 100% original price
- GPRD PHN Duration/Split
- Vaccine duration 10 years
The probability of not surpassing the unofficial Belgian threshold of €30,000 is 94.5% from a TPP healthcare perspective.
Discussion and conclusion

- Base case ICER of €6,799 per QALY well below commonly accepted CE threshold of €30,000

- Model strengths
  - Pivotal clinical trial data
  - Country specific data wherever possible
  - Ageing of population considered
  - Direct & indirect effect of vaccination incorporated
  - Great level of detail: different pain severity levels, HZ & PHN duration
  - Complete and robust sensitivity analysis
  - Content validation

- Model limitations
  - PHN proportion not available for Belgium → derived from the UK
  - Patient-level data available for HCRU not available for Belgium (→ Delphi as alternative)

- Further research on budget impact required