Commercialisation Strategy for Orphan and Rare Disease Products – Incorporating the Payer Perspective

A report by RJW&partners

Thursday 20th March 2014
16:30 - 18:00

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- Introduction and methodology
- Payer Objectives and Attitudes – Survey Insights
- Incorporating the Payer Viewpoint
- Conclusions
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RJW & partners is a consultancy specialised in providing pricing and market access advice

We specialise
- Pricing and market access only
- Industry, payer
- Strategic focus
- Europe, US, Asia-Pacific

The Benefit of Experience
We carried out an online survey for this workshop

- RJW & partners carried out an online survey of 9 ex and current payers between 24\textsuperscript{th} January 2014 and 27\textsuperscript{th} February 2014

- The payers were selected for the survey based upon the seniority of their former or current position and their level of expertise in pricing and market access

- The survey contained 10 questions of differing format and allowed for both quantitative and qualitative responses

- The geographical scope is listed in more detail on the next slide, but included 9 global markets

- The responses have been anonymised in accordance with good market research principles
The survey covered nine markets

Participants

- Ex-President of the Transparency Commission
- Ex-President of the Italian Society of Pharmacology
- Ex-Ministry of Health (Chief specialist in P&R)
- Director Catalan Agency for HTA and research
- Ex-Board Member of the TLV
- SMC Economic Assessor
- Ex-Secretary of CFH
- Ex-Head of the GKV Spitzenverband
- Pharmacy Director of a Large Managed Care Organisation (MCO)
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“What are your three main concerns about orphan drugs?”

- Opportunity Cost
- Safety
- Blurring of orphan/ultra orphan
- Immature/Poor Data
- Limited Clinical Effectiveness
- Expansion of Patient Population
- Cost/Affordability

Unprompted answers
“Do you feel the current prices charged for orphan drugs are sustainable in the future?”

“Absolutely not….the US payer system is heading towards some kind of QALY or cost effectiveness measures and drugs that cost $300,000 / year and are not curative will not be paid for in the near future.” Pharmacy Director, MCO, USA
“Do you feel the current prices charged for orphan drugs are sustainable in the future?”

“The high prices per patient can't be justified by health benefits.” Ex- Board Member of the TLV, Sweden

“For many reasons the business model is unsustainable; as orphan drugs proliferate, the overall cost of is going to be a significant share of the expenditure. It is ethically questionable and there is no real innovation any more.” Director Catalan Agency for HTA and research, Spain

“In the end with the introduction of more orphan drugs, costs will become too high.” Ex-secretary of CFH, Netherlands

“Price decrease is needed, if more rare diseases are to be treated.” Ex MOH, Poland
Question 3

“Will the payer environment become tougher towards orphan drugs? What will be main hurdles to access?”

“Pressure on prices will become higher and higher and target populations increasingly restricted.”
Ex-President of the Transparency Commission, France

“In the short term, for Germany the legally set barrier of 50 million Euros will be reduced likely by half in the mid term, there will be a societal debate about rationing.”
Ex-Head of the GKV Spitzenverband, Germany

“A real concern is the value of the therapy and we will begin to question this as more drugs become available.”
Ex-President of the Italian Society of Pharmacology
“What proportion of orphan drugs are supported by an adequate evidence base for reimbursement?”

- 0% (0 responses)
- 10% (1 response)
- 45% (4 responses)
- 45% (4 responses)

“It is a very mixed picture for orphan drugs as a whole. When it comes to ultra orphan drugs, there are few of these drugs with an evidence base at all sufficient for reimbursement, especially those that impact more on HRQoL than survival.”

Pharmacy Director, MCO, USA

“Very few orphan drugs have demonstrated their value in terms of clinical benefit for patients; most use intermediate criteria for the marketing authorisation and there is a clear gap between registration and HTA evaluation.”

Ex-President of the Transparency Commission, France
“How impactful do you find anecdotal evidence such as patient case-studies on decision-making?”

- 67% Very Useful
- 22% Useful
- 11% Not Very Useful
- 0% No Impact

“I actually think this is useful if obtained in as scientific a way as possible to ensure it is representative of all patients with the rare condition. It is more useful with ultra-orphan drugs with a poor evidence base due to very low numbers.” SMC Economic Assessor, UK

“We look at PRO data, but it has never made a difference on tier of preferred status.” Pharmacy Director, MCO, USA

“We’ve all learned that there is anecdotal evidence for anything you want.” Director Catalan Agency for HTA and research, Spain

“Anecdotal evidence is a contradiction in terms.” Ex-Head of the GKV Spitzenverband, Germany
“Could you please rank the following in terms of priority to fund?”

<table>
<thead>
<tr>
<th>Rank</th>
<th>Disease</th>
<th>Average Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Oncology</td>
<td>7.44</td>
</tr>
<tr>
<td>2</td>
<td>CV Disease</td>
<td>5.67</td>
</tr>
<tr>
<td>3</td>
<td>Diabetes</td>
<td>5.11</td>
</tr>
<tr>
<td>4</td>
<td>Mental Health Disorders</td>
<td>4.89</td>
</tr>
<tr>
<td>5</td>
<td>Rare Diseases</td>
<td>4.78</td>
</tr>
<tr>
<td>6</td>
<td>Asthma</td>
<td>4.22</td>
</tr>
<tr>
<td>7</td>
<td>Obesity</td>
<td>2.44</td>
</tr>
<tr>
<td>8</td>
<td>Smoking Cessation</td>
<td>1.44</td>
</tr>
</tbody>
</table>
“Do you envisage the use of financial arrangements such as PAS to be the rule in orphan diseases? Why?”

- 33% Yes
- 67% No

““This will increasingly become a way to make orphan drugs cumulatively more affordable in terms of budget impact, but not as a way to make many ultra-orphan drugs cost-effective.”
SMC Economic Assessor, UK

“They will become almost mandatory.”
Ex-secretary of CFH, Netherlands

“No absolutely. We are already using them in oncology and I would expect the same in rare diseases.”
Pharmacy Director, MCO, USA
“Do you think that drugs going off-patent creates room for the funding of new orphan drugs?”

“Only a separate budget for orphan drugs can allow for funding of more drugs for rare diseases.” Ex-MOH, Poland

“Although it is a possibility, I would prefer to use for innovative drugs in the same field.” Ex-President of the Italian Society of Pharmacology, Italy

“I don’t think payers should think in silos in terms of rare disease budgets. It should be about society and political willingness to pay.” SMC Economic Assessor, UK
“Do you think that drugs going off-patent creates room for the funding of new orphan drugs?”

- Patent expiry is freeing up limited funds, but these are by no means guaranteed for rare disease products

- Healthcare systems are wrestling with a large number of innovations to deal with ageing populations

- All these innovations have to be funded from existing budgets so there is competition for funding

- The high price of rare disease treatments coupled with the increasing number of diseases identified, puts payers in a difficult position

“Today we talk about the price of drugs in terms of affordability—tomorrow subject will be sustainability. The price of any drug is magical…. but what is not magic is the epidemiology and budget impact, those figures are very real.” Director Catalan Agency for HTA and research, Spain
“Which is more important to you – (a) the cost per patient? Or (b) the overall budget impact?”

11% Cost per patient
22% Budget Impact
67% Both

Budget Impact. It shows expenditures with estimation of population, so gives an assumption to create a risk-sharing scheme.” Ex-MOH, Poland

“I would say both are important; you cannot consider one without knowing the other, but cost per patient is perhaps slightly more important. Budget impact is just a blunt measure of sustainability, but we cannot forget about it.” Director Catalan Agency for HTA and research, Spain

“Cost per patient is most important for assessing cost-effectiveness and has been the most important especially in the UK. However, going forward overall budget impact along side benefit per patient is likely to be most important.” SMC Economic Assessor, UK
“How can the pharmaceutical industry improve the way they communicate with payers?”

- 41%: Pro-active engagement
- 25%: Transparency
- 17%: Data Collection
- 17%: Prepare & understand payer requirements

“More openness in disclosure of data is required. Prepare well in advance to try and meet payer evidence requirements e.g. collect HRQoL data for rare disease drugs that impact on patient HRQoL.” SMC Economic Assessor, UK

“By being trustworthy and acting responsibly; because market access and reimbursement conditions are quite comfortable. It is in the industry’s interest not to ask too much of patients or the SHI.” Ex-Head of the GKV Spitzenverband, Germany
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Each orphan disease is rare, but having an orphan disease is not unusual

- Rare disease: one affecting less than 5/10,000 European people; many diseases affect less than 1/100,000
- However:
  - 5,000 to 7,000 distinct rare diseases
  - 30 million Europeans have a rare disease of some kind

Source: Rare Diseases: Understanding this Public Health Priority, EURORDIS, 2005
Pharmaceutical treatments for orphan diseases are becoming less rare

Source: Orphanet: Lists of rare diseases in Europe, 2013
As the orphan product numbers increase, payers get more nervous about the overall budget impact.

Source: Adapted from Orphanet: Lists of rare diseases in Europe, 2013
Orphan drug expenditure is expected to increase to a higher level of total pharmaceutical spend.

**Budget impact of orphan drugs as percentage of total pharmaceutical spend (2002 - 2020) in the Eurozone & UK**

Payer expectations of orphan drug expenditure are higher than predicted levels of total pharmaceutical spend

Budget impact of orphan drugs as percentage of total pharmaceutical spend (2002 - 2020) in the Eurozone & UK

A recent report from the BIA in the UK highlights the political interest for rare disease

The report comes ahead of the formal consultation on the methodology and process behind NICE’s new Highly Specialised Technology evaluation programme

- **68% of MPs** agree that access to treatments on the NHS for very rare diseases should be based on clinical need and not the NHS’s ability to pay.

- **63% of MPs** disagree that there should be a maximum price per patient for treating people with very rare and complex diseases.

- **Almost half (49%)** of MPs who expressed a preference said that NICE should not apply its standard mathematical methodology to evaluating very rare diseases, while just over a fifth (22%) agreed that it should.

“I think it is effectiveness not price that should be the criterion” **Labour MP**
The gap between regulatory and payer requirements is widening and needs bridging – the 6MWT example

The 6 Minute Walk Test is a good example of a clinical endpoint which is a benchmark in regulatory approval, but difficult for payers to use in their assessment.

<table>
<thead>
<tr>
<th>ERT</th>
<th>Improvement over Baseline 6MWT (m)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Revatio</td>
<td>45</td>
</tr>
<tr>
<td>Aldurazyme</td>
<td>38</td>
</tr>
<tr>
<td>Adempas</td>
<td>36</td>
</tr>
<tr>
<td>Tracleer</td>
<td>35</td>
</tr>
<tr>
<td>Elaprase</td>
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<tr>
<td>Adcirca</td>
<td>33</td>
</tr>
<tr>
<td>Letairis</td>
<td>31</td>
</tr>
<tr>
<td>Lumizyme</td>
<td>28</td>
</tr>
<tr>
<td>Elosulfase alfa</td>
<td>23</td>
</tr>
<tr>
<td>Tyvaso</td>
<td>20</td>
</tr>
<tr>
<td>Remodulin</td>
<td>10</td>
</tr>
</tbody>
</table>

In the future, payers may not accept evidence based on distance in meters alone.

► What does this mean to the patient in day-to-day life?
► Why should they pay for 10m or even 45m improvement?
► The 6MWT is a regulatory endpoint and is not so good for market access.
Orphan drugs are not always seen as having incremental value as the UK example below shows

<table>
<thead>
<tr>
<th></th>
<th>NICE</th>
<th>SMC</th>
<th>AWMSG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orphan products by indication subject to appraisal</td>
<td>18 (26%)</td>
<td>56 (82%)</td>
<td>51 (75%)</td>
</tr>
<tr>
<td>Of these: recommended</td>
<td>7 (39%)</td>
<td>14 (25%)</td>
<td>12 (24%)</td>
</tr>
<tr>
<td>Of these: restricted</td>
<td>5 (28%)</td>
<td>14 (25%)</td>
<td>9 (18%)</td>
</tr>
<tr>
<td>Not Recommended</td>
<td>6 (33%)</td>
<td>27 (48%)</td>
<td>30 (59%)</td>
</tr>
</tbody>
</table>

“I think the picture is mixed across countries; and the distinction needs to be made between orphan and ultra-orphan drugs. In the UK there is a general lessening of the barriers to ultra (very rare) orphan disease drugs recently, but possibly as a counter less acceptance of less rare but still 'orphan' disease drugs.” SMC Economic Assessor, UK
The impact of the disease and the clinical benefit for patients need to be stronger linked.

“It is a common problem and a mistake companies make in not building a bridge between the description of the disease and the clinical benefit to patients.” Ex-Board Member of the TLV, Sweden

“You often have data contained within the natural history study and phase I & II trials. You should use this to strengthen the case for a product and show the possible long-term effects.” Ex-NICE TAC Member, UK
Companies need to be open in explaining limitations of data and remove uncertainty for payers

- Explain why data gaps exist and steps taken to mitigate this
- Justify why clinical endpoints were selected and how they are relevant to the patient population in question
- Use clinical data to model long-term trends if possible
- If dosing is an issue, reassure payers about patient characteristics to provide certainty on budget impact

Companies should avoid being perceived as trying to cut corners
Anecdotal evidence such as patient case-studies can be useful but only when used in the right way.

A delicate balance exists between showing payers the human impact of a disease and being seen as trying to evoke sympathy.

However, it is important to emphasize that anecdotal evidence is needed to fill gaps in clinical evidence.

“It is important to avoid the temptation to give lots of details on the severity of disease. Presenting parameters which are not influenced by the treatment may lead to an impression that the drug does not do very much.” Ex-President of the Transparency Commission, France

“It can play a minor role in giving people a feeling of severity of disease. It is not a problem to show pictures of patients – but don’t overemphasise this angle. Any case-studies should be in a sober fashion and are obviously better in a publication.” Ex-Secretary of CFH, Netherlands
Approaches in terms of data submission need to be tailored to market requirements – the Polish example

This example from Poland shows that there is no point here in focusing on cost-effectiveness.

- Payers in Poland want to know about budget impact, price relative to other therapy and justification of price.
- The clinical aspects are important; but a large focus is on the financial elements.

“This is orphan drugs we are talking about; cost-effectiveness doesn’t make sense – so show me budget impact and price information – this is what we care about in Poland.” Ex-MOH, Poland
It is important to make clear to payers that prices for orphan products are reasonable

- Payers are concerned that companies are unable to justify the high price for orphan drugs
- The recent NICE decision on Soliris, highlights that in a market where this was not a requirement, payers are wanting to establish how companies justify high prices
- It is vital to demonstrate to payers that the price of orphan drugs are reasonable:
  - A product is priced at a level comparable to other similar accepted therapies
  - The price of a product represents a fair ROI given the small number of patients, severity and unmet need
  - The company have invested in expensive clinical trials
  - The company have invested in a facility to produce the product

“We estimate (Soliris) would cost the NHS about £58 million in the first year, rising to over £80 million in 5-years, we need more information. Our independent advisory committee has therefore asked for clarification from the company on aspects of the manufacturing, research and development costs of a medicinal product for the treatment of a very rare condition.” Sir Andrew Dillon, NICE
Payers need to be reassured that patient numbers and budget impact will not be out of control

### Projected

<table>
<thead>
<tr>
<th></th>
<th>Year 1</th>
<th>Year 2</th>
<th>Year 3</th>
<th>Year 4</th>
<th>Year 5</th>
</tr>
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<tbody>
<tr>
<td>Patient Numbers</td>
<td>10</td>
<td>12</td>
<td>15</td>
<td>18</td>
<td>18</td>
</tr>
<tr>
<td>Budget Impact</td>
<td>€5m</td>
<td>€6m</td>
<td>€7.5m</td>
<td>€9m</td>
<td>€9m</td>
</tr>
</tbody>
</table>

### Actual

<table>
<thead>
<tr>
<th></th>
<th>Year 1</th>
<th>Year 2</th>
<th>Year 3</th>
<th>Year 4</th>
<th>Year 5</th>
</tr>
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<tbody>
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<td>15</td>
<td>18</td>
<td>20</td>
<td>22</td>
<td>25</td>
</tr>
<tr>
<td>Budget Impact</td>
<td>€7.5m</td>
<td>€9m</td>
<td>€10m</td>
<td>€11m</td>
<td>€12.5m</td>
</tr>
</tbody>
</table>

Payers biggest fear is uncertainty; with orphan drugs, due to the high price of medicines, even a small miscalculation on numbers or dosing can have a large impact on the healthcare system.

“The Ministry have spent a lot of time and energy on Myozyme and have learnt their lesson. They do not believe there is clinical rationale for double dosing of the product in the Netherlands.” Ex Ministry of Health, Welfare and Sport (VWS)
Some issues, which although not specific to a product, are likely to arise too in negotiations

- These are the kind of issues payers put forward to highlight high prices, reiterate limited budget and to put pressure on companies.

- It is important that companies are prepared to deal with these questions.

“I do not buy the argument that the budget impact is low. We have a number of rare diseases and it really aggravates payers that you claim that budget impact is only small so we should pay for it.” Ex-Head of the GKV Spitzenverband, Germany.
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In summary, payers are becoming tougher towards orphan drugs

• The increasing number of rare diseases is forcing payers to view orphan drugs in a new light and they are becoming increasingly sceptical about the prices charged in relation to the clinical benefit offered.

• There is space for innovation and patent expiry is freeing up funds – but rare diseases are competing with other therapy areas for limited budget.

• The bottom-line is that as rare disease spending becomes a higher proportion of pharmaceutical spending, payers will need to take action to curb this trend.
What does this mean for companies developing orphan drugs?

There are a number of steps that companies can take to ensure that when arriving at market, they have taken the necessary actions to optimise market access and understand the payer viewpoint.

- Justify the R&D investment and be as open and transparent as possible
- Ensure evidence generation is appropriate and reflects regulatory and payer demands
- Build the bridge between the nature of the disease and the clinical benefit to the patient
- Rationalise pricing strategy & acknowledge the changing payer environment
- Ensure you understand your customers needs

“I can sum it up simply….BETTER PREPARATION!! Understand our needs and take the necessary actions.” Director Catalan Agency for HTA and research, Spain
Thank you for your time!

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