



How to provide sustainable access to OMP at national level?

*10th EPPOSI Workshop on Partnering for Rare Disease
Therapy Development*

Monday 26- Tuesday 27 October 2009

Andrea Rappagliosi
VP European Government Affairs
GlaxoSmithKline
Chair of EuropaBio





Rare Diseases: Europe's challenge

Four pillars

1. Communicating the value of biotechnology innovation for healthcare systems
2. Shaping European Union policy to ensure that emerging biotechnology solutions reach patients
3. **Delivering the European Union's vision for orphan drugs to patients with rare diseases**
4. Promoting reward for innovation as key success factor to improve progress in medicine and patient safety – taking account of biotech medicines specificities



And a Joint EFPIA-EBE / EuropaBio Task Force on Rare Diseases & Orphan Medicinal Products



High Level Pharmaceutical Forum

October 2nd, 2008, Forum final Report:

➤ “Rec. 7.3: Member State authorities, companies and the Commission **should strengthen their efforts to ensure access to orphan medicines in all EU Member States**. They are therefore called upon to take up the appropriate ideas developed in the Working Group Pricing”.

➤ endorsement of the paper: *Improving access to orphan medicines for all affected EU citizens*

“To promote the sustainable development of valuable orphan medicines and to improve sustainable access to these medicines for all affected citizens in the EU.”

Pharmaceutical
FORUM



High Level Pharmaceutical Forum

“Bottlenecks”

- The development of a medicine for an orphan indication remains a **risky enterprise**
- Assessing the clinical added value of innovative medicines has proven to be a **difficult task**
- Pricing and reimbursement decision-making is an area of **increasing sensitivity** within almost all of the European Member States



“Potential ways forward”

- Establish **early dialogue** between companies and pricing and reimbursement authorities
- **Exchange of knowledge** amongst Member States and European authorities on the scientific assessment of the clinical added value of orphan medicines
- Promotion of the initial uptake of orphan medicines through **conditional pricing and reimbursement decisions**
- Building EU-level **awareness and expertise** on orphan diseases

“The first step to wisdom is getting things by their right name”

Chinese proverb



- Policy-makers face **tremendous challenges** when making recommendations for the adoption of new therapies to address rare diseases.
- The **perceived value of a therapy** may differ depending on whether one is a payer, a patient, a family member, or a physician **involved in the healthcare of a patient**.
- Where healthcare allocation decisions are **judgemental and values driven**, the fullest possible **transparency and stakeholder involvement** are basic and necessary components.



Orphan Drugs in context: linking access to sustainability in Healthcare

2009 - 2014 scenario under two **coexisting** main drivers:

1. **Centralization of Value Assessment;**
2. **Fragmentation of Payers.**

Centralization of Value Assessment, would include: HTA and Pricing Networks/Initiatives such as: EUnetHTA, MEDEV, EU Network of Pricing Competent Authorities ("Slovenian Initiative"), AGREE Collaboration, Nordic Collaboration on medicines, UK - France - Germany Collaboration,...

Fragmentation of Payers, would include: regionalization, tenders, new access interlocutors (beyond regulators and healthcare authorities, healthcare policy-makers, payers and patient groups other constituency such as regional/local administrators and/or hospital administrators are playing an increasing role in the valuation process of medicines), rebates, price per volume, pay per performance...

Orphan Drugs: linking access to sustainability in Healthcare II



Centralised Value Assessment: Fragmentation of Payers:

1. **EUnetHTA Network 2010/12:** Core HTA dossier, Capacity building for MSs, RE for Pharmaceuticals. (MSs & DG Sanco).
 2. **EMA Initiative** – Getting new medicines faster to patients, anticipate payers input in the regulatory process, scientific capability, “new paradigm” (EMA, Regulatory Bodies & DG Enterprise).
 3. **Swedish Presidency initiative:** Assessing drug effectiveness in real life setting (post MA); Pilot projects in Orphans, Cancer, Biologics (November '09).
 4. **EURORDIS / CAVOD:** facilitate informed decision, MSs commitment to common assessment report, use review of scientific data at time of MA
1. **Consolidated procurement:** e.g. AP-HP (Paris) and the Marseille Hospital-Buying Group, France;
 2. **Contracting/discounting** on branded products required for formulary placement: e.g. Germany;
 3. **Regional level formulary management and tendering:** e.g. Italy;
 4. Application of **regional technology assessment** which result in specific localised data requirement: e.g. Catalonia, Spain...

Building a sustainable access system for ODs in Europe: a few shared principles?



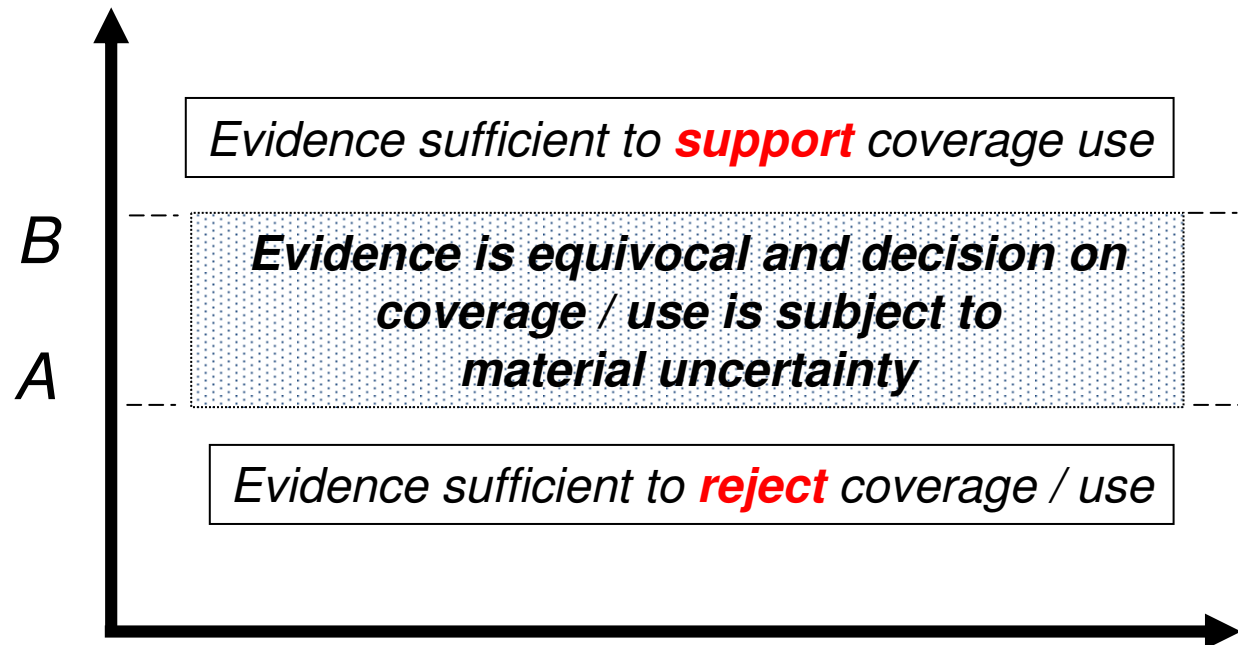
- The price of a orphan drug in each indication should always closely reflect its value:
 - a. Value should be **demonstrable**
 - b. “Value” as **perceived/accepted** by all stakeholders (e.g. payers, patients)
- Value changes over time but pricing tends to be “fixed”:
If the demonstrated value of a drug **changes over time**, its price should change accordingly.
- Open issues:
 - a. **Risk and uncertainty**: over drug value before, during and after patient access.
 - b. **Financial risk and Affordability**.

Assessing the « Value » of innovative drugs: where Uncertainties lie



- Therapies which have the potential to offer **significant health or economic benefits**;

- Therapies where the **balance of uncertainty** suggests that the outcomes of the CED process will confirm the presence of a **significant clinical or economic benefit**;



- Therapies where the source of uncertainty around the clinical or cost/effectiveness of a technology is identifiable, can be overcome through **additional evidence generation** and is the main source of equivocality in a coverage decision.

(See Hutton, Trueman, Henshall: *International Journal of Technology Assessment in Health Care* 23:4 2007)

Addressing uncertainties to ensure patient access



- **Performance-based agreements** provide a guarantee on the product's clinical performance and may differ on the basis used to define the performance and/or on who assesses the performance (***Risk & Uncertainty***);
- **Financial-based agreements** guarantee the product's financial impact and differ on the financial basis they use – drug's price per unit, cost per patient or the total expenditure for a drug or a product class (***Financial & Affordability***);
- **“Holistic” approaches** consist in offering additional services such as patient education. Though these have been mainly an uptake tactic or a part of a performance- or financial-based contract, one could envision them as a more systematic P&R contract at a national level.

(LIF – IMS Innovative contracting in support of value-based pricing in Sweden – Phase 1 – 2009)



Contract type	Contract examples	Motivations for entering into contract	Level of support for value-based pricing	Summary of contract terms	Benefit
Outcome / Behaviour Guarantee	Velcade (UK)	Concerns over value proposition	Blend of upfront price cut & payment by results	Price cut to achieve reimbursement/ Patients showing a full/partial response are funded	Manufacturer gains access
	Actonel (DE)	Concerns over value proposition	Blend of price cut ¹ and payment by results	Manufacturer pays if no. of bone fractures is not reduced compared with generic alendronate	Manufacturer gains access
Biomarker/ Clinical Endpoint	Lipitor (UK)	Concerns over inappropriate use	Usage restricted based on performance	Usage restricted to certain population in order to guarantee a pre-defined goal for population	Manufacturer gains access
	Aricept (CN)	Concerns over inappropriate use/ treatment benefit	Blend of upfront rebate and payment by results	12 weeks free sample upfront/ Aricept only reimbursed for patients demonstrating agreed upon MMSE ² score after 12 weeks	Manufacturer gains reimbursement
Patient Satisfaction	Levitra (DN)	Attempt to induce patients to treatment	Payment by results/satisfaction	Forms were given to patient with prescription – patient could request a refund from Bayer	Manufacturer improves uptake
	Lucentis (DE)	Concerns over value proposition	Payment by results/satisfaction	Patients signed a consent form in order to allow comparison of clinical efficacy of wet AMD drugs	Manufacturer gains access
Price Cap/ Differentiation	-	-	-		
Cost/ Treatment Cap	Lucentis (UK)	Payer concerns over budget impact	Treatment capped at proven optimal utilisation	Ranibizumab is reimbursed by the NHS up to the 14th injection	Manufacturer gains broad access
	Erbix (UK)	Concerns over value proposition/ Concerns of inappropriate use	Treatment capped linked with quantity utilisation	Rebate offered in the form of free stock based on quantity utilisation at a rate of 16% per patient	Manufacturer gains access
Budget/ Expenditure Cap	Revlimid (UK)	Concerns over value proposition	Full access for limited period of time	NHS fund Revlimid for the first 2 years (equivalent to 26 cycles of treatment) Celgene pays after this	Manufacturer gains access
	Sutent (UK)	Concerns over value proposition	Blend of higher value placed on end of life treatment & upfront rebate	First cycle of treatment offered free of charge to achieve cost per QALY/ new NICE criteria for EOL treatments (lower cost per QALY threshold)	Manufacturer gains access
Value-added Services	Anti-TNFs (NL)	Concerns over value proposition	Value-added services forming part of a 'value package'	Value package brought value to the patient and encouraged patient membership with Dutch health insurers that offer the 'value package'	Manufacturer gains access & improves uptake
	Diovan (US)	Concerns over efficacy	Blend of 'value package', payment by results & upfront rebate	Free 30 days trial (rebate), free blood pressure monitoring (added service) & 4 months funding by Novartis if patient failed to reach goal	Manufacturer improves uptake

DRAFT

¹ Price cut was is due to jumbo reference pricing (not a traditional agreement)

² MMSE = Mini Mental State Examination



Performance-based agreements

**Biomarker/
Surrogate/
Clinical
endpoint**

**Clinical
Outcome/
Behavioural**

**Patient
Satisfaction**

**Basis of the
performance**

**Who
assesses
performance**

Example

*Markets/
stakeholders
experienced*

Measurement of a biochemical, considered as surrogate to patient's outcome	Health worker, e.g. physician, nurse	<i>HbA1c reduction in diabetes</i> <i>DAS18 or ACR50 in RA</i>	<i>UK, PCTs</i>
Patient-related outcome or event		<i>Amputations in diabetes</i> <i>Fracture in osteoporosis</i> <i>Smoking cessation</i>	<i>Germany, KK</i> <i>US MCOs, Health insurers</i>
Patient satisfaction with the drug	Patient	<i>Past agreements in lifestyle indications: e.g. erectile dysfunction</i>	<i>US</i>

Budget-holders / access stakeholders

National P&R stakeholders



INNOVATIVE AGREEMENTS

Financial-based agreements

	Type of cost basis	Cost level	Example	Markets/ stakeholders experienced
Price Cap	Price per unit of per pack	At a drug's subpopulations level	<i>Price cap for a specific patient subpopulation</i>	N/A
Cost/ Treatment Cap	Price per patient per year	Drug's level	<i>14 doses course reimbursed – MNF paying beyond for Lucentis</i>	UK, NICE/DoH
	-Utilization-based: # of doses/ year -Non-utilization-based: X€/ year		<i>PPPY set at €16,000 (Tarceva)</i>	UK, NICE/DoH
Budget/ Expenditure Cap*	Total expenditure regardless utilization & price	Drug's or drug class's level	<i>Limit on total expenditure for anti-TNFs</i>	Australia, PBPA
			<i>Limit on subpopulations</i>	Australia, PBPA

Budget-holders/ access stakeholders

LIF IMS 2009

National P&R stakeholders

Overcome traditional pricing setting to improve uptake of orphan drugs



By:

- **delivering** evidence which proves a benefit for patients in the real life-setting that cannot be demonstrated at the time of the marketing authorisation (CED, RSS);
- **removing** cost (or deliver evidence to demonstrate removal of cost) from the healthcare system at the time of the marketing authorisation (PBS);
- **removing** uncertainty about the total cost of a therapy measured in real-life setting (CSS);
- **setting** dedicated funding mechanisms and distribution path for ODs;
- **breaking** the international reference pricing barrier;
- **rethinking** the use of HTA (e.g. OLS “innovation pass”)*

* **“Innovation pass”**. This will be a three-year initiative for selected medicines, which will be funded for time-limited use across the NHS, from a new ring-fenced budget, without going through a NICE appraisal .

« Coverage criteria sit aside the flow of money »



Eddy, D. M. (1996). "Benefit language: Criteria that will improve quality while reducing costs". *JAMA*, 275, 650-657.

- ▶ Ensuring timely access to and rationale use of medicines for all people is a difficult goal in itself;
- ▶ Changing relationship between the public and private sectors has become a critical success factor especially in rare diseases;
- ▶ Long-term strategic dialogue should be focused on building trust, understanding the mutual benefit and adding value to patient access; and
- ▶ Reliability, consistency and integrity from both sides are key but:



Allocation of appropriate and adequate funding within the healthcare system is paramount



*" Let us stop talking about me.
Let's talk about you.
What do you think about me?..."*

Bette Midler



Managing Uncertainty from a Public Health perspective: the « Value » of Orphan Drugs

Discussion/Negotiation points:

- What is “**sufficient**” at different assessment points?
- How can the **timing of data collection** and associated **regulatory and payers decisions** be improved to capture the benefits, risks and value to optimize patient care?
- How can **pre- and post-marketing evidence** requirements be better adapted to serve the need of physicians, patients and payers?
- How can we **manage regulatory and reimbursement decision making** that better rewards and promotes innovation/progress in medicine that benefits patients?



Assessing the therapeutic « Value » of Orphan Drugs: the issues at stake

- Societal cost **vs.** cost of traditional therapy (**financial**);
- Treatment **vs.** no treatment / **health economics needs a Comparator**;
- **Major** contribution to patient care **vs.** traditional efficacy standards;
- **Effectiveness by** randomised controlled clinical trials **vs.** small number of patients **and ethical issues related to life threatening or chronically debilitating conditions (see EMEA Guideline 27/07/06 Clinical Trials in Small Populations)**;
- **Lack of dialogue** between **regulators** and **assessors** on minimum data requirements and **scant attention** paid to phase IV trials / observational cohorts.



Assessing the added therapeutic « Value »: can an Orphan Drug provide the “**minimum evidence expectations**” required?

- Randomized CTs **difficult to conduct** (often individual observational studies, published case reports, opinion of experts, anecdotal reports);
- Biomarker and surrogate endpoints often **not validated**;
- Rarity of patients **does not allow comparative analysis** throughout all the stages of the disease progression (including best supportive care);
- Poor epidemiological data and disease history due to **limited diagnostic skills**;
- **Lack of scientific understanding** of the disease (know-how).