Brussels, 13 May 2015

Call on EU National Competent Authorities for Pricing & Reimbursement to support:

1. **The establishment of a table for price negotiation with a group of Member States**
2. **The scaling-up of the pilots on Early Dialogue between payers and developers of medicinal products**

We are writing to you on behalf of **EURORDIS ([1]) (European Organisation for Rare Diseases) and EPF ([2]) (European Patients' Forum)** in order to drive your attention to the need for establishing new mechanisms that would improve access to medicinal products for patients in Europe while addressing the upcoming challenges in terms of sustainability of the healthcare systems ([3]).

Bringing together different stakeholders to discuss within the EU Processes of the Pharmaceutical Forum ([4]) with the Working Group "Improving Access to Orphan Medicinal Products for Patients in Europe", and thereafter of the EU High Level Group on Corporate Responsibility in the field of Pharmaceuticals, specifically within the Working Group on a "Mechanism of Coordinated Access to Orphan Medicinal Products (OMPs)" ([5]) - the so-called MoCA process - has helped establishing in recent years a new culture of dialogue. This process has raised expectations in terms of truly improving access to OMPs.

Orphan Medicines share commonalities with gene therapies and cell therapies (ATMPs), Paediatrics, Precision Medicines and highly innovative/high price medicines. These products, **most often targeting small populations, are mainly medical specialties supplied in a hospital framework and are therefore delivered by medical experts addressing complex conditions**. The medical practices are progressively converging throughout the EU, therefore **the data generated from both clinical studies and post-marketing phases are collected by these same experts within those hospital centres.**

In a context of fast scientific advances, improved dialogue and emerging platforms for discussion between healthcare professionals, patients, decision-makers, industry, and progressively EMA and HTA bodies, as well as payers, we would like to call on National Competent Authorities to support the two proposals described below.

These proposals seek to foster cooperation through the establishment of a structured dialogue between the Competent National Authorities for Pricing & Reimbursement of pharmaceuticals and other relevant stakeholders. The core objective is not only to enhance the functioning of the Internal

([1]) www.eurordis.org
([2]) http://www.eu-patient.eu/
([3]) Shining a light in the black box of **orphan drug** pricing Picavet E, Morel T, Cassiman D, Simoens S. Orphanet J Rare Dis. 2014 Apr 27;9:62. doi: 10.1186/1750-1172-9-62.
Market watch: Are **orphan drug** companies the pick of the pharmaceutical industry? Morel T, Popa C, Simoens S. Nat Rev **Drug** Discov. 2014 Jan;13(1):10. doi: 10.1038/nrd4205. No abstract available.
Reconciling uncertainty of costs and outcomes with the need for access to **orphan** medicinal products: a comparative study of managed entry agreements across seven European countries. Morel T, Arickx F, Befrits G, Siviero P, van der Meijden C, Xoxi E, Simoens S. Orphanet J Rare Dis. 2013 Dec 24;8:198.
Cost-effectiveness assessment of **orphan** drugs: a scientific and political conundrum. Simoens S, Picavet E, Dooms M, Cassiman D, Morel T. Appl Health Econ Health Policy. 2013 Feb;11(1):1-3. doi: 10.1007/s40258-012-0004-y. No abstract available.
([4]) http://ec.europa.eu/enterprise/sectors/healthcare/files/docs/pharmaforum_final_conclusions_en.pdf
([5]) http://ec.europa.eu/enterprise/sectors/healthcare/files/docs/orphans_report_en.pdf

Market, but also to ensure that national systems achieve an adequate balance between cost-containment, pharmaceutical innovation and patients' access to medicines ([6]).

1. Establishing a "table for price negotiation" with a core group of volunteering Member States:

The growing opportunities of research translating into new treatments for patients with unmet medical needs represent **a great perspective in terms of Public Health outcomes**. Innovative therapies to address high unmet medical needs are coming to the market.

The impact that they have on healthcare budgets is still "absorbable" for national healthcare systems but they are increasingly raising **new challenges both in terms of high price per patient and high impact on healthcare budget**, **thereby generating unequal access across Europe**. It has been estimated that in the European Union, approximatively 30% of patients do not have access to the OMPs they need ([7]).

The challenge around sustainability is becoming pressing. A new model has to be set up in order for society to be able to pay for and provide access to treatments which will generate important medical benefit and health outcomes for patients.

We are therefore calling on National Competent Authorities to create a table of negotiation on pricing based on value assessment, volume and post-marketing evidence generation. This "negotiating table" would allow for enhanced collaboration at EU level between industry and payers to address sustainability issues and ultimately lead to improved access to medicines for patients and improved patient health outcomes. This table could be established in the first place by a core group of "willing Member States" and could progressively integrate more countries on a product by product basis.

This new model to be established is particularly relevant in the rare diseases field for the two main following reasons:

- The model will need to address specific challenges in small populations, which is the case for OMPs, medicinal products for paediatric use and precision medicines;
- At the time of the initial (conditional) market authorisation, there is a high level of uncertainty, which poses new challenges to payers.

A first core group of Member States forming a "coalition of the willing" has expressed readiness to embark in a process of increased collaboration, involving patients, industry, payers, national authorities and HTA bodies. Based on our knowledge, five Member States (Belgium, as the initiator of the process in 2010, The Netherlands, Austria, Italy and Portugal) could form this core pioneering group. Then, on a product by product basis, all EU Member States could be invited to join "table of negotiation on pricing"; hence the number of countries participating to the negotiation would vary from products to products, but having a core group of countries always taking part, while progressively refining the processes and creating a common culture and trust.

Based on EURORDIS' one to one discussions with CEOs and leaders, a large part of the industry seems to be quite interested by a European approach to the market rather than at scattered national level, especially in the field of orphan medicinal products. The main incentive within the EU Regulation on

([6]) http://ec.europa.eu/enterprise/sectors/healthcare/competitiveness/pricing-reimbursement/index_en.htm
([7]) http://www.eurordis.org/content/survey-patients%E2%80%99-access-orphan-drugs-europe

OMPs is the 10 or 12 years market exclusivity, but **the European Commission does not provide a mechanism to have a real access to the EU market.** Most of the national price & reimbursement negotiations for orphans are taking place a long time after the 180 days proposed in the Directive on Transparency of measures regulating prices of medicinal products ([8]).

A European collaborative approach to price negotiation and market entry would accelerate market access and patient access, thereby generating quicker revenues and return on investment for the producers, secure a certain volume, reinforce the launch effect, reduce the administrative burden and negotiation steps - in exchange of some level of price reduction. It would also enable a more rapid and more robust post-marketing data collection and re-assessm**ent.**

This approach can only be pursued if there is wide acceptance by all parties involved of the two following principles:

1) **Pricing discussions are based on a value assessment – especially for products in areas with small populations and high uncertainties – and are linked to the post-marketing evidence generation;**
2) **There is a need to accept - by all involved parties – that prices will possibly be fluctuating over time: this means that prices may increase or decrease after the first setting of a price.**

2. Fostering Early Dialogue between payers and industry

a. Through the implementation of the MoCA pilots:

It is more than five years now that the Working Group (WG) on a Mechanism of Coordinated Access to OMPs, established within the Process of Corporate Responsibility in the field of Pharmaceuticals and launched under the **Belgian Presidency of the EU Council in 2010**, has gathered the most relevant stakeholders, including for the first time HTA bodies and payers. The WG has been meeting on a regular basis to reflect and develop proposals on a way to create voluntary collaboration at EU level in order to improve access to OMPs for rare disease patients. Two years ago, **in April 2013, the final Report from the MoCA Working Group was published concluding that enhanced collaboration and coordination would lead to improved access to OMPs for patients**. The Report also identified that defining the (added) value of a new OMP represents an important aspect for improved access.

In order to achieve this goal, the MoCA group proposed **a European Transparent Value Framework** as the basis for collaboration between different Member States and other stakeholders towards a **common assessment of the value** of orphan medicinal products, bearing in mind that this value may evolve over time, depending on the evidence generated all along the life-cycle of a medicine.

From the beginning, **the MoCA process has been conceived as an "Early Dialogue" process, on the basis of voluntary collaboration, increased mutual trust and understanding, within the existing legislative framework, and with no binding commitment for parties involved**. This early dialogue and enhanced cooperation would help responding to the challenges linked to bringing treatments to small populations, in areas of high unmet medical needs, high uncertainties and high prices.

It is currently felt by all the stakeholders who participated to the MoCA process **that now is the time for a new series of pilots to be thoroughly implemented in a more structured and better supported way in order to generate concrete results and learn from these experiences**. Today, some maturity

([8]) http://ec.europa.eu/enterprise/sectors/healthcare/files/docs/transpadir_finalprop01032012_en.pdf

and agreement on the main concepts around the MoCA has been reached; the process needs to be further supported and substantiated with concrete pilots.

We are therefore calling on National Competent Authorities to support more broadly the MoCA Pilots which has to be pursued within the MEDEV (Medicines Evaluation Group) as originally envisaged, in an open and flexible way.

b. Through the participation of representative of payers to EMA & HTA Parallel Scientific Advice as well as to the Scientific European Early Dialogue of the EUnetHTA:

The pilots of EMA & HTA Parallel Scientific Advice started in 2010 and are now a routine practice with approximatively 55 pilots to date. They have become mainstream ([9]) with a large support from EMA, Commission, all HTA agencies, industry at large, overcoming the initial scepticism, resistance and cautiousness. A next step, will be to have EMA-EUnetHTA Parallel Scientific Advice, hence between to the European institutions.

The HAS (Haute Autorité de Santé, France) on behalf of the EUnetHTA is conducting since 2014 the project on Scientific European Early Dialogue (SEED) [10]with over 20 pilots in one year. Few additional pilots are directly conducted by the EUnetHTA. The next EUnetHTA Joint Action, starting in 2016, does plan to have an intensive number of SEED ([11]) every month with product developers.

One of the limit and missed opportunity is the absence of payers so far in this two innovative and successful early dialogue processes with product developers.

We are therefore calling on National Competent Authorities to engage into these EMA – HTA Parallel Scientific Advice and EUnetHTA Scientific European Early Dialogue. The representation of payers could be through the MEDEV or through the core group forming the table of negotiation.

Overall, all parties will gain from an early dialogue between payers and product developers. In itself, this participation enables payers to perform a horizon scanning of products under development. Payers will acquire a better knowledge on the disease or condition, on the product, on the therapeutic indication pursued, on the strategy of the company particularly with regards to its clinical development plan and regulatory approach. Payers will be able to express their questions, concerns, expectations early on e.g. acceptable level of uncertainties, need for a registry, study on living with the disease, estimation of hospital costs saved, etc. Product developers will acquire an earlier uptake on what to do to address payers concerns and build solutions within the clinical research so to streamline the development and optimise the allocation of resources.

This approach is a must when bringing to market innovative products at the end of phase 2 with convincing but limited data and high uncertainties, when conditional approval is envisaged, when authorising a gene or cell therapy which may require a high tech hospital environment limited to few countries, hence requiring an anticipation of the economic model and route of access for patients.

([9]) http://www.ema.europa.eu/docs/en_GB/document_library/Report/2014/05/WC500166228.pdf
([9]) http://www.earlydialogues.eu

3. Main elements that are currently being explored in different EU platforms and need to be integrated within a new model:

1) There is a need to recognise that, in the area of therapies for small populations, the evidence generation is a continuum all along the life-cycle of the asset. In fact, the data that are collected in clinical studies, within a homogeneous patient group selected according to specific common criteria, do not reflect the reality of the medical use in real-life setting. It is therefore necessary to place the product on the market (which is restricted by definition) earlier, as soon as a satisfactory efficacy has been demonstrated, at least in one sub-target patient population and then collect real world data/evidence in order to refine the safety/efficacy evaluation, define the target patient groups, the effectiveness, as well as the best place of the treatment within the therapeutic strategy. This will help defining the optimal practice of care.

2) It is important to support and promote the development of the Medicines Adaptive Pathways to Patients (MAPPs) approach, in particular at the EMA (Scientific Advice and Adaptive Licensing), at the HTA level (Early Dialogue, adapted core value dossier and European common assessment report), but also with payers. "Only patients can legitimately determine how much risk or harm they are willing to accept for a given benefit. Patients know better that anyone which trade-offs between the benefits and the risks/uncertainty are acceptable" ([12]). This is why the risk/benefit assessment at the CHMP needs to take into account the patients' position in a context of higher uncertainties. This will help payers to take well-informed decisions.

3) A mechanism based on the MoCA process should be developed while taking into account the recent trend towards Medicine Adaptive Pathways to Patients. In this context, the **link between the Table for price negotiation and post-marketing evidence generation has to be underlined: negotiations between payers and industry to determine the price, with the participation of experts and patients, based on the value assessment tools of medicines (such as the EPARs, HTA reports, European transparent Value Framework), together with a certain degree of transparency on costs, and an estimation of the volume of patients to be treated in Europe, has to be linked to the generation of post-marketing evidence.** Price and post-marketing evidence generation should be closely linked so that prices will fluctuate based on re-assessments at key time-points over the life cycle of the medicine. This approach calls for close collaboration with EMA and HTA European collaborative work, in order to align post-marketing requirements.

Looking forward to hearing from you soon,

Yours sincerely,

Yann Le Cam
Chief Executive Officer
EURORDIS – Rare Diseases Europe

Nicola Bedlington
Secretary General
European Patients' Forum

([12]) http://static.correofarmaceutico.com/docs/2015/05/05/informe_anual_2014_ema.pdf