POLICY BRIEF

Towards a pharmaceutical legislation that truly enhances public health and ensures sustainable health care systems in Europe

Europe needs a modern, long-term sustainable regulatory framework for pharmaceuticals that truly enhances public health for the European population, while strengthening the competencies and decision power of Member States, responsible for national health care systems. The current revision of the pharmaceutical legislation (including the general pharmaceutical legislation, legislation for orphan medicinal products and medicinal products for paediatric use) brings new opportunities for targeted stimulation of pharmaceutical development, and for strengthened accessibility of clinically relevant – safe, effective and cost-effective – medicinal products that reach the intended patient populations, now and in the future.

Key messages

The Swedish Association of Local Authorities and Regions (SALAR), member organisation for the 21 regions responsible for health care in Sweden, want to see the following five key messages being reflected in the revised pharmaceutical legislation.

1. The European pharmaceutical legislation needs to **consider the broader spectra of the pharmaceutical system and the contexts of national health care systems**, where new medicines are being introduced – beyond the suboptimal focus on development and authorisation of new medicines. This is important for efficient, safe and reasonably priced medicines to reach the whole way to intended patients. This is also a prerequisite for the **long-term sustainability of national health care systems in EU Member States**.
2. The regulatory framework needs to **steer towards authorisation of new medicines that addresses truly unmet medical needs**, clearly defined from patient and health care perspectives. This includes more extensive requirements of **proven added clinical benefit for patients** with unmet medical needs, taking into account all kinds of available treatment options for specific patient populations – not only authorised medicines on the European market. A more restrictive application of the term unmet medical need is needed in order for EU orphan incentive to be used effectively and in a way that stimulates development of relevant pharmaceuticals for Europe.
3. Requirements for market authorisation of new medicinal products need to be clearly linked to **relevant and robust clinical evidence, including proven safety and efficacy with clinically relevant endpoints, prior to market authorisation**. This will better enable medicinal products with added clinical benefit to reach patients in various EU Member States and will also contribute to maintaining the trust in European institutions as well as Community codes and procedures.
4. The European pharmaceutical legislation needs **to strengthen availability of both older and established treatment options as well as new medicines in health care**. The legislation's focus on industrially produced – commercial – medicinal products for human use intended to be placed on the European market should neither result in the crowding out of established medicines, nor hinder health care providers to find novel uses for existing medicinal products or impede clinically driven innovation, development and use of other treatment options – **beyond industrially produced and EMA authorised medicinal products**. The possibility for national exceptions needs to be clarified and broadened. Furthermore, pharmaceutical supply chains need to be secured and strengthened, with legally clarified responsibilities and repercussions with regard to manufacturing, warehousing and distribution chains for both old and new medicinal products.
5. The regulatory framework needs to **promote inter-changeability and availability of generic medicinal products and biosimilars** on the European market, when patents expire. Incentive schemes and market exclusivity for brand-name companies (patentees) should not hamper the development and availability of these medicines. This is key for competition and the functioning of the pharmaceutical market in Europe.

The content of the European legislation impacts the availability of medicinal products in national health care systems and does, in large parts, also affect what and how treatment options can be made accessible to and reach patients who need them. The current legislation has been successful with regard to the establishment of the Community code and common framework for market authorisation and availability of industrially produced medicinal products intended for human use, and commercialised and marketed on the European market. Incentive schemes for research and development has contributed to scientific breakthroughs and pharmaceutical development.

However, the European regulatory framework has not been able, in a satisfactory way, to target truly unmet medical needs of patients, nor has it been able to consider and build on perspectives that are relevant for national health care systems in EU Member States. Market mechanisms necessary for the functioning of the pharmaceutical market in Europe have been given insufficient attention which will, in the longer term, pose a threat to the sustainability of national health care systems.

ABOUT MEDICINAL PRODUCTS

Medicinal Product Any substance or combination of substances presented for treating or preventing disease in human beings. Any substance or combination of substances which may be administered to human beings with a view to making a medical diagnosis or to restoring, correcting or modifying physiological functions in human beings is likewise considered a medicinal product. (Directive 2001/83/EC (Article 5))

Orphan medicinal products, "orphan drugs", are medicinal products which have been granted orphan designation by EMA. The criterion for designation builds on the condition being rare (not more than five in 10 thousand persons in the Community), or for the medicinal product being intended for life-threatening, seriously debilitating or serious and chronic conditions. The criteria are also that no satisfactory method of diagnosis, prevention or treatment of the condition in question has been authorised in the Community, or, if such method exists, that the medicinal product will be of significant benefit to those affected by that condition. (Regulation (EC) No 141/2000)

The initial intention of the regulation was to stimulate development of medicinal products for conditions which occur so infrequently that the cost of development and bringing to the market a medicinal product to diagnose, prevent or treat the condition would not be recovered by the expected sales of the medicinal product, so that the pharmaceutical industry would be unwilling to develop such medicinal products under normal market conditions. These market conditions no longer apply. Today's orphan designations are used for both rare and ultra-rare, untreatable conditions, as well as for medicinal products for sub-groups of common and treatable conditions. The orphan drug designation further admits incentive schemes and granted market advantages such as market exclusivity, excluding other competitive medicinal products from the market. Orphan medicinal products are also more commonly introduced with very high prices from the pharmaceutical companies which in many cases hampers patients' access to treatment. The orphan drug market has grown into an expanding and lucrative segment of the pharmaceutical market – partially driven by regulatory incentives globally.

Medicinal products for paediatric use addressing paediatric indications and are intended to be used in a part of or the whole population of children (0-18 years). Are, similar to orphan drugs, associated with various types of incentive schemes and market advantages. Regulation (EC) No 1901/2006

Market authorisation for medicinal products intended for human use within the Member States occurs in accordance with the European regulatory framework legislation. The European Commission, through the European Medicines Agency (EMA), is responsible for the authorisation procedures for i.a. technologically advanced medicinal products, medicinal products consisting of new active substances or being developed with significant therapeutic, scientific or technical innovation. The procedure is managed in a centralised process and also includes medicinal products with orphan designation (orphan drugs), paediatrically approved pharmaceuticals and ATMP. (Regulation (EC) No 726/2004)

Exceptions to the EU regulatory framework A Member State may, in accordance with legislation in force and to fulfil special needs, exclude from the provisions of the regulatory framework for medicinal products that are supplied in response to a bona fide unsolicited order, formulated in accordance with the specifications of an authorised health care professional and for use by his individual patients on his direct personal responsibility. This is essential for national health care systems as it provides treatment options for patients, beyond industry driven and commercial medicinal products approved for the European market. (Directive 2001/83/EC (Article 5))

ABOUT EUROPEAN LEGISLATION

The scope of European legislation builds on determined areas of, delimitations of, and arrangements for exercising **Union competencies in relation to EU Member States**, as defined in the Treaty of the Functioning of the European Union. This also applies to the pharmaceutical legislation. In terms of public health, the EU and its Member States **share competencies**. EU efforts build on principles of "common safety concerns in public health matters" and, more specifically defined in the area of pharmaceuticals, for "setting high standards of quality and safety for medicinal products and devices for medical use". Valuations and pricing thus fall outside of the scope of Union competencies.

Union action can **complement national policies** for the purpose of improving public health and preventing illness and diseases but shall **respect the responsibilities of the Member States** for the definition of national health policies and for the organisation and delivery of health services and medical care. The responsibilities of the Member States shall include the management of health services and medical care and the allocation of the resources assigned to them. The Union has **exclusive competencies** over the establishment of competition rules necessary for the functioning of the internal market, including the pharmaceutical market.

This principle of **proportionality** states that Union action shall not exceed what is necessary to achieve the objectives of the Treaties. The principle of **subsidiarity** states that decisions should be taken as openly and as closely as possible to the citizens and only if such action cannot be achieved at a more decentralised level in Member States. The two principles are derived from the Treaty of the European Union and govern the scope and use of Union competencies.

(More information about the division of competencies can be found in the Treaty of the Functioning of the European Union, Article 168 and Articles 2(5), 6(a) and 4(2)(k), as well as Article 3(1)(b); and Treaty of the European Union, Articles 5 and 10(3))

Introduction

The European pharmaceutical legislation consists of a regulatory framework for medicinal products in the EU. During the 2022/2023 the European Commission is expected to present revisions on the current legislation, including the legislation on orphan drugs and medicines for peadiatric use.

During the past two decades the regulatory framework for medicinal products in Europe has become more and more centralised, while **stimulation of research and development** have been introduced to promote pharmaceutical development intended for the European market. This has taken place at a time of rapid scientific development and breakthroughs. The importance of a EU common framework cannot be stressed enough, and has been key for the ability of Member States to manage such development. Incentive schemes in combination with i.a. simplified regulations for clinical studies, flexible evidence requirements and adaptive pathways for earlier market authorisation have been introduced with the purpose to increase availability of new medicincal products in Europe.

However, *availability* **of new medicines is not the same as the use of new medicines and de facto patient access (***"accessibility"***)**. The European regulatory framework has in this regard failed in securing the functioning of the complete system, from research and development to market authorisation, implementation and use of new medicinal products in clinical practice. One key explanation to this is that the **current regulatory framework is lacking a clear health care perspective**. Far from all medicinal products that are authorised at European level are clinically relevant from a health care perspective, and many new medicines are approved with limited documentation and clinical evidence, which translates into great uncertainty when it comes to their intended use. Furthermore, not all medicinal products are introduced to the market and those that are introduced not seldom come with increasingly high prices from the pharmaceutical companies. In combination with the uncertainties of actual safety and efficacy, this results in greater difficulties of solid health economic evaluations and decision making for introducing a medicine into clinical practice. Consequently, national health care systems are faced with greater risks of misallocation of resources and crowding out of other pertinent health care interventions.

The regulatory framework has also proven to be **vulnerable to unintended use, or misuse, by pharmaceutical companies** who gain advantages from the broad application of orphan drug designation criteria and the generous incentives that comes with it. Numerous examples of "regulatory innovation" show that new orphan drugs are being approved in areas where treatment options already exist. This sometimes leads to impaired access to well-established, well-functioning and cost-effective treatment options to broader patient populations.

The focus on development of new medicinal products for patient sub-groups of common diseases rather than more targeted focus on new treatments for truly unmet medical needs for patients with rare diseases has also been recognised by patient organisations in Europe such as EURORDIS. The organisation stresses the importance for national, European and global authorities to curb this trend, many times packaged as under the term "precision medicine". This kind of regulatory ingenuity does not only impair the health and care of patients in Europe, but it also contributes to a malfunctioning pharmaceutical market and inflates company pricing of medicinal products.

Currently, **the European pharmaceutical legislation builds on an industry perspective on medicinal products** as the regulatory framework assumes market authorisation of industrially produced medicinal products intended for human use, commercialised and marketed on the European market, as the main process for availability of new medicines to patients in Europe. This is executed through the mandate given to the European Medicines Agency (EMA) and with the purpose of setting high standards of quality and safety for medicinal products. The focus on industry perspective **however disregards, to a great extent, both academia and health care and their important role when it comes to research, development, and innovation within the pharmaceutical field** – many times as driving forces in terms of development of new therapies and treatment options for patients.

Historically, health care professionals and health care providers could apply science and proven experience in the search for new areas of use for older and well-established medicines and also drive the development of new, more technologically advanced therapies. This generated new treatment options for patients with rare diseases and severe conditions, e.g. for patients with transthyretin-related familial amyloid polyneuropathy and multiple sclerosis (off label in line with science and proven experience) and advanced cell therapies and lifesaving treatment for patients with severe burns (hospital exemption for ATMPs). Today, these kinds of possibilities are severely limited unless driven by commercial purposes.

More and clearer pathways for approval and use of both new and older – safe and effective – treatments are needed at the national levels, beyond the commercially driven pathway. The exclusion from the European legislation (expressed in article 5, Directive 2001/83/EC) is too vaguely formulated and has not resulted in broader use of non-commercialised medicinal treatment options within national health care systems.

A European regulatory framework which primarily builds on industry perspectives – and thus steers national health care systems towards the use of commercial medicinal products – **results in de facto limitations of how EU Member States can execute their national competencies** with regard to decision making and the management and resource allocation for health services and medical care. This is not sustainable for national health care systems. For Sweden this also hampers principles of local governance, the free right of prescription for health care professionals, and the possibility of choosing from different types of safe and effective treatment options (not only EMA approved and commercialised medicinal products). These limitations also impact on the possibilities of managing cost-effective health care and undermines efforts towards maximised health outcomes within the publicly funded health care system.

EXAMPLES OF "REGULATORY INNOVATION" WITHIN THE LAW – WHOSE UNMET NEEDS ARE BEING ADDRESSED BY THE REGULATORY FRAMEWORK?

Chenodeoxycholic acid Leadiant An older medicinal product developed in the 1970s and used "off label" for treatment for a range of bile duct diseases. In 2017 the medicinal product was authorised for a rare subgroup of bile duct disease (smaller patient population), based on a register study with 35 patients. It was granted orphan designation with market exclusivity. The older medicinal product has since been withdrawn from the market. Sharp price increases were introduced by the company and apply also for the broader patient population (when used as "off label") which has resulted in affordability and accessibility challenges.

Amglidia An older medicinal product for diabetes in tablet form (glibenclamide) which has been used "off label" but was later deregistered as a product. In 2018 an oral solution of the medicinal product was granted market authorisation for new-born babies, diagnosed with diabetes. This product was granted orphan designation with market exclusivity, based on data from published studies where i.a. 10 patients had been treated with both oral solution and administered as a crushed tablet form of the medicine (considered as satisfactory treatment). Added clinical benefit of the oral solution could not be proven in the studies.

Verkazia A medicinal product consisting of the known substance ciclosporin, for treatment of an allergy induced eye disease affecting children and adolescents. The condition is rare but can be treated satisfactorily with the medicinal product Ikervis, also containing the substance ciclosporin, and EMA approved for a broader patient population (same market authorisation holder). With Verkazia, the company has sub-targeted the paediatric population (smaller patient population) for market authorisation and has thereby been granted orphan designation and market exclusivity.

Focus areas for legislative action – EU pharmaceutical strategy leads the way

The current European pharmaceutical strategy was launched in 2020. The strategy is described by the European Commission as a patient-centred strategy aiming to secure quality, efficacy and safety of medicinal products. The strategy contains four main area of focus, including suggestions for legislative action, that aims to ensure access to new medicines at reasonable and affordable prices for patients while supporting the competitiveness, innovation, and sustainability of the European pharmaceutical industry. The strategy also calls for greater effort for crisis preparedness and response and strengthening the role and independence of EU on the international arena.

The pharmaceutical strategy has been well received from different stakeholders. Nonetheless, great discrepancy remains with regard to specific interventions and legislative action that are necessary from the perspective of different stakeholders, i.a. patient representatives and pharmaceutical industry. In Europe, voices are also raised on the need for clearer health care and payer perspective within the pharmaceutical area. E.g. affordability cannot only be seen from the perspective of patients but also need to consider national health care systems and different kind of payers such as tax payers and insurance payers. Sustainability is not only of essence from an industry perspective but also from a health care perspective. These dimensions are key for enhanced access to new medicine and treatment options for patients in Europe – through a suitable, credible, and long term sustainable regulatory framework for medicinal products in Europe.

Call for legislative measures that incorporates national health care perspectives

SALAR, member organisation for the 21 regions responsible for health care in Sweden, want to see a pharmaceutical legislation that enables the use of a variety of medicines and treatment options in the care and treatment of patients in Sweden and in other EU Member States.

The following five key messages therefor needs to be reflected in the legislative action and revision of the regulatory system for new medicines in Europe.

1. A European legislation that considers the broader spectra of the pharmaceutical system

The European legislation needs in a clearer way take the broader context of national health care systems, where new medicinal products are being introduced. From research, development and market authorisation of new medicines which is a subject to a joint Community code, to introduction, use and patient access of new medicines which is managed by national health care systems in EU Member States, according to national competencies.

Market authorisation is key in order for pharmaceutical companies to market and sell medicinal products in Europe and is therefore of importance for the availability of medicines in the European market. At the same time, the prerequisites for market approval also affects how new medicines are being adopted by health care systems and becoming accessible to patients. E.g. through the evidence levels prior to market approval and accepted uncertainties regarding safety and efficacy. The regulatory framework is also precedent to what and when incentive schemes are being used and in what cases competition restriction measures and market benefits are granted. The de facto possibilities of health care systems to lead research, development, innovation and the ability to choose the right type of treatment option for the right patient – based on needs – has to be safeguarded in the legislation. This requires a more holistic approach in the European legislation. As such, the revision of the pharmaceutical legislation should not only aim at increasing available medicines and setting high standards of quality and safety for medicinal products but needs an overarching goal of contributing to the long-term sustainability of national health care systems. This creates conducive conditions for patient accessibility of new medicines and is the path towards enhanced public health in Europe.

National competencies and responsibility for health care as well as the possibility of local governance and de facto subsidiarity – in national health care systems in EU Member States – needs to be safeguarded in the revision of the pharmaceutical legislation.

2. A shift towards medicines for truly unmet medical needs

Incentive schemes for the development of medicinal products should be based on truly unmet medical needs – premiering development in areas where real treatment gaps exist – and thus result in new medicines that reach the whole way to the patients.
The term unmet medical need ought to emanate from patients' real needs and therefore also consider the broader health care perspective by i.a. relating to all types of treatment options available for the patient population – not only commercial medicinal products approved for the European market. Greater emphasis and requirements of proven added clinical benefit for patients is also key, e.g. in the form of increased length of disease-free or progression-free survival; safer and more efficient ways of restoring, correcting or modifying severe medical conditions; as well as freedom from debilitating adverse effects of treatment.

A more precise definition with a patient-oriented approach for how to determine orphan designation would premiere and stimulate research and development in areas where the needs are greatest.

SUGGESTIONS FOR CHANGE OF FOCUS IN THE CRITERA FOR ORPHAN DESIGNATION

FROM A COMMERCIAL FOCUS ON MEDICINAL PRODUCTS	TO A MORE PATIENT-ORIENTED FOCUS
Medicinal products intended for life-threatening, seriously debilitating or serious and chronic conditions.	Medicinal products intended for life-threatening, seriously debilitating or serious and chronic conditions (remains unchanged).
For rare conditions (not more than five in 10 000 persons in the Community). Or (if the condition is not rare) It is unlikely that the marketing of the medicinal product in the Community, without incentives, would generate sufficient return to justify the necessary investment.	For rare conditions (not more than five in 10 000 persons in the Community).
There exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorised in the Community. Or (if such method exists) The medicinal product is assumed to be of significant benefit to those affected by that condition.	There exists no satisfactory method – authorised or otherwise established in health care within or outside the Community - for diagnosis, prevention or treatment of the condition in question. Or (if such method exists) The medicinal product has proven to have added clinical benefit for patients who suffer from the condition in question.

This kind of approach would also be better suited for the incentives and market advantages that are currently associated with the medicinal products with orphan designation. This would also steer the pharmaceutical industry and the associated multi-billion financial investments towards relevant products and a clearer focus for future development. In the long-term this also bring more relevant and competitive pharmaceutical companies.

This suggestion needs to be understood in the light of the current generous incentives that have been introduced to stimulate pharmaceutical development for orphan and paediatric use, i.a. extended scientific advice, prolonged patent and market exclusivity, lower regulatory fees. These incentives have been effective but have also been overused, not the least when it comes to orphan drugs. The medicinal products that are covered by the incentives are not seldomly associated with higher price expectations from the pharmaceutical companies which means de facto double compensation, first through the regulatory incentive schemes and market advantages in the phase for research, development and market approval, and later in terms of introduction to higher prices and expectations of higher reimbursement. This hampers patient access which in the end means that the initial incentives have been used in vain.

3. Increased focus on satisfactory, relevant and robust – clinical evidence for market authorisation

It is of great importance that the regulatory system for market authorisation of new medicinal products ensures sufficient levels of clinical evidence, for patients and for health care providers and payers. This is particularly key also from an affordability perspective. Uncertainties of clinical benefits in combination with high prices from pharamceutical companies inhibits the possibilities of prioritisation and decision making in terms of introducing and adoptiong new medicines in national, regional and local governance structures in EU Member States, which in the end hampers patient access. The Community code and processes for market authorsation therefore needs to incorporate perspectives, needs and specific considerations from national HTA authorities, authorities responsible for pricing and reimbursement, payers as well as health care providers and patients – to ensure that the requirements for documented clinical evidence prior to market authorisation are relevant also for decision making processes on introduction and adoption of new medicinal products in health care.

This suggestion needs to be understood against the backdrop of current approach to evidence requirements at European level, with shorter and more adaptive pathways towards market authorisation with increasing number of medicinal products being approved with limited clinical evidence regarding safety and efficacy. It is certainly positive that value creating medicines reach the market in a timely manner, but in practical terms the fast-tracked market approvals at European level can also results in lengthy processes and delays in patient access, at national level, in the EU Member States. It would here be desired to see a more restrictive approach to the application of adaptive pathways and a clear link to areas with truly unmet medical needs (according to suggestions made in the previous point). As such, truly unmet medical needs would be a defining criterion for what kind of medicinal products that require a more urgent management of the market authorisation procedure.

SUGGESTIONS FOR A CLEARER CORRELATION BETWEEN LIMITED EVIDENCE AND CONDITIONS FOR MARKET AUTHORISATION AND INTRODUCTION IN HEALTH CARE SYSTEMS IN EU MEMBER STATES

LIMITATIONS IN EVIDENCE LEVELS	RESULTS IN	
Limited study design with regard to scope, inclusion criteria, comparative data, and follow-up time for clinical studies prior to market authorisation.	Limited scope of the market authorisation with regard to approved indication, in line with applied limitations in the clinical studies.	Other medicines and treatment options that are established in health care systems – within or outside of the Community – are not out-crowded and can be made available to patients in EU Member States.
Conditional approval or approval under exceptional circumstances with requirements of additional data on the safety and efficacy of the medicinal product in question.	Time limited and binding follow-up on evidence requirements in the approval. Withdrawal of granted approvals, market exclusivity and other incentive schemes if the follow-up is not adhered to or if data on safety and efficiacy is not sufficient. Market approval is not fully recognised until converted into a standard market authorisation.	
Market authorisation is granted based on short term and limited evidence and absense of clinically relevant comparative data.	More restrictive assumtions on safety and efficacy in health technology assessment and economic evaluations. Lower initial net prices for payers.	

When medicinal products are approved despite high level of uncertainty regarding safety and efficacy it is difficult to assess the clinical benefit as well as potential adverse safety considerations of a new medicines compared to other already existing treatment options. In particular, health economic evaluations and cost-effectiveness analysis – assessing the safety and efficacy in relation to the price – becomes a challenge for national health care systems. In Sweden for example, the use of value-based pricing and possibility to prioritise treatment options in ways that ensures maximum health outcomes for the population, for each Swedish crown spent, is undermined. Uncertainties with regard to safety and efficacy implies higher risks of mis-prioritisation of health care resources and, as a result, risks of crowding out other health care interventions for other patient groups. A greater transparency around documented clinical evidence used as a basis for market approval is desired from a health care perspective.

Furthermore, the applied study design, inclusion criteria for the study population, relevant control groups as well as scope of the clinical study with regard to number of patients included and time for follow-up of results from the studies need to better correspond with the scope of the market approval granted in terms of intended indication and conditions for introducing a medicinal product on the European market. The withdrawal of medicinal products that are not delivering according to expected safety and efficacy need to be applied in a more systematic way than what is currently the case.

4. Increased availability of both old and new treatment options within national health care systems

The revised pharmaceutical legislation needs to create mechanisms that maintain older, established, well-proven and effective medicines on the market while at the same time harnessing the research, development, innovation and proven experiences of using various medicines within the health care systems. This needs to be understood in the light of the primarily commercial perspective of the current legislation. To safeguard access to older medicines (sometimes with expired patents) as well as other treatment options give increased possibilities of clinical practitioners to choose among various kind of treatment options when deciding on a course of treatment. This would result in greater access to treatment options for patients in Europe.

It is here important to note the regulated definition of medicine is not limited to only commercial medicinal products and a modern regulatory framework should be able to relate to the use of non-commercial medicinal products and/or commercial medicinal products that are not primarily intended for the European market. The exclusions from the European regulation that is articulated in "Article 5" of the general pharmaceutical legislation (Directive 2001/83/EC) therefore needs to be clarified in ways that grant national health care systems the right to secure availability and access to safe, effective and cost-effective medicinal treatment in a more predictable way and in larger scale. There is a need of clarifying roles and responsibilities in relation to national competent authorities and an expressed legal mandate for national actors to manage health care applications of approval for the use of medicinal products in new areas (health care-driven "repurposing" processes) or new medicinal products developed through research and innovation within health care system (e.g. hospital exemption ATMPs).

This has the potential to contribute to great value for patients where treatment gaps currently exist, foster cost-effective use of resources within national health care systems, disseminating good clinical praxis within the EU, while medicinal products that are unlikely to reach the market without targeted incentives could still be made available and accessible to patients who need them.

It is therefore unfortunate that the pharmaceutical companies associations are arguing for the opposite and call for legislative measures to restrict the prescription of medicinal products outside of market authorised indications (off-label), limit the use of pharmacy prepared medicines and medicines that are not approved specifically for the European market including older and established medicines that have been withdrawn from the European market – as well as hospital exemption ATMPs. Harder restrictions would result in extensive consequences for treatment options available for patients. Health care providers would be regulatorily steered towards commercial medicinal products and EU Member States would have national competencies restricted with regard to delivery of health services and medical care as well as prioritisation and allocation of resources. In Sweden this would also mean a de facto limitation of the free prescription right and the use of a range of well documented treatment options while such regulatory restriction also risks reducing innovation capacity and incentives within national health care systems.

Lastly, it is also key for the regulatory framework to address the need for a reliable pharmaceutical supply in Europe with legally clarified responsibilities and repercussions with regard to manufacturing, warehousing and distribution chains for both old and new medicinal products. It is necessary that the new legislation addresses the need of a more robust supply of pharmaceuticals in Europe. It is also key that requirements for environmental risk assessments for medicinal products are strengthened, from manufacturing to actual use.

5. Increased availability of interchangeable medicines, generic medicinal product and biosimilars

To maintain the possibility of applying interchangeable medicines and ensuring availability of generic medicinal products and biosimilars – i.e. copies of medicinal products whose patents have expired – is a key legislative action. This is also important for the competition on the pharmaceutical market in Europe. Well-functioning incentive schemes for research and development as well as marketing of generic medicinal products and biosimilars is of essence for the future-proofing of the regulatory framework.

Sweden has today one of the most effective generics markets in Europe where the pharmacies can exchange the prescribed medicinal products against an equivalent medicines with a lower price. This results in sizeable cost savings and can free resources for other medicinal products or for other health care interventions. Experiences and lessons learned from Sweden could be applied in other EU Member States as a way to promote cost-effective use of medicinal products in Europe. For biological medicines – which includes the growing number of increasingly lucrative medicinal products – there is currently some challenges with regard to competition after patent expiry, which is hampering the development of biosimilars.

Targeted legislation measures are thus needed to stimulate and premiere the development of generic medicinal products as well as biosimilars. The new pharmaceutical legislation therefore needs to promote the possibility to introduce these kind of medicines on the European market. Competition after patient expiry is an important factor for the balance and functioning of the pharmaceutical market.

To further enhance the patent protection and market exclusivity of brand-name companies (patentees), as the pharmaceutical companies have advocated for, would lead to reduced availability and patient access to these medicines and have an extensive budget impact for national health care systems in EU Member States, even after patients have expired. In addition, the discerning trend of competition restriction collaborations between brand-name companies and generica companies – with the aim of delaying the introduction of generic medicinal products – needs to be curbed from a regulatory perspective.

Conclusions

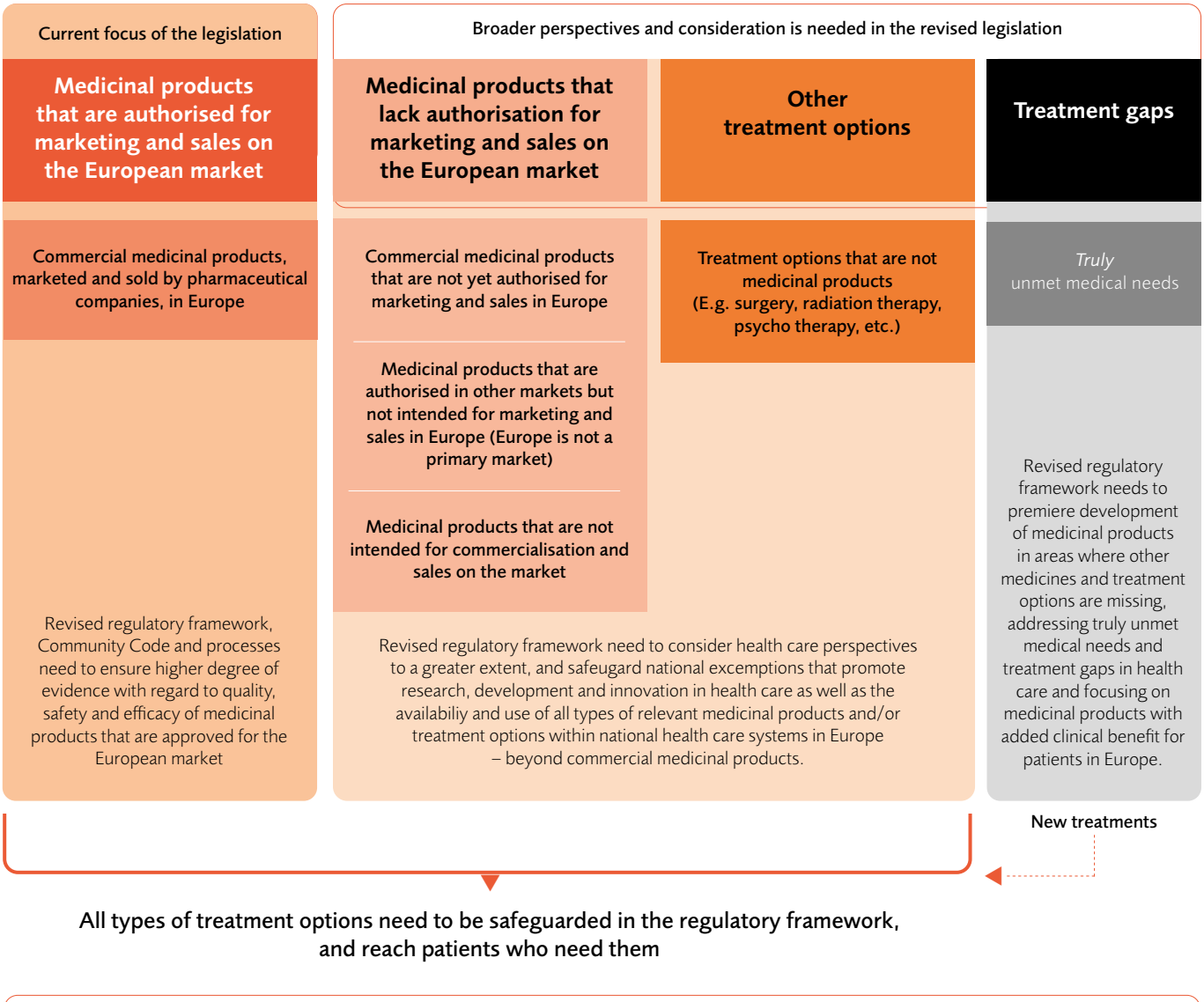
The importance of a EU common framework in the pharmaceutical area has been key for the joint capacities of EU Member States to manage the development of new medicinal products. The availability of new medicines have increased, yet a clear patient and health care perspective have so far been missing in the pharmaceutical legislation. The consequences of this can now be seen at national level, within the national health care systems in Europe. Many EU Member States are struggling with sustainable ways of patient access for new medicinal products as well as access to other relevant treatment options. Sweden is no exception.

It is therefore time for a pharmaceutical legislation that strengthens the conditions for national health care system and truly enhances sustainable public health in Europe, today and in the future.

SALAR stresses the importance of the new pharmaceutical legislation to take into account and build on the national competencies of EU Member States when it comes to the organisation and delivery of health services and medical care. SALAR calls for legislative measures that strengthen the EU Member States in taking on these responsibilities and the capabilities of national health care systems to give patients access to care and treatment based on their individual needs.

ILLUSTRATIVE OVERVIEW:

A European pharmaceutical legislation with a clear patient and health care perspective, that takes greater consideration to the broader spectra of the pharmaceutical system and national health care systems in the revision of the regulatory framework



Europe needs a modern and long-term sustainable regulatory framework for both market approval of medicinal products that are intended for marketing and sales at the European market, as well as conducive conditions for research, development, innovation and use of medicines that are not intended for commercialisation and sales in Europe or that are yet to be granted market authorisation for the European market. The pharmaceutical legislation need to consider the importance of national health care systems' continued access to other treatment options – beyond medicinal products – as a way to address patients' needs. A modern regulatory framework therefore needs to aim for more targeted European incentive schemes for new medicines, in areas where truly unmet medical needs apply and treatment gaps exist.

The pharmaceutical industry join forces with patient organisations for legislative action – Consequences for national health care systems

EURORDIS, an alliance of over 1000 patient organisations with focus on rare diseases, is an active voice in the European arena. Equally, the European Federation of Pharmaceutical Industries and Associations (EFPIA) has become a prominent and influential actor in pharmaceutical matters. Both parties have joined forces and made a joint statement including legislative measures for the revision of the European regulatory framework, with the aim to foster broader and faster patient access to medicines for rare diseases.

Low price and high price corridors for medicinal products in Europe ("tiered pricing") – Suggestions that limit Member State competencies on pricing and reimbursement and reduce possibilities for fair pricing for payers.

The **tiered pricing** concept for low price and high price corridors, developed by EFPIA and the pharmaceutical industry, and proposed by EURORDIS and EFPIA, is launched as "equity-based pricing" and "solidarity among EU Member States". The concept assumes establishment of **price corridors with confidential net prices – proposed by the companies** – according to "best price" principles from the industry, where differential pricing would be based on wealth and as a way to meet the varying ability to pay for medicines in Europe. Factors such as gross national income and human development index would be used to determine the relative prices for different countries.

> In practical terms, the suggestion implies greater influence over pricing from the pharmaceutical industry. The proposal does not address the underlying challenges of pricing and disregards the mere fact that ability to pay for medicine is not based on aggregated figures such as gross national income, but is a matter of budget constraints within the national health care systems – a fact that applies to all EU Member States. The proposal means higher risks for less transparent pricing, a reduced possibility for competitive exposure and price pressure. Neither does it bring any guarantees for more reasonable pricing from a payer perspective. For countries with higher economic wealth the proposal is likely to lead to even higher prices.
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> For Sweden this would also mean a divergence from the value based pricing and reimbursement of medicinal products and the legislated requirements of cost-effectiveness in health care. A mismatch between the ability to pay within national health care systems and the pricing of companies will by extension affect patients in Europe and result in higher financial burden on taxpayers and insurance policy holders. It does neither result in broad nor speedy access to medicines for patients. Furthermore, pricing is part of national competencies

Evaluation of medicinal products at European level – Suggestions that hinders contextually relevant evaluations and poses limitations on cost-effective use of resources for medicines in Member States.

The parties also propose further **harmonisation between EU Member States on value assessments and greater EU-level influence and guidance over health technological assessments, pricing and reimbursement procedures for orphan medicinal products.** For example, joint EU-level clinical assessments are suggested to supersede national clinical assessments used in pricing and reimbursement processes. Increased flexibility in terms of evidence requirements for rare diseases and orphan medicinal products are proposed, including direct linkages between the EMA labelling from the market approval and the scope of reimbursement at national level. The parties also wish to see greater use of adaptive processes for value assessments and decision-making regarding reimbursement, using real world evidence as a way to manage uncertainty over time (similar to the adaptive pathways for market approvals). Furthermore, **novel payment and pricing models** such as outcomes-based payments, over-time payments, indication and combination-based pricing, and subscription payments are assumed to address clinical and financial uncertainty, affordability constraints, or issues linked to medicines being used across indications and combinations, and thus ultimately contribute to accelerating patient access.

> The proposals are partially derived from the truly unmet medical needs apply and treatment gaps exist. 2021/2282 on HTA, health technology assessment, but also extend to areas relating of national competencies where EU Member States are responsible and mandated. In essence, the suggestions lack a clear health care and payer perspective. For value assessments to be relevant for decision making at national level, it is key that such assessments are contextually relevant and continue to build on national circumstances, conditions and processes. The use of adaptive pathways for market approval has proven insufficient with regard to the actual withdrawal of medicines that fail to generate satisfactory follow-up evidence on clinical benefits. The risk is that the same inefficiencies will arise for value assessments,

pricing and payment under such adaptive schemes. The consequences for payers within national health care systems is that resources can no longer be purposefully prioritised and allocated according to patient needs and principles of cost-effective use of resources, crowding out other health care interventions for other patient groups. A such, the long term sustainability of national health care systems will be undermined which would negatively affect public health in Europe.

The proposals also disregard the underlying problems with regard to patient access: Clinical evidence at the time of market approval, ambiguity in terms of clinically relevant endpoints and added clinical benefit over other treatment options, uncertainty regarding safety and efficacy over time – in combination with high prices from the companies – implies multiple uncertainties. For adaptive value assessments, conditional reimbursements and novel payment models to be feasible in practice, the net prices from companies need to be substantially reduced from today's price levels. Certainly, without eliminating the pharmaceutical industry's possibilities to make ends meet and make profit. As a balanced proposal, EURORDIS vision paper "Rare 2030" raises a suggestion for greater transparency in research and development costs as a basis for reasonable pricing of medicines for payers, while companies could still make profit, and without limiting patient access.

Incentive schemes, data and patent protection and market advantages – Suggestions that impedes pharmaceutical development and limits health care providers' use of different types of treatment options, beyond commercial medicinal products approved for the European market.

EFPIA has also proposed suggestions that include continued and increased investments and **incentives for research and pharmaceutical development** and wish to see **expedited processes for market approval** and possibilities of even lower evidence requirements at the time of approval, with reference to the processes for approval of covid-19 vaccines and possibilities of real world data follow-up from use in clinical praxis.

These proposals aim to stimulate the increased quantity of medicinal products, approved for marketing and sales at the European market, but does not necessarily mean that relevant medicines are made available to patients. Too broad incentives bring increased risks of inaccurate, non-targeted, pharmaceutical development in Europe. Too low evidence requirements create greater uncertainty in the later stages of decision-making for introduction and use of new medicines and can de facto inhibit or delay patient access.

EFPIA also want to see a greater **data and patent protection** as well as extended mechanisms for market exclusivity as a way to secure the **competitive advantages for market authorisation holders.** Furthermore, the industry is calling for **legislative limitations to the possibility of national exceptions** to the EU-common regulatory framework.

These proposals pose great concern from a health care and payer perspective for many reasons. First, it risks hindering the development of generic medicines and biosimilars. Secondly, it implies great limitations on the use of different types of treatment options within national health care systems. Although referred to as a matter of quality, safety, efficacy, it is important to note that not only – and far from every – industry developed, commercial, medicinal product approved for the European market, guarantee quality, safety and efficacy for patients. Medicines that are not intended for commercial purposes – researched and developed by academia and health care providers – can also be of uttermost relevance as a treatment options. They can be equally of high quality and safe and effective – sometimes even well-proven in clinical practice – and commonly both medically and financially motivated as treatment option. Steering national health care systems towards commercial medicinal products is therefore not recommended. The risks associated with this is also that market mechanisms fail and competition on the pharmaceutical market is weakened. The EFPIA proposal is thus contra productive from both a patient perspective and a health care perspective.

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