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Remissutskick av EU-läkemedelslagstiftning: Kommissionens förslag på förordning och direktiv om humanläkemedel

Diarienummer: S2023/01768

Merck, Sharp & Dohme (Sweden) AB has been asked to respond to the attached proposal.

Introduction

The Swedish life science sector is home to one of the world's most innovative ecosystems. Pro-innovation policies, multi-stakeholder partnerships and strong R&D investment have all contributed to making Sweden a global leader in oncology, neuroscience, genomics, and diagnostics.

The pharmaceutical industry constitutes a significant part of this ecosystem and of the Swedish economy. With 15,000 employees of which 3,000 are working in R&D, the Swedish pharmaceutical industry annually contributes 56bn SEK to GDP and has made pharmaceuticals the 3rd largest export item. Even more importantly, this has allowed for Swedish patients to gain fast access to innovative treatments, medicines, and vaccines.

Pro-innovation policies help pharmaceutical companies bring innovation to patients faster through e.g., clinical trials. Sweden has for long been a strong proponent and defender of strong patent protection and pro-innovation policies, not only nationally but also internationally.

The European Commission's revision of the pharmaceutical legislation is a rare opportunity for Sweden and the EU to strengthen incentives for innovation, improving access to new treatments and addressing unmet medical needs.

A number of the measures proposed by the European Commission are positive and important steps to further strengthening European competitiveness, improving access to innovation and modernizing pharmaceutical regulation.

However, the current shape of some proposed changes to the legislation are cause for concern and risk having a detrimental effect on access and innovation. Therefore, MSD as a company and as part of the wider industry has put together a number of constructive suggestions for changes that we believe would

greatly contribute to a stronger and more innovative European pharmaceutical sector where patients get fast and equitable access to innovative treatments, medicines and vaccines.

General Input

MSD is committed to European prosperity, and we continue to believe that this once in a generation reform driven from Brussels is the chance to modernise how we authorise medicines in the EU. We recognise the expertise of the EMA network and look forward to a closer collaboration with the aim of **supporting innovation** (e.g., through phased review). We also welcome leaner procedures at the EMA and **updating to adapt to the digital era** (e.g., digital submissions; use of electronic patient information). The increased focus on **real-world evidence** is a welcome step forward. We urge the legislators to ensure that the same quality and regulatory standards apply when using Real-World Evidence (RWE) and that companies remain in the driving seat of label updates.

Furthermore, it's important that Europe contributes its fair share when it comes to supporting research and the development of innovative medicines. We operate globally and we only take positive investment decisions if we expect that the total global sum of incentives will make this investment sustainable. This is why we are very concerned about the foreseen reduction of Regulatory Data Protection (RDP) – which is a major incentive for R&D. On the other hand, we welcome the thinking behind a transferable exclusivity voucher to foster interest in antimicrobial research (AMR). It could be strengthened further – and we hope that it focuses attention even more on AMR.

We are present in all EU countries and as a company, we always work hard to ensure patients have access to our medicines. Sometimes access delays are beyond our control. We are committed to the concrete solutions put forward by EFPIA (the European innovative industry association) to improve access to medicines across Europe. These solutions lie outside of the legislation and of this reform. RDP modulation will not improve access for European patients. We support the EFPIA discussion on a solidarity mechanism based on Equity Based Tiered Pricing and call on Member States, the European Parliament and the European Commission to engage in a meaningful discussion on how this model could be used to support access across the EU.

Specific Input

EMA Structure

- We welcome the proposal to streamline the EMA governance (including the reduce timelines for the assessment process) and committee structure.

- We welcome many aspects of the proposed legislation including, phased reviews [Reg Article 6(2)], codification of PRIME in law [Reg Article 60], Exceptional Circumstance marketing authorisations (MA) for new indications [Reg Article 18], CMA for new indications [Reg Article 19] and the new Temporary Emergency Marketing Authorisation (TEMA) [Reg Section 3] and would welcome the following changes:

    - Expand the scope of the expedited iterative scientific dialogue with regulators (regulatory support)
    - Expand scope of Accelerated Assessment Pathway to new indications and line extensions
    - Expand scope of Phased Review (=rolling review) to products of major interest and new indications and line extensions

Electronic product information

Electronic delivery of product information (patient leaflets) provides significant advantages for patients and healthcare professionals, industry, regulators and the environment by offering accessible and up-to-date information on a medicine. Electronic delivery of product information strengthens the supply chain by mitigating and preventing shortages and contributes to environmental sustainability. The proposed legislative revision [Dir Article 63] acknowledges the importance of electronic product information, makes the future transition from paper to electronic product information possible and increases the flexibility to make patient information more impactful. However, the proposed gradual implementation, driven by Member States' readiness, could be challenging to operationalize, particularly if the Member State by Member State implementation period extends over a lengthy hybrid period. To address these elements and to leverage the advantages of electronic product information in mitigation of shortages, we suggest the proposal is further adapted to:

- Allow **Healthcare Professional administered products** (i.e. products that are not intended to be delivered to the patient for self-administration), and **including vaccines**, to be transitioned first with a short implementation window due to multiple positive pilot experiences already in place.

- Keep the “Member State by Member State” **implementation phase as short as possible** and considering pragmatic implementation needs such as in the case of multi-country packs.

- Find a solution in each country to make paper patient leaflets available to those who need them, as no patient should be left behind.

Real-World Evidence (RWE)

MSD welcomes RWE in the legislation to make the EU regulatory framework more efficient and competitive including accepting, per Legal basis, the use of RWE for the regulatory decision-making process.

Overall, we call for the appropriate **involvement of the MAH in the decision-making process of implementing RWE-based changes in the product label** and **transparency on data that is** not owned by MAH but is used by Regulators. Updating a MA-license with real world evidence (RWE) could impact the product label and potentially post-approval activities. If RWE studies generated by 3rd parties are considered, those studies should be subject to the same regulatory standards.

Furthermore, we would like the proposal to also take into consideration the key elements outlined below:

- MSD proposes that the Marketing Authorization Holder (MAH) should, as legally liable and responsible for the product, have access to the data sources and analysis of RWE information for their products, and should be involved in the decisions of their own product labels.
  This proposal is connected to Article 166 of the Regulation on Personal health data where it is stated that the Agency may consider and decide upon additional evidence available, independently from the data submitted by the marketing authorization applicant or marketing authorization holder. On that basis, the Summary of Product Characteristics (SmPC) shall be updated if the additional evidence has an impact on the benefit-risk balance of a medicinal product.

- Common agreed methods, data quality standards and guidelines should be developed in order to leverage the power of RWE and the underlying data on which it is based and build healthcare decision makers’ trust in using it.

- Ensure all evidence streams, irrespective of origin, are subject to a consistent level of rigorous scientific review according to same standards.

- Article 48 of the proposed Regulation lays out the proposed regulatory framework to support repurposing of already authorised medicines. According to this, the concerned MAHs would not be able to have a role in the decision on the inclusion of a new indication in the summary of product characteristics (SmPC) and patient information leaflet of their product, based on data generated by a third party. On the contrary, we propose that measures to stimulate repurposing need to closely involve relevant MAHs in the process and build on a non-binding system for scientific assessment of evidence for repurposing.

Paediatric medicines

- A robust framework for Mechanisms of Action (MoA) Paediatric Investigation Plans (PIPs) is essential to ensure that this new obligation is effective to achieve its purpose and manageable for developers. With this increased obligation should come an increased reward and we are calling for a twelve months' Supplementary Protection Certificate (SPC) extension for MoA PIPs.

- Where the EMA requests PIP modifications based on external scientific evidence (not generated by the PIP holder) there must be a consultative and collaborative process with open scientific discussions and sharing of information with the PIP holder. The applicant's right to request a re-examination of the EMA's decisions on PIP applications and modifications should be reinstated.

Regulatory Data Protection (RDP)

The reduction of the RDP baseline from 8 to 6 years is a step in the wrong direction, reducing the attractiveness of the EU as a location for R&D investment. RDP is a key, inevitable ex-ante consideration for R&D investment in Europe – as the last-to-expire protection and key driver for approximately 1/3 of innovative medicines – and is particularly important for advanced, complex therapeutics with a long or difficult development time. Where patent/SPC protection may not be reliable or last long enough due to extended development or approval time, RDP is a guaranteed period of exclusivity on which businesses can reliably plan investment and mitigate associated risks.

We call for maintaining a **strong baseline for regulatory data protection**.

- Shortening the RDP baseline protection period and recuperating it only under complex and unpredictable conditions will discourage innovation efforts. Patient access to medicine will not increase as conditions are linked to different and mostly national processes, which are not fully under the control of the MAH.

- To limit incentives only for treatments that fit a certain narrow definition of Unmet Medical Need (UMN) risks excluding the development of important therapies for patients. The development of medicines takes many years and is always done with the ambition to address an UMN. It is however impossible to know in advance whether a particular investment will eventually address a specific UMN.

The **RDP baseline protection period should be increased to 10 years**, and we call to;

- Change the obligation "releasing and continuously supplying**"** in each and every MS" to regain 8 years RDP to a commitment to filing for pricing and reimbursement within two years of product approval, in order to gain an additional 2 years of RDP.
- Review the link of RDP to unmet medical need as well as the definition of this to encourage all innovations.

Transferable Exclusivity Extension (TEV)

We welcome the proposal on TEV. It is essential that any pull incentive meets certain criteria:

- Incentivizes innovation and appropriate use: an incentive large enough to incentivize sustainable innovation, aligned to the EU contribution or fair share of the needed global incentive. Delinked from revenue and therefore aligned to stewardship;
- Value for money: represents a proportionate cost to society and an efficient approach;
- Predictability: provides clarity for all stakeholders, including innovators, the generic industry and payers;
- Feasibility: is implementable given the current context, framework, and policy debate; and
- Supports timely access: can be implemented relatively quickly in the EU, given the urgency to address the AMR threat, and contributes to patient access through the increased supply and availability of new antimicrobials.

The additional incentives outlined in the Council Recommendation have the potential to serve as valuable complementary tools to the TEV, in ensuring sustainable supply and facilitating access to new antimicrobial treatments.

There is a need to improve the conditions surrounding the TEV, to ensure that TEV provides an effective tool to incentivize the development of new antimicrobial treatments. This includes:

- Incorporate a provision for the periodic review of the incentive program after 15 years, based on predefined outcomes. A 15-year sunset clause lacks predictability does not align with the research and development (R&D) timeline and fails to account for the possibility that no alternative incentives may be successfully implemented during this period.
- To expand the pool of eligible products for TEV and maintain predictability for generic manufacturers, consider enabling the attachment of a TEV to any product that retains at least 2 years of regulatory or IP protection (such as RDP, SPC, or patents).

Shortages & Supply Chains

The EU pharma reform is an opportunity to work together to tackle shortages. Each shortage is unique and has to be considered. The EU can bring value through:

- The creation of a **harmonised EU prevention and mitigation system**, based on a **standard definition of a shortage**, and an **interoperable IT European monitoring/ notification system**: shortage information should be uploaded onto a common IT portal to ensure a streamlined and effective alert system as well as an alignment across the data provided from different sources and based on a consistent and workable definition of medicine shortages. The proposed obligation of 6 months prior notification of shortages for all medicines is in most situations not feasible. We recommend keeping the mandatory **notification timeline at 2 months** as is currently in the legislation and opening the system for voluntary earlier notifications to ensure that the very limited cases of shortages that can be anticipated several months in advance are reported as soon as information is available.

- **Increased transparency and understanding of patient demand, through timely (current and forward looking) epidemiological data**: the European Centre for Disease Control (**ECDC**) should aim for timely release of modelling data covering patient needs and hospital capacity in the Member States, but also combining any such forecasting data with real data on usage (consumption), and other relevant data that can provide information on supply.

- **Use of the European Medicines Verification System (EMVS) for medicine shortage prevention and monitoring of marketing authorisation holders' supplies to wholesalers and pharmacies**: the data stored in the EMVS could provide timely intelligence regarding the number of packs for all prescription products being supplied by manufacturers on the various EU markets, number of packs dispensed in national pharmacies, number of packs exported (and/or imported), as well as on the level of stocks present in the supply chain at country level. The real time information in the EMVS data repositories can be analysed according to very granular time frames (per day, per week, per month etc.) as well as per region (postal codes). Wholesalers and traders as well as National Competent Authorities have access to the data stored in National Medicines verification Systems.

- Shortage Prevention Plans (SPP) for all products are not an effective way of preventing shortages. **We propose a risk-based approach focusing on critical products/critical shortages leading to the implementation of targeted SPP** through a collaborative process, and the management of safety stocks on a risked-based approach: we support the development of a fit-for-purpose SPP in a common format for a risk-based selection of medicines, i.e., history of supply issue and patient impact. SPP should be kept by the MAH and made available upon request by authorities during inspections and kept confidential given the sensitive information they include. A clear harmonised list of critical products is needed to ensure a consistent approach at EU level.

The Environment

- MSD is committed to minimising our impact on the environment. Furthermore, we work diligently to ensure that environmental risk assessments (ERAs) are available for all the products we put on the market. In principle, we agree with most of the intentions pursued by the European Commission in their proposal.

- We want to ensure that any additional requirements are manageable and would not unintentionally delay access for patients, as patient benefit should always prevail. Some justified delays in submitting ERAs must remain acceptable and there must be the opportunity to discuss any environmental risk identified based on scientific data.

- Our highest concern relates to the ability to revoke, suspend or vary an existing MA based on data submitted by third parties. A due process needs to be established for the MAH to present its data and argue its perspective on environmental risk considering potential risk mitigation measures before an MA may be affected. Patient benefit should always prevail - ERA should not be put at the same level as efficacy, safety, quality.

- A periodic renewal of ERAs is acceptable as long as timelines are predictable and allow sufficient time for data collection (e.g. 5 years). We support the fact that legacy products will now be covered by the legislation. We also agree with the intended system of monographs, provided they are based on the information that is already made public by the EMA.

- As part of the extended ERA concept, the ERA should evaluate the impact of active pharmaceutical ingredients (APIs) instead of single medicinal products to capture the latest environmental information and accurately assess potential risks from all medicinal products.

About MSD

For more than 130 years, we have brought hope to humanity through the development of important medicines and vaccines. We follow the science where we can make the greatest difference, now and in the future. We aspire to be the premier research-intensive biopharmaceutical company in the world – and today, we are at the forefront of research to deliver innovative health solutions that advance the prevention and treatment of diseases in people and animals.

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