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## Urgent need to define unmet medical needs in cardiovascular diseases

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In 2020 the European Commission announced a major review of the European Union's (EU's) pharmaceutical legislation and in March 2023 adopted a proposal for a new Directive and a new Regulation, which will revise and replace the existing one (Regulation 726/2004 and Directive 2001/83/EC) and the legislation on medicines for children and for rare diseases (Regulation 1901/2006 and Regulation 141/2000/EC), respectively.(1)

The proposed revision builds on harmonisation that has been already achieved for the authorisation of medicinal products. As stated in an Explanatory Memorandum to the Directive of the European Parliament and of the Council "The overarching aim of the reform is to ensure that patients across the EU have timely and equitable access to medicines. (...) **A harmonised approach at EU level also provides greater potential for incentives to support innovation and for concerted action to develop medicinal products in areas of unmet medical needs.**"(2)

In this context, "Unmet Medical Need" (UMN) means that there is a gap or deficiency in the available medical options for preventing, diagnosing, or treating a specific health disorder, and this gap represents a need that has not been covered by current medical approaches. The concept of UMN has important implications not only in the regulatory frameworks of the European Medicines Agency (EMA) but also for European innovators, researchers and clinicians. Regulators use it now mostly, but not exclusively, in the context of orphan medicinal products. In general terms however, it is applicable

to a wide range of situations where existing diagnostics, interventions or therapies are incapable to adequately address a particular health condition or disease.

The term is all but unambiguous; indeed, a recent review yielded 16 definitions of UMN, based on various criteria.(3) Regulators work on scoring and grading systems to better define what UMN really are. So far, with the adopted paradigm, the results are not particularly favourable for the cardiovascular community. Indeed, the Belgium's National Institute for Health and Disability Insurance (INAMI-RIZIV) in its 2023 edition has proposed a ranked list of UMN. There are no cardiovascular diseases on it, despite mentioning non-orphan, non-rare conditions such as Alzheimer disease or treatment resistant depression.(4) This does not look too good for cardiologists, especially considering that Belgium wants to make UMN one of the central themes of the Belgian Presidency of the Council of the European Union in 2024 and methodology developed may be applied at the EU level. (5)

The proposed revision of the EU pharmaceutical legislation puts a concept of UMN and high UMN at a centre of its legislation, focusing on medical products for paediatric use, and orphan indications, rewarding new drugs for patients with rare diseases who don't have any other treatment options. It is certainly not promising for cardiovascular patients. In 2022 there were no new cardiovascular drugs recommended for marketing approval among the 89 positive EMA recommendations for authorization, including 41 containing new active drugs (6) Analysis of the first 5 years of experience of EMA PRIME scheme, which was set up in March 2016 to provide early and enhanced scientific and regulatory support to medicines that have the potential to significantly address patients' UMN, revealed particularly alarming numbers. Of note, there were 384 PRIME requests received by EMA between 1 January 2016 and 30 June 2021 and out of those only 20 were for cardiovascular diseases and just 2 (!) were granted eligibility to the PRIME Scheme – which is a mere 0.5% of all submissions. For comparison, out of 111 requests for oncology drugs 27 were granted eligibility to the PRIME Scheme – which is in an order of a magnitude higher!(7) At the same time cardiovascular diseases

remain the number one killer in Europe and a pressing public health challenge due to existing UMNs and inequalities in access to optimal care.(8)

From the point of view of the cardiovascular community there is a need to work with patients, regulators, payers and other stakeholders to identify unmet needs in cardiovascular medicine from patient's, clinicians', societal perspective to reverse the declining trend in cardiovascular innovation. A single definition of UMN may be challenging and there is a clear necessity for the cardiovascular community to shift the paradigm from where it is now to where it ought to be - to include cardiovascular patients and their care in the centre of European pharmaceutical policy.

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