



WHITE PAPER | 2021

# Creating a **European ecosystem** for safe, timely and affordable patient-centric innovation

The Value Added Medicines Group, a Medicines for Europe sector group, calls on the European Union to foster continuous innovation on well-established substances and increase patient access to Value Added Medicines.

## Key messages:

Value Added Medicines should be recognised as a separate group of medicines in EU legislation, linking approval procedures, innovation frameworks and reimbursement processes to create an ecosystem that delivers better health to patients, solutions for healthcare systems and fair returns on R&D investments.

We recommend the establishment of a new, simplified regulatory pathway for VAMs, defined under a new Article 10.7 of the EU Directive 2001/83/EC, and built on three pillars:

- 01 Design a fit-for-purpose regulatory framework that will enable clarity early in the development.
- 02 Recognise VAM as a category of innovation with proportionate incentives.
- 03 Recognise and define value for healthcare systems.

## How can Value added medicines make a difference to patients and healthcare systems during a pandemic and beyond?

Value Added Medicines (VAM) can deliver important benefits to patients, healthcare professionals, payers and healthcare systems, as a whole, in a sustainable and affordable way. Value Added Medicines present an opportunity to innovate on off-patent molecules and to bring treatments for indications which have no approved therapies and reduce unmet medical need (repurposing/repositioning), build on existing medicine to allow for patient-centric design or address healthcare inefficiencies (drug reformulation) and combine medicine and different services that can substantially improve treatment outcomes (complex combinations).



## REPOSITIONING - FINDING NEW INDICATIONS TO ADDRESS UNMET MEDICAL NEED

Repurposing remains a largely untapped, affordable and safe treatment approach to address unmet medical needs. **Dexamethasone is an affordable steroid** that is commonly used. **Repurposed for Covid-19 treatment**, it has been shown to reduce deaths by one-third in hospitalised Covid-19 patients receiving mechanical ventilation and one fifth in hospitalised Covid-19 patients receiving oxygen without invasive mechanical ventilation.

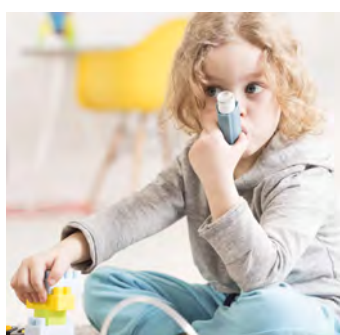
Source: [RECOVERY trial](#)



## REFORMULATION - FACILITATING PATIENT TREATMENT IN A HOME CARE SETTING

Covid-19 dramatically reduced accessibility of care and changed patients' needs in a number of ways. Value Added Medicines can support patient-centered reform of care with medicine reformulation and offer patients new ways to administer their own treatments at home and avoid in-person hospital visits. **Reformulation of chemotherapeutics that offer reduction of toxicity and potential for hospital admission** historically faced challenges with recognition of value, were recommended in the pandemic over the "standard" chemotherapeutics.

Source: [IQVIA](#)



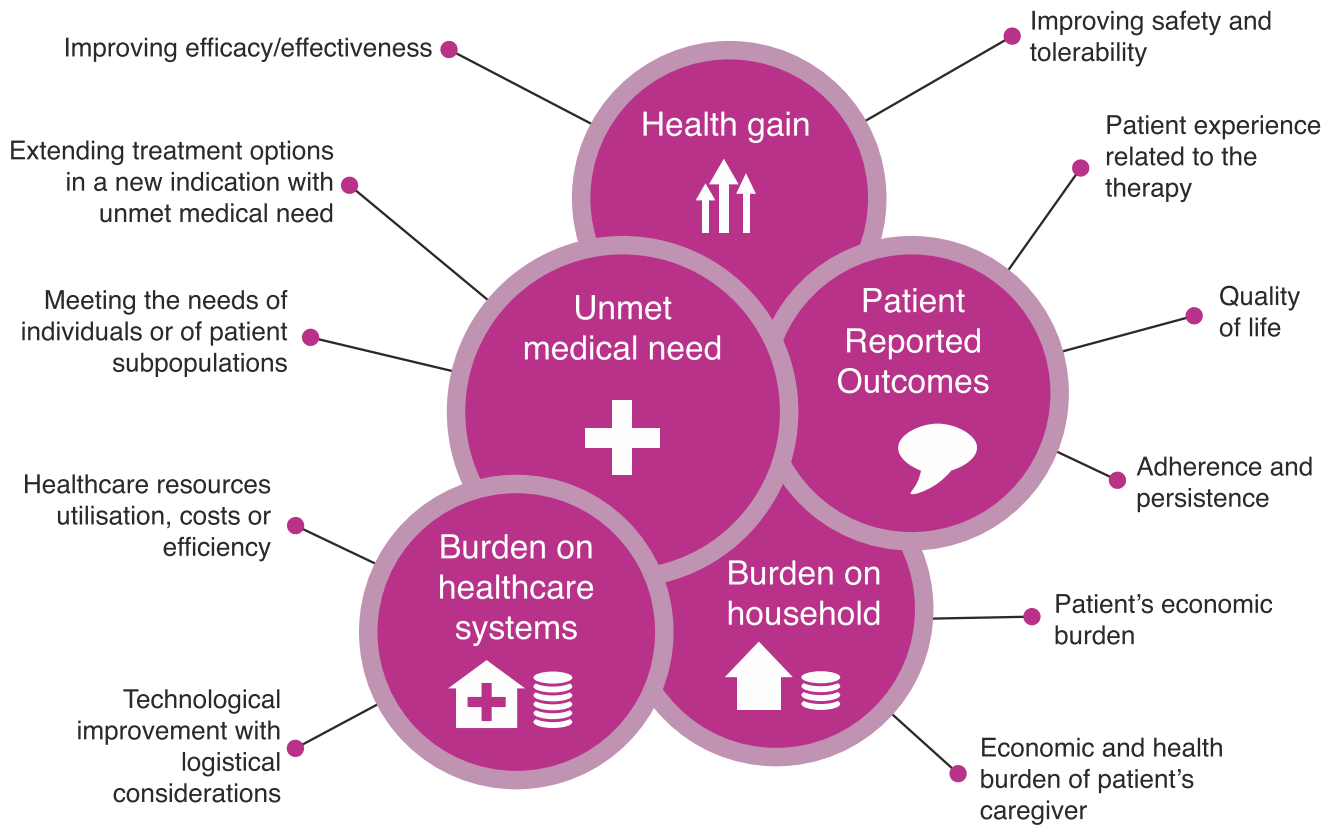
## COMPLEX COMBINATIONS - UTILISING DIFFERENT RESOURCES TO DELIVER THERAPY

Combining two or more substances or combining substances with services, digital components or devices: **Digital Value Added Medicines**, combine medicines with innovative technological solutions and can support the patient-HCP relationship and improve treatment adherence in a remote care setting. **Combination with devices** (inhalers) is explored to find Covid-19 treatment options for patients to be taken at home and prevent the need for admission.

Source: [Principal trial](#)

# Continuous innovation matters to patients and health care sustainability

Another advantage of value added medicines is that they often build on existing knowledge of a medicine with an already well-established safety profile. This reduces research and development times and lowers cost, favouring more accessible innovation. The benefits for patients and health care systems can then be maximised in various ways, including:



\* Identified Value domains as per proposed Core Evaluation framework for Value Added Medicines<sup>1</sup>

1 Petykó, Z. et al: Proposal for a Core Evaluation Framework of Value Added Medicines. Value in Health, Volume 23, S659 - S660.



## RE-EVALUATING THE CURRENT INNOVATION MODEL

The European Commission's recently adopted **Pharmaceutical Strategy for Europe<sup>2</sup>** prioritises the need for **affordable and available medicines that contribute to the sustainability of healthcare**. Re-evaluating the current innovation model should lead to a greater focus on ways to stimulate innovation across the lifecycle of medicines and especially on off-patent molecules.

## A FLOURISHING PHARMACEUTICAL SEGMENT IN UNITED STATES

The Value Added medicines innovation ecosystem in Europe markedly contrasts with that in the **United States, which already, today, has a flourishing value added medicines segment** based on its framework legislation that encourages innovation on off-patent molecules. The **dedicated regulatory pathway, 505(b)(2), offers a clear framework for companies to invest in innovation, for payers to recognise its value and for patients and prescribers to have access to better treatments<sup>3</sup>**.



2- [https://ec.europa.eu/health/human-use/strategy\\_en](https://ec.europa.eu/health/human-use/strategy_en) , accessed in Feb 2021

3- Presentation IQVIA at Value Added conference 2019, Brussels, Belgium: estimated that 70% of the total Value Added Medicines market is in concentrated in the US.

# The current EU pharmaceutical framework fails on continuous innovation on well-established substances

Multiple attempts to foster innovation on well-established (often off-patent) molecules have failed in Europe. Even in clearly designated priority areas of the current legislation, such as paediatric indications. The Paediatric-Use Marketing Authorization (PUMA)<sup>4</sup> introduced incentives to stimulate off-patent development but failed to deliver sufficient results for children, as this provision has been used only 6 times<sup>5</sup>, despite a clear need. **By recognising VAMs in their own right, the EU can remove the barriers to continuous innovation:**



## 1. THE CURRENT APPROVAL PROCESS IS TOO CUMBERSOME

At present, there is no specific regulatory pathway for Value Added Medicines. Several legal bases can apply for Value Added Medicines to be registered in the EU. The consequence is a high complexity for the applicant – different pathways require different levels of evidence and developers often need to seek regulatory advice to determine which legal pathway would be most suitable for their product. This wastes resources and adds to the complexity and cost of the development. As continuous innovation is based on well-established substances, regulatory requirements should be further tailored to provide clarity for VAM developers by increasing **predictability of required evidence and development costs and regulatory timelines.**

4- PUMA = Paediatric-Use Marketing Authorization. The EU Pediatric Regulation No. 1901/2006 introduced the Pediatric-Use Marketing Authorization (PUMA) for medicines that have been authorized and can no longer be covered by a supplementary protection certificate (SPC) or a patent (European Commission, 2017). A PUMA offers incentives like automatic access to the centralized procedure, a partial fee exemption and a 10-year period of data and marketing protection.

5- Verbaanderd C, Rooman I, Meheus L, Huys I. On-Label or Off-Label? Overcoming Regulatory and Financial Barriers to Bring Repurposed Medicines to Cancer Patients. *Front Pharmacol.* 2020 Jan 31;10:1664. doi: 10.3389/fphar.2019.01664. PMID: 32076405; PMCID: PMC7006723.



## 2. THE ABSENCE OF INCENTIVES FOR CONTINUOUS INNOVATION

The current legislative framework encourages innovation in new chemical or biological entities and research for rare diseases or subsets of diseases. The EU pharmaceutical legislation also encourages follow-on competition at patent expiry with clear regulatory and market pathways for generic and biosimilar medicines, thereby massively increasing patient access to medicines. However, **the development of Value Added Medicines requires additional evidence generation when compared to traditional follow-on products, with further complexity, costs and prolongation of the development.** Existing regulatory incentives in the EU framework, such as one year of non-cumulative data exclusivity for a new indication on a well-established substance<sup>6</sup>, have failed to stimulate more development - this pathway has never been used<sup>7</sup>. Value added medicines innovation is not sufficiently encouraged under either the generic, biosimilar or originator framework.



## 3. THE VALUE, BENEFITS AND INVESTMENTS IN VAMS ARE NOT RECOGNISED IN THE EU MARKETS

Following on from the EU legal framework, there is a confusion in EU markets regarding the fair valuation of VAM innovation. The value assessment process is heterogeneous across EU Member States and Value Added Medicines are often categorised as generic medicines<sup>8</sup>, because the innovation is on an off-patent molecule, with no process/framework in place to recognise their additional value in a proportionate way. In other instances, VAM manufacturers are faced with requests for evidence in HTA processes that are designed for originator pharmaceuticals and therefore demand disproportionate evidence generation which is not fit for purpose and prevents affordable innovation from reaching patients. There are some positive developments, for example in Belgium, where value added medicines are defined in the legislation as a separate class of medicines where the value added aspect of the medicine (compared to “standard” generic) is justified through pragmatic scientific arguments. By establishing an EU level recognition of VAM, Member States can develop proportionate mechanisms to reward this kind of innovation.

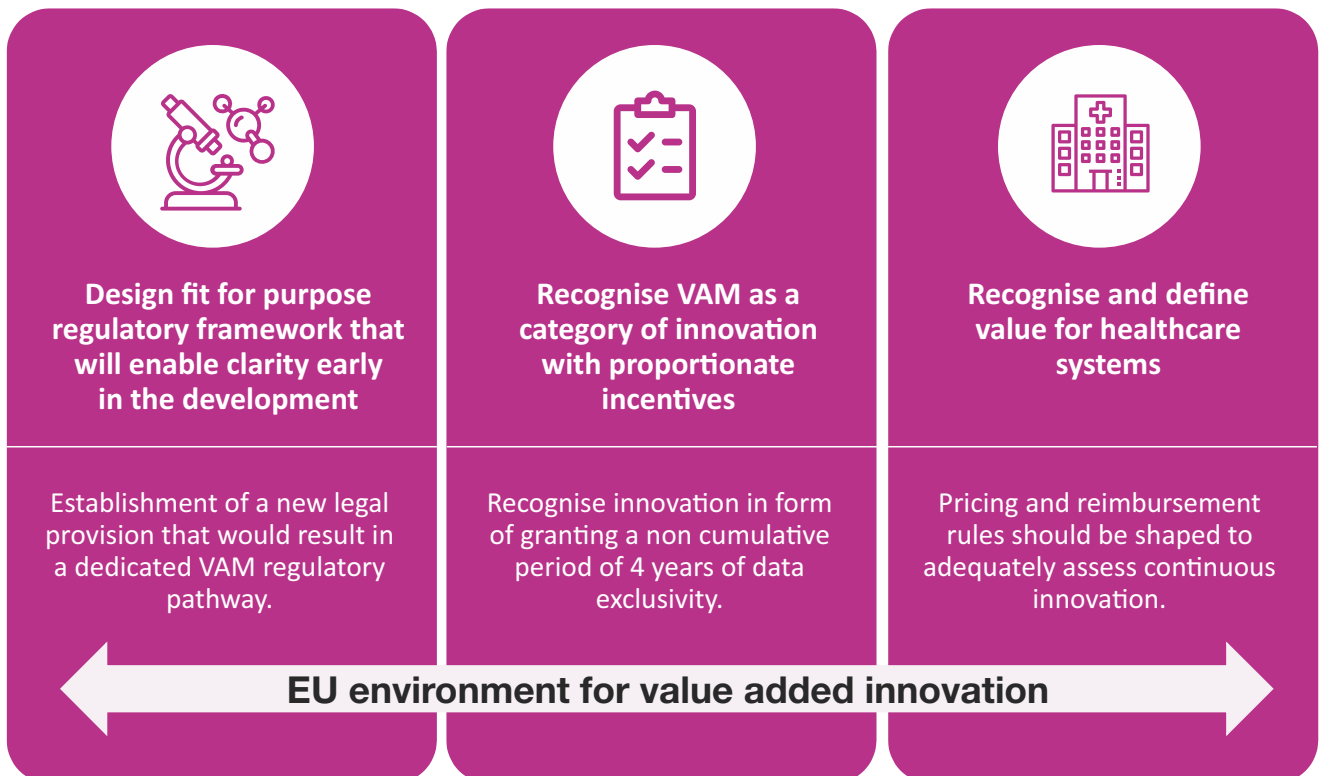
6- Reference – EU Directive 2001/83/EC Article 10.5,

7- Copenhagen Economics: Study on the economic impact of supplementary protection certificates, pharmaceutical incentives and rewards in Europe, May 2018

8- Typically, this means a generic reference price based on an internal reference price system.

# EU Pharmaceutical Strategy: a historic opportunity for R&D investment on off-patent medicines and better treatment of patients

The new Pharmaceutical strategy for Europe targets unmet health needs and the accessibility and affordability of medicines. Value added medicines are defined as an accessible, affordable innovation to address health needs that are especially important to larger patient populations in both, communicable and non-communicable disease management. By tailoring the system of incentives provided by the EU pharmaceuticals framework to support innovation throughout a molecule’s lifecycle, we can achieve a competitive and resource-efficient EU pharmaceutical industry while delivering medicines to satisfy the unmet need and improve the lives of patients in Europe.





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We recommend the establishment of a new, simplified regulatory pathway for VAMs, defined under a new Article 10.7 of the EU Directive 2001/83/EC, and built on three pillars:



## 1. DESIGN A FIT-FOR-PURPOSE REGULATORY FRAMEWORK THAT WILL ENABLE CLARITY EARLY IN THE DEVELOPMENT

Establishment of a new legal provision for a dedicated regulatory pathway that includes new, pragmatic methods of evidence generation and assessment for affordable and sustainable continuous innovation. This should be accompanied by early dialogue with regulators, breaking silos, increased cooperation between all healthcare stakeholders and fit-for-purpose scientific advice, so that developers will be able to gain clarity and invest in a Value Added Medicine that will best benefit patients and society, as a whole.



## 2. RECOGNISE VAM AS A CATEGORY OF INNOVATION WITH PROPORTIONATE INCENTIVES

Value Added Medicines should be recognised as a separate category of innovation with incentives to encourage further development of Value Added Medicines in Europe.

We propose that, for the innovation on well-established substances, a non-cumulative period of 4 years of data exclusivity be granted, subject to certain conditions and provided that the additional value that is delivered by the innovation can be demonstrated by appropriate data.

**We propose Data exclusivity as an incentive, as it is already an established incentive in the pharmaceutical framework in the US<sup>9</sup> and the introduction of a similar concept in Europe would bring us a step closer towards global convergence and set a level playing field for EU industry.**

It is important to note, that data exclusivity does not prevent competition from taking place, as it does not translate into preventing other manufacturers from entering the market (as would be the case with market exclusivity).

The purpose of this proposal is to stimulate innovation where it is not currently encouraged. It is not the intent of this proposal to encourage the further extension of exclusivities for medicines that have already benefited from a substantial exclusivity period. We therefore consider that the global marketing authorisation (GMA) concept should continue to apply and that data protection would not apply to data that was previously used within the GMA (i.e. no further protection for studies already benefiting from exclusivity). The proposed framework should not facilitate the delay of the off-patent competition. Appropriate safeguards should be included to ensure the benefits of this framework are fully realised and a level playing field is created that encourages all medicine developers to continuously innovate on off-patent medicines.



### 3. RECOGNISE AND DEFINE VALUE FOR HEALTHCARE SYSTEMS

Improving the EU pharmaceutical framework will need to be followed by the adoption of an evaluation framework for Value Added Medicines.

The decision-making process should consider **relevant value dimensions** that demonstrate the benefits of Value Added Medicines in different purchasing/procurement mechanisms which **should be defined with healthcare stakeholders**: regulators, patients, healthcare professionals and payers. Patient preferences and unmet needs should be considered and accounted for in

9- US FDA 505(b)(2) Guidance for industry <https://www.fda.gov/media/72419/download> , accessed February 2021

regulatory and reimbursement decisions across the lifecycle of the medicine. Ideally, value evidence requirements and evaluation should be streamlined in an early scientific and HTA/payer dialogue. The cost of evidence generation would need to be proportionate to the claimed benefit and the price premium in play<sup>10</sup>. To secure more development in repurposing, it is crucial that national authorities commit to exploring ways to prioritise the use of such approved medicines over the off-label use of unapproved products.

Member States should recognise medicines registered under the VAM pathway as a separate class of medicines. Therefore, **pricing and reimbursement rules should be shaped to adequately assess continuous innovation and adjusted to the specificity of Value Added Medicines**: a different rule and assessment process should be established, as the current pathways for generic medicines (e.g. internal price referencing, mandatory discounts) or innovative medicines (e.g. clinical benefit) are not appropriate for VAMs.

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10- Zsuzsanna Ida Petykó, András Inotai, Anke-Peggy Holtorf, Diana Brixner & Zoltán Kaló (2020) Barriers and facilitators of exploiting the potential of value-added medicines, *Expert Review of Pharmacoeconomics & Outcomes Research*, 20:3, 229-236, DOI: 10.1080/14737167.2020.1758558



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