Value Added Medicines: The Need to Establish One Common Terminology for Repurposed Medicines

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BACKGROUND

- Value added medicines embrace the concept of drug repurposing of existing molecules which is a well-known concept for many years and are defined as "*medicines based on known molecules that address healthcare needs and deliver relevant improvements for patients, healthcare professionals and/or payers*" [1].
  - Lots of interest have been gained in this field over the last years *(through availabilities of public and open source data, as well as technological advances in disease pathogenesis, genomics and bioinformatics)* and an increasing collaboration is emerging between public and private sectors to support drug repurposing [2-5].
- However, contrary to products like generic medicines, biosimilar medicines and hybrids, no regulatory definition has been set for repurposed medicines.
- Value added medicines are not always recognised and rewarded at their full potential value, creating a disincentive for further development.

OBJECTIVE

- The objective of this study was to propose a common typology for value added medicines allowing for better assessment of their value.

METHODS

- A comprehensive literature review was conducted in Medline, Embase, Cochrane databases, Generics and Biosimilars Initiative (GaBI), Google Scholar, European Medicines Agency, European Commission websites and available grey literature to identify the different nomenclatures describing the concept of value added medicines and to propose a common typology.
  - The search was conducted in English language, limited to publications released between 2000 to December 2015 (cut-off date of the search).
  - The search strategy included preliminary free search terms ('marginal innovation', 'incremental innovation', 'adaptive innovation', 're-innovation', 'hybrid products', 'drug repurposing', 'drug reformulation', 'drug repositioning') and was complemented with additional free search terms found in the literature.

RESULTS

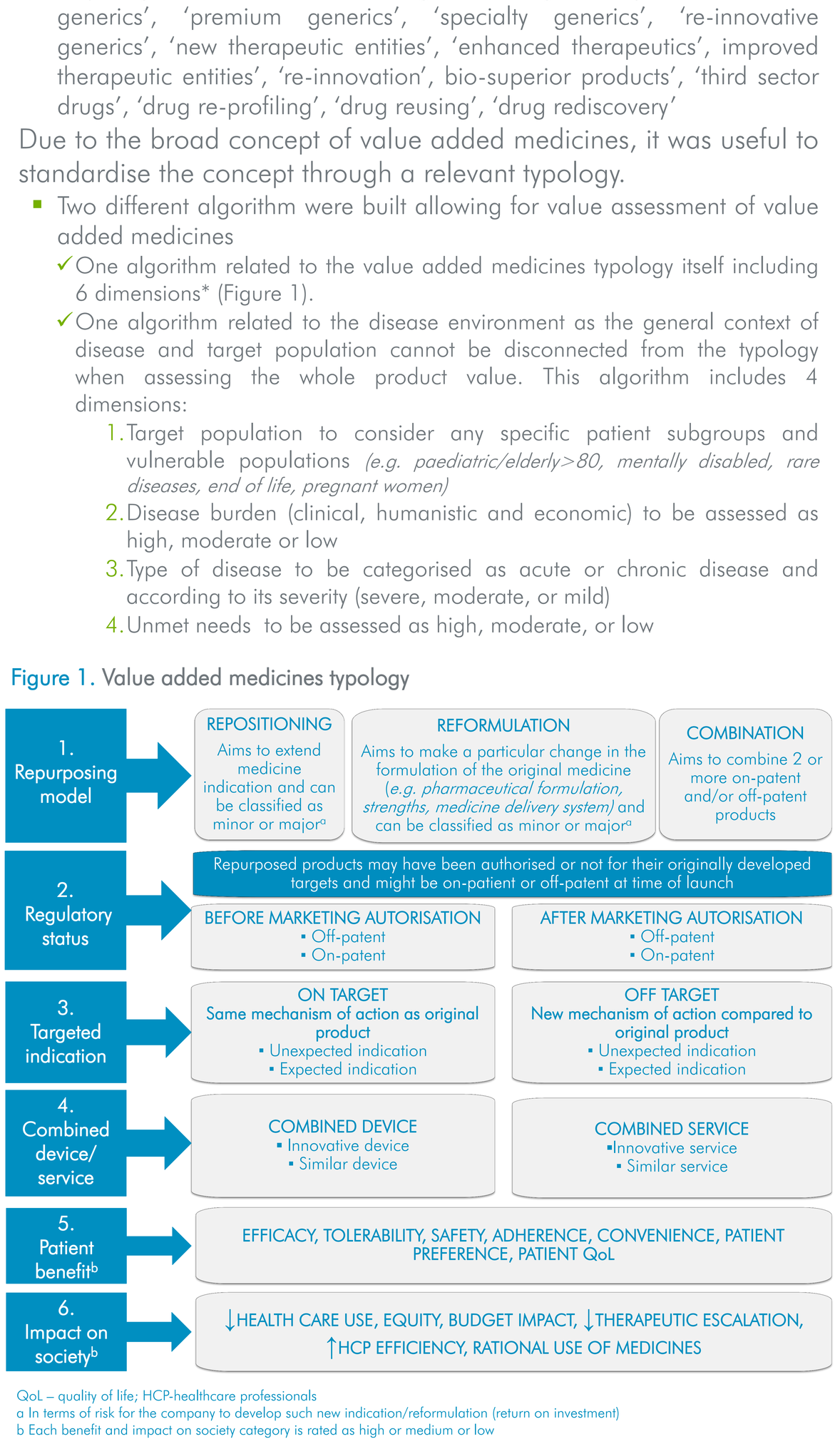
- Various nomenclatures have been used to describe the concept of drug repurposing in the literature with more or less broad definitions, either based on outcomes, processes, or being mix of both (*some examples provided in Table 1*).

Table 1. Examples of nomenclatures/definitions for the concept of drug repurposing

Definition based on	Nomenclature	Definition (s)
Outcomes	Enhanced therapeutics	"*Drug products derived from existing generic drugs that provide additional benefits to the patients and the healthcare system*" [6].
Processes	Incremental innovation	"*Either new approved drugs created from an already existing molecule or approved modifications to existing drugs.*" There are 5 types of incremental innovation: 1. New dosage form: which affects the dosage route, the dosage form and the does amount 2. New formulation: how the chemicals in the drug are combined to produce the drug 3. New combination: creation of combination drugs from existing molecules 4. New indication: using an existing drug to treat a different condition 5. New active ingredient: drugs that contain the same active moiety but include a different enantiomer, racemate, salt, ester, complex, chelate, or clathrate [7]
Outcomes /Processes	Bio-superior products	"*Intended to have attributes that are better than the first-generation product (…)* *A bio-superior utilises cutting-edge technologies such as protein engineering, and novel drug formulation and delivery approaches to enable its superiority over a first-generation product, possibly improving its efficacy or safety profile or improving administration route or reducing dosing frequency*" [8]

- Additional terms found in the literature included:
  - 'super generics', 'added value generics', 'generic plus', 'innovative generics', 'premium generics', 'specialty generics', 're-innovative generics', 'new therapeutic entities', 'enhanced therapeutics', improved therapeutic entities', 're-innovation', bio-superior products', 'third sector drugs', 'drug re-profiling', 'drug reusing', 'drug rediscovery'
- Due to the broad concept of value added medicines, it was useful to standardise the concept through a relevant typology.
  - Two different algorithm were built allowing for value assessment of value added medicines
    - ✓One algorithm related to the value added medicines typology itself including 6 dimensions* (Figure 1).
    - ✓One algorithm related to the disease environment as the general context of disease and target population cannot be disconnected from the typology when assessing the whole product value. This algorithm includes 4 dimensions:
      1. Target population to consider any specific patient subgroups and vulnerable populations *(e.g. paediatric/elderly>80, mentally disabled, rare diseases, end of life, pregnant women)*
      2. Disease burden (clinical, humanistic and economic) to be assessed as high, moderate or low
      3. Type of disease to be categorised as acute or chronic disease and according to its severity (severe, moderate, or mild)
      4. Unmet needs to be assessed as high, moderate, or low

Figure 1. Value added medicines typology



QoL – quality of life; HCP-healthcare professionals
a In terms of risk for the company to develop such new indication/reformulation (return on investment)
b Each benefit and impact on society category is rated as high or medium or low

**This algorithm is based on a previous work conducted by Susana Murteira and Creativ-Ceutical as part of thesis research (Murteira S, Ghezaiel Z, Karray S, Lamure M. Drug reformulations and repositioning in pharmaceutical industry and its impact on market access: reassessment of nomenclature. Journal of Market Access & Health Policy 2013, 1: 21131.)*

CONCLUSIONS

- This harmonised typology for value added medicines might allow better differentiating these products and enhancing their value assessment.
- While no regulatory definition for value added medicines, the recent European Commission STAMP initiative related to repurposing of established medicines raised this issue and will consider the opportunity to provide a definition.

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ISPOR 19th Annual European Congress, Vienna, Austria, OCT 29 – NOV 02, 2016. PHP139.

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