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 the availability of public and open source data, as well as technological advancements 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 terminology for value added medicines allowing for better assessment of their value.

METHODS
• A comprehensive literature review was conducted in Medline, Embase, Cochrane databases, Genetics 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 terminology.
  • 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

<table>
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<tr>
<th>Definition based on</th>
<th>Outcomes</th>
<th>Processes</th>
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<tr>
<td>Outcomes</td>
<td>Enhanced therapeutic value</td>
<td>Incremental innovation</td>
<td>Repurposing of existing medicines</td>
<td>Bio-superior products</td>
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<td>&quot;Drug products derived from existing generic drugs that provide additional benefits to the patients and the healthcare system.&quot; [6]</td>
<td>&quot;Either a new approved drug created from an already-existing molecule or approved modifications to existing drugs.&quot; There are 5 types of incremental innovation: 1. New dosage form, which affects the dosage route, the dosage form and the dosage amount 2. New formulation: how the chemicals in the drug are combined to produce the drug 3. New combination: combination of two existing medicines 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 structure, moiety, salt, ester, complex, chelate, or clathrate&quot; [7]</td>
<td>These must be: a) approved medicines, b) approved modifications, c) approved indications, d) larger potential for benefit 1. New mechanism of action compared to the original drug, 2. Improved strength and/or off-patent 3. New indication 4. New active ingredient</td>
<td>&quot;Intended to have attributes that are better than the first-generation product (…) A bio-superior utilizes cutting-edge technological of 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.&quot; [8]</td>
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REFERENCES
1. Medicine for Europe. What is value added medicines. 2016, [Internet].
7. Hu H. Incremental Innovation and Pharmaceutical Productivity. 2014, [Internet].
8. M, H. Bollinga a biologics pipeline portfolio. Drug Discovery World website, 2011, [Internet].

CONCLUSIONS
• This harmonised terminology 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.

REFERENCES
1. Medicine for Europe. What is value added medicines. 2016, [Internet].
7. Hu H. Incremental Innovation and Pharmaceutical Productivity. 2014, [Internet].
8. M, H. Bollinga a biologics pipeline portfolio. Drug Discovery World website, 2011, [Internet].

(Supporting information)

Additional terms found in the literature included:
• 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, and life, pregnant woman
    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