Pharmaceutical Directive – Article 84

Repurposed medicinal products

Affordable innovation that addresses patient needs

Directive Article 84 - Repurposed medicinal products Affordable innovation that addresses patient needs

The revision of the pharmaceutical legislation should address **patient needs and the accessibility and affordability of medicines**. This is especially important as **out of 7000 diseases with a known molecular basis, only around 500 have approved treatments**[1].

Many existing treatments can be improved leveraging modern technologies for today's health needs:

- **Reducing adverse effects**, for example **for women, who experience 60% more adverse effects than men**[2].
- **Optimising life-saving treatments**, such as for oncology, where a substantially modified version of a **medicine for breast, pancreatic and lung cancer improved efficacy by 50%**[3]**.**
- **Supporting patients in adhering to their chronic treatments**, such as in cardiovascular diseases, where a combination product **helped reduce cardiovascular events by 30%**[4]**.**

Due to a **lack of appropriate treatments**, many diseases are managed with off-label or un-licensed medicines, with varying degrees of supportive evidence, which could prove a **significant risk to patients**. At the same time the **price of novel medicinal products** poses a challenge for many healthcare systems in terms of affordability, which restricts the access to a small proportion of the affected patient population.

Value added medicines, which are obtained by repurposing off-patent molecules can serve as an alternative, affordable type of innovation to address these challenges, making a difference in the daily lives of patients through:

1. **New indications**

Most new indications are added on label 7-8 years before loss of exclusivity. As recognised by the European Commission **new indications can be discovered at the end of the (patent) life cycle of a medicine.** However, due to a market failure of our current system, very few new indications are added on label at the end of the patent protection period. **This is a huge loss for public health.**

Added value in a health crisis → Dexamethasone, an affordable steroid normally used to treat inflammatory conditions (such as allergic disorders and skin conditions) and severe autoimmune diseases (ulcerative colitis, arthritis, lupus, psoriasis, and breathing disorders), was **repositioned for Covid-19 treatment, as it was shown to reduce deaths by 1/3 in hospitalised Covid-19 patients receiving mechanical ventilation in ICU (Intensive Care Unit)**[5].

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[1] Online Mendelian Inheritance in Man, Morbid Anatomy of the Human Genome
[2] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1873702/
[3] https://www.ema.europa.eu/en/documents/assessment-report/abraxane-epar-public-assessment-report_en.pdf
[4] ISPOR EU 2022, J of Hypertension V41 No 1 2023
[5] Source RECOVERY TRIAL.

2. New pharmaceutical forms

The development of new pharmaceutical forms, such as switching from adult forms to adapted oral solutions can help tremendously in addressing the **huge needs for appropriate medicines for children**.

There are **many other examples where changes in pharmaceutical forms bring significant improvements** for patients and health systems.

Added value in addressing AMR → The rise in antimicrobial resistance has led to many severe infections where existing antibiotics no longer work, mostly affecting vulnerable immunocompromised patients. Changing the pharmaceutical form to an **inhalable formulation for amikacin**, an antibiotic usually used as an intravenous injection, allowed **3 times more effective treatment[6] for resistant pulmonary infections.**

Added value for healthcare professionals → Building on Covid-19 lessons learned, moving care closer to patients by using self-administered pharmaceutical forms, **can greatly reduce burden on patients, on healthcare professionals and health systems**. According to NHS data, in England alone switching to ready to administer formulations can **save the time for 4,000 nurses per year as well as free up 1 million beds.**

3. New methods or routes of administration

This is the way that the medicine enters the body and can have a significant influence how the medicine acts and how it affects patients.

Added value for health systems → Several years ago, a company introduced a new version of the antirheumatic drug, methotrexate. Instead of being taken orally in a tablet form, it is available as a pre-filled auto-injector. The previous oral tablets often caused unwanted side effects, particularly in the stomach, which often led patients to switch to expensive biologic treatments. **With this new formulation, patients have experienced improved treatment outcomes, allowing them to stay on treatment for 1-2 years longer than with the oral version[7], which reduced the financial burden on healthcare systems, as patients can be treated effectively with a more affordable option.**

The budget impact of introducing this affordable innovation meant savings of tens of thousands of euros per patient per year.

4. Posology

The dose and timing for administering the product can be relevant to address adherence which negatively impacts health outcomes but also bring huge additional costs to the EU system of around **125 billion euros[8].** However, often, changes in posology also arise due to better formulations of the medicine.

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[6] https://www.ema.europa.eu/en/documents/assessment-report/arikayce-liposomal-epar-public-assessment-report_en.pdf

[7] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5394544/

[8] https://ilcuk.org.uk/125-billion-lost-each-year-due-to-non-adherence

Added value in mental health → For **patients suffering from schizophrenia**, the **use for long-acting anti-psychotics,** has been shown to **significantly improve patient outcomes while also reducing healthcare costs by 1/3[9].**
Added value in oncology → A reformulation of a **medicine used to treat leukaemia, enabled effective treatment for an additional 20% of patients[10]**, that were not receptive to this lifesaving treatment with the original medicine. This was done by improving the way the medicine was absorbed in the body, which resulted in a lower dose needed. This **resulted in a change of posology**, because of the dose, but did not result in a change in method, route, or form of administration.

The **development of these medicines takes 5-10 years,** requiring lengthy non-clinical and clinical trials. The **research and investment** is **significant and can amount to tens of millions of euros[11].**

For companies to make these **high-risks investments** and bring these products to European patients, **we need a more systematic approach to this class of medicines**, which we can now achieve through the revision of the pharmaceutical legislation.

MEDICINES FOR EUROPE RECOMMENDATIONS

The Commission recognises the importance of repurposed value added medicines as a source of affordable innovation and their value for patients, their caregivers, and the healthcare systems with **non-cumulative 4-year data protection period which only protects the new studies conducted,** as **set out in Article 84 of Directive 2023/0131.** This is an excellent basis for supporting the development of alternative affordable sources of innovation brought by value added medicines.

In addition, the legislation should:

- Clarify the article to **allow all new uses** brought through repurposing to be considered, including **changes in methods or routes of administration, posology, or pharmaceutical form**.
- Align to the established regulatory concept of **significant benefit,** as defined in the EMA guidelines, which encompasses both clinical and patient centered benefits such as easier access to treatment (home vs hospital administration), improvements in adherence or patient quality of life.
- Ensure that the **article is not misused for evergreening practices**, by also excluding products which have benefitted from market protection and making the link to the concept of a global marketing authorisation in Article 84(1) point b.

[9] https://pubmed.ncbi.nlm.nih.gov/35395757/
[10] https://pubmed.ncbi.nlm.nih.gov/37789147/
[11] https://www.fast.nl/wp-content/uploads/2024/03/Fast-EN-Position-paper-Drug-repurposinginteractief.pdf