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High cost oncology drugs without proof of added benefit are burdening health systems

Research into rational use of expensive oncology drugs in clinical practice can benefit health systems and patients

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In recent decades, drug discovery and development has undergone remarkable progress, leading to groundbreaking biomedical innovations such as targeted therapies, cell and gene therapies, and mRNA vaccines. But this surge in advances has posed a challenge for health systems, leading to increasing budgetary distress because of the high numbers of innovative, albeit costly, drugs entering the market.[1-5] This challenge is particularly pronounced in oncology. The share of oncology products entering the global drugs market increased from 30% in 2010 to 50% in 2020, and global spending on these drugs is projected to rise from $164bn in 2020 to $269bn by 2025.[6,7] In this context, research into the rational use of expensive oncology drugs is needed to ensure that budgets of health systems are well spent.

Oncology drugs are increasingly approved through expedited pathways to ensure timely access to treatments (for unmet medical needs such as rare cancers with no satisfactory treatment options). These approvals are often based on less comprehensive evidence, such as that obtained from single arm trials, and/or derived from surrogate endpoints.[2,8-12] Inherently, this evidence introduces uncertainty during drug reimbursement evaluations, hampering assessments of added benefit and contributing to the high number of negative evaluation outcomes for these drugs.[9,13-16] In this context, a lingering question remains: do the considerable private and public resources invested in these promising yet costly "high end" drugs genuinely translate into clinical and societal benefits?

In response to ongoing debates about the effect of drug policies on health systems, Leufkens and colleagues explored potential scenarios for the future of pharmaceutical and social policy in 2030.[7] One scenario envisions health systems progressively "deprioritising the high end," anticipating a shift towards prioritising public health and primary care over early disease interception with highly innovative technologies—thereby challenging the prevailing emphasis on high end oncology drugs.

While the scenario presented by Leufkens and colleagues might seem unlikely to some in high income countries, support is growing for this line of thinking.[9-11,16-19] Critics argue that current policies on marketing approval and reimbursement within many health systems may inadvertently offer patients access to expensive drugs with limited benefits but often substantial toxicity, fostering false hope in patients while potentially displacing other healthcare options. Some research has focused on rational use of these drugs in clinical practice to evaluate the clinical uncertainties and financial risks associated with these costly drugs. For example, the SONIA study in the Netherlands found that initiating CDK4/6 inhibitors as second line treatment for HR+/HER2- advanced breast cancer led to substantial cost savings of approximately €25m over the trial's duration without compromising clinical outcomes.[20-22] These findings challenge conventional guidelines recommending upfront use of CDK4/6 inhibitors as first line.[23] Illustrated by rational use studies like SONIA,[17,24-27] exploration of efficient drug administration and dosing strategies hold significant potential in reducing healthcare costs while retaining, or even enhancing, patient benefits.

Our research article, published in *The BMJ* (doi:10.1136/bmj-2023-077391), provides an extensive overview of oncology drugs approved by the European Medicines Agency between 1995 and 2020 and confirms that, despite regulatory approval, a considerable number of oncology drugs show limited added benefit. This was particularly pronounced in cases where drugs had been approved through expedited regulatory pathways that are inherently associated with less comprehensive evidence. While these pathways aim to accelerate the availability of drugs for unmet medical needs, they often lead to situations where expensive drugs fail to deliver substantial clinical benefits to patients.

Our study also reveals that oncology drugs, even those with minimal or no added benefit, recover their estimated research and development costs within a median time of three to four years, and more than 90% recover these costs within eight years. Hence, oncology drugs often not only reach the market while lacking proof of added benefit but also succeed in recovering their research and development costs in a relatively short period. All this raises serious questions about the alignment of marketing approval and reimbursement policies with the actual clinical benefit offered to patients. Following the scenario envisioned by Leufkens and colleagues, health systems—even those of high income countries—may ultimately fail to keep up with high cost oncology drugs without proof of added benefit.[7]

Our study underscores the challenges in incentivising the development of drugs that clearly address critical unmet medical needs, highlighting a policy gap between drug approval and reimbursement on the one hand and patient and societal benefit on the other. Bridging this gap requires recognition of the problem and active engagement and policy

refinement by all stakeholders involved. Positive steps are being taken, such as a decision by the Dutch Society for Medical Oncology to tighten the acceptance standards for oncology drugs by revising its PASKWIL criteria (referring to palliative, adjuvant, specific side effects, quality of life, impact of treatment, and level of evidence).[28] At EU level, Belgium has committed to prioritise research and innovation in the area of unmet medical needs during its presidency of the Council of the EU,[29 30] and a proposal for reformed EU pharmaceutical legislation contains new definitions of unmet medical need and—for orphan drugs—high unmet medical need.[31-35] Nevertheless, accelerating approval of innovative drugs also remains popular, as seen in the various new expedited approval procedures proposed for the new EU legislation.[31 32 35] In the UK, marketing approval and reimbursement agencies have collaboratively introduced the Innovative Licensing and Access Pathway (ILAP).[36] One of the ILAP criteria requires provision of evidence of likely patient benefit, preferably based on input from patients or patient organisations, and to be evaluated upfront by both marketing approval and reimbursement agencies. But the question remains whether ILAP will deliver on its promise and can effectively balance expedited patient access with clinical benefits.

We urge policymakers to consistently reassess both ongoing and new initiatives aimed at ensuring fair, affordable, and sustainable patient access to innovative and expensive drugs. Additionally, we emphasise the importance of investigating and promoting the rational use of these drugs in clinical practice. This approach strives for a future where drug development and limited resources align more closely with real world benefits to patients.

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