The DRUG Access Protocol: access inequality and European harmonisation

We commend the initiators of the DRUG Access Protocol (DAP) for their efforts to combine earlier access to medicine with structured data collection.[1] Although this is a novel programme in the Netherlands, similar programmes covering compassionate use, evidence generation, and reimbursement are already in effect in England (Early Access to Medicines Scheme) and France (L'Accès Précoce).[2,3] The benefits of the DAP in providing conditional reimbursement of registered drugs and thereby creating access are evident. However, the effects of the protocol in the setting of compassionate use (typically free of charge) require further exploration.

First, the current set-up of access to compassionate use in Europe has led to a patchwork of national access pathways. The DAP could further complicate the process of obtaining access to compassionate use, by introducing a novel national pathway specifically for oncology. Pharmaceutical companies without local presence or sufficient resources might prefer to provide access in countries with easier access pathways, which raises issues of equity in patient access. With the harmonisation of clinical trials through the Clinical Trial Regulation and health technology assessments through the EUnetHTA initiative, we believe the need grows for compatible compassionate use legislation, rather than further diversifying pathways.

Second, the DAP poses additional hurdles and workload to oncologists and companies as participation does not guarantee regulatory approval for compassionate use. Because this protocol is a voluntary, cooperative initiative and not a legally mandated pathway, regulatory approval still must be obtained separately. This workload might deter rather than expedite access, especially for patients and oncologists in less specialised centres. The benefits of additional evidence generation might not outweigh the extra paperwork and research strains imposed on patients and physicians. In a broader context, the changing nature of compassionate use programmes to provide research rather than treatment has been a growing source of concern among bioethicists.[4]

In recent years, there has been increased interest in compassionate use programmes to generate evidence on safety and efficacy that supports trial results. The Compassionate Use Guidelines of the European Medicines Agency from 2007,[5] which do not mention the collection of efficacy data, seem out of date. We hope a guideline revision will clarify the value of compassionate use as real-world evidence, shed light on the concerns of equity to access raised above, stimulate harmonisation of access pathways, and incorporate the experiences from the DAP.

TBP works part-time for expanded access service provider myTomorrows, in which he holds stock and stock options (<0·01%); he is contractually free to publish, and the service provider is not involved in any of his past or ongoing research, nor this Correspondence. DGJC received payments for lectures for Takeda, outside the submitted work. CAU-dG has received unrestricted grants from Boehringer Ingelheim, Astellas, Celgene, Sanofi, Janssen-Cilag, Bayer, Amgen, Genzyme, Merck, Glycostem Therapeutics, AstraZeneca, Roche, and Merck. CAU-dG, JvR, and TBP work under a Dutch government grant from HealthHolland. In this grant, they specifically research legal, ethical, policy, and statistical issues of evidence generation in compassionate use programmes (EMCLSH20012). HealthHolland is a funding vehicle for the Dutch Ministry of Economic Affairs and Climate Policy that addresses the Dutch Life Sciences & Health sector.

*Tobias B Polak, David G J Cucchi, Joost van Rosmalen, Carin A Uyl-de Groot
t.polak@erasmusmc.nl

Erasmus School of Health Policy & Management, Erasmus University Rotterdam, Rotterdam, Netherlands (TBP, CAU-dG); Department of Biostatistics (TBP, JvR), and Department of Epidemiology (TBP, JvR), Erasmus Medical Centre, Rotterdam, Netherlands; Real-World Data Department, myTomorrows, Amsterdam, Netherlands (TBP); Department of Haematology, Amsterdam UMC, Vrije Universiteit Amsterdam, Cancer Centre Amsterdam, Amsterdam, Netherlands (DGJC)

1 Zeverijn LJ, van Waalwijk van Doorn-Khosrovani SB, van Roy AAMGP, et al. Harmonising patient-access programmes: the Dutch DRUG Access Protocol platform. *Lancet Oncol* 2022; **23:** 198–201.
2 Haute Autorité de Santé. Authorisation for early access to medicinal products. June 17, 2021. https://www.has-sante.fr/upload/docs/application/pdf/2021-08/authorisation_for_early_access_to_medicinal_products_has_assessment_doctrine.pdf (accessed Feb 8, 2022).
3 Polak TB, Cucchi DGJ, van Rosmalen J, Uyl-de Groot CA. Real-world data from expanded access programmes in health technology assessments: a review of NICE technology appraisals. *BMJ Open* 2022; **12:** e052186.
4 Chapman CR, Moch KI, McFadyen A, et al. What compassionate use means for gene therapies. *Nat Biotechnol* 2019; **37:** 352–55.
5 European Medicines Agency. Committee for Medicinal Products for Human Use. Guideline on Compassionate Use of Medicinal Products, Pursuant to Article 83 of Regulation (EC) No 726/2004. https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/guideline-compassionate-use-medicinal-products-pursuant-article-83-regulation-ec-no-726/2004_en.pdf (accessed Feb 8, 2022).