Copenhagen Economics

EXPENSIVE INNOVATIVE TREATMENTS: HOW TO INCREASE PATIENT ACCESS AND AVOID CONDITIONAL REIMBURSEMENT APPROVALS

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28 October 2020

INNOVATIVE TREATMENTS ARE INCREASINGLY EXPENSIVE

The emergence of gene therapies and other novel treatments has made new and innovative medicines increasingly expensive. Besides the high costs associated with R&D, clinical trials, and marketing authorisation, developing new treatments involves a great deal of uncertainty. Only 68% of orphan medicinal products make it past development, and 22% of those that do, do not reach marketing approval.[1]

Although technological development often makes medicinal devices smarter, it also makes them more expensive. High costs and the uncertainty of putting new treatments on the market is particularly problematic for treatments indicated for rare diseases since the high upfront costs are sought to be recouped from a small number of patients.

INNOVATIVE TREATMENTS ARE SOMETIMES ONLY APPROVED FOR REIMBURSEMENT FOR NARROW PATIENT POPULATIONS

Faced with increasingly tight budget constraints, national health authorities sometimes approve new therapies for reimbursement only for narrow patient populations with specific characteristics. Here are a few examples:

- HAE is a rare, severe, and potentially life-threatening disease, characterised by excessive swelling ('attacks') of various body parts. Lanadelumab (Takhzyro™) has been shown to significantly reduce the mean attack rate.[2] Lanadelumab indicated for HAE has been approved for reimbursement in the UK by NICE, but only for patients "[…] having two or more clinically significant attacks […] per week over eight weeks […]"[3] and in Denmark for patients with at least four attacks per month.[4] Based on real-world evidence from the US and the Nordic countries, a cut-off point

of eight attacks per month would benefit 6% of the UK patient population.[5]

- Idiopathic pulmonary fibrosis (IPF) is a chronic, progressive, and fibrotic lung disease.[6] Pirfenidone (Esbriet®) indicated for IPF is only approved for reimbursement in the UK for patients with a forced vital capacity (FVC)[7] between 50% and 80% predicted[8], which conflicts with early care of patients with higher FVCs[9].
- Acute myeloid leukaemia (AML) is a disease in which cancer cells are found in the peripheral blood and bone marrow. AML is divided into different subtypes including acute promyelocytic leukemia (APL), which constitutes approximately 10% of AML cases.[10] Gemtuzumab ozogamicin (Mylotarg™) has been approved for reimbursement in The Netherlands for previously untreated CD33-positive AML, except for APL.[11] This conditional approval for reimbursement persists even though Gemtuzumab ozogamicin has proven safe and effective in patients with high-risk APL.[12]

National health authorities often justify these conditional approvals for reimbursement based on a cost-benefit analysis and/or uncertainty about efficacy. The patients in the subgroups where treatment is not reimbursed are essentially denied access to a treatment that could provide improvements in health and quality of life due to treatment costs and the uncertainty of how large the treatment effects will be.

NARROW PATIENT ACCESS HAS ADVERSE EFFECTS

Conditional approvals for reimbursement have adverse effects on all stakeholders:

- Patients who are denied access to innovative treatments miss out on potential health and quality of life improvements, and in some cases, on the chance to survive.
- Producers and manufacturers obtain a lower revenue and have a harder time recouping the investments made to develop the innovative treatments.
- Healthcare professionals have fewer treatments options available to tailor their treatment of patients and less autonomy to do so.
- Healthcare payers lose out on avoidable healthcare costs associated with current treatments as well as potential healthcare savings from reduced use of healthcare services associated with the disease and comorbidities.

CONDITIONAL APPROVALS FOR REIMBURSEMENT RELY ON SIMPLIFIED PROXIES OF DISEASE BURDEN

How can patients, producers and manufacturers, healthcare professionals, and healthcare payers avoid a situation where finite health budgets available to payers mean that new innovative treatments are conditionally approved for reimbursement, making them unavailable to all patients who could benefit?

Conditional approvals are suboptimal because they rely on imperfect proxies of the disease's burden. Returning to the example of HAE; using the number of attacks as an indicator of disease severity reflects only one aspect of the burden this disease has on HAE patients for two reasons: first, individuals with fewer attacks can be more affected than individuals with more attacks depending on attack severity, impact on the patient's life, and more. Second, the number of attacks only reflects how patients are affected *during* an attack and does not capture the burden of the disease *in between* attacks on overall quality of life, work capabilities, mental health, and more. These factors affect the patient's health and well-being as well as contribute to the overall costs of the wider health and social care system.

The disease burden in-between attacks may be a particularly important aspect when moving from treating a disease to curing a disease with gene therapy, for example: not only does the patient avoid the health consequences of the disease, they are also no longer burdened by concerns and other negative consequences of living with a chronic disease.

> **Imagine living with a severe and chronic condition that impacts your health and limits your quality of life. Then imagine that it can be treated, but you can't get treatment because those who produce it and those who buy it cannot agree on something as simple as the price.**

An approach that considers the 'average' patient may not provide precise enough information on the efficacy of these new and innovative treatments for *individual* patients; uncertainty may exist about how individual patients will respond to a new treatment. Some patients may reap large benefits from the new treatment, while others experience little or no benefit.

TOOLS EXIST TO HELP IMPROVE ACCESS TO INNOVATIVE TREATMENTS

Basing reimbursement on a holistic view of consequences of innovative treatments on patients and society can help avoid patients being restricted access to life-saving and life-changing treatments. For example, real-world data from surveys can provide valuable insights into the total cost of using innovative and often expensive treatments as well as the cost savings, health gains, and quality of life improvements associated with them.

If payers are concerned about the risk of paying for all patients for something that might only work for some, tools such as value-based health care (VBHC) can help mitigate this risk. Innovative pricing agreements based on VBHC can help ensure that payment for innovative treatments is based on the *individual* value provided to patients. An example of such agreements is the recent approval for reimbursement of voretigene neparvovec (Luxturna®) in Denmark indicated for a rare inherited retinal disease due to mutations in both copies of the RPE65 gene which inevitably cause blindness.[14] The innovative pricing agreement is based on rates that are only paid if the treatment works for the individual patient.

Partnerships between healthcare payers and producers can help both parties engage in mutual beneficial procurement agreements. However, such models require a higher level of mutual trust between payers and providers than we often see today.[13] An effective dialogue between patient organisations, producers, and national health authorities about costs, benefits, and, more importantly, risk can help pinpoint the consequences of allowing more patients access innovative treatments and facilitate the development of a mutually beneficial VBHC arrangement.

Imagine living with a severe and chronic condition that impacts your health and limits your quality of life. Then imagine that it can be treated, but you can't get treatment because those who produce it and those who buy it cannot agree on something as simple as the price. There are opportunities to better use the finite budgets available to health authorities. By collecting and using real-world evidence, health systems can better understand patients' needs and base reimbursements on the holistic consequences of new and innovative treatments.

FOOTNOTES

[1] Copenhagen Economics based on historical average success rates from EMA data between January 1995 and May 2020, see https://www.ema.europa.eu/en/medicines/download-medicine-data.

[2] Banerji, A., Riedl, M. A., Bernstein, J. A., Cicardi, M., Longhurst, H. J., Zuraw, B. L., Davis-Lorton, M. (2018); et al. Effect of Lanadelumab Compared With Placebo on Prevention of Hereditary Angioedema Attacks: A Randomized Clinical Trial. Jama, 320(20), 2108-2121, see https://jamanetwork.com/journals/jama/article-abstract/2716564.

[3] NICE (2019). Lanadelumab for preventing recurrent attacks of hereditary angioedema, see https://www.nice.org.uk/guidance/TA606/chapter/1-Recommendations.

[4] The Danish Medicines Council (2020). Baggrund for Medicinrådets anbefaling vedrørende lanadelumab som mulig standardbehandling til forebyggende behandling af arveligt angioødem, see https://medicinraadet.dk/media/kfshf5hu/baggrund-for-medicinraadets-anbefaling-vedr-lanadelumab-til-arveligt-angiooedem-vers-1-0_adlegacy.pdf (in Danish).

[5] Copenhagen Economics based on the HAEA and CE survey (2018) and HAEi and CE survey (2019) of 833 patients in total with HAE type 1 or 2. The share is based on patients who are currently using on-demand treatment only (n = 316) and patients using prophylactic treatment, who recall a period without access to their prophylactic treatment (n = 279). In the former group, 17 patients report 8 or more attacks in the month before the survey. In the latter group, 18 patients report 96 or more attacks per year (8 attacks per month times 12 months) in the period without access to their prophylactic treatment. Combining these groups yields a share of patients with 8 or more attacks per month of (17+18)/(316+279) = 6%.

[6] Richeldi, L., Collard, H. R., & Jones, M. G. (2017). Idiopathic pulmonary fibrosis. The Lancet, 389(10082), 1941-1952, see https://www.sciencedirect.com/science/article/abs/pii/S0140673617308668.

[7] The maximum amount of air that can forcibly be exhaled after taking the deepest breath possible.

[8] NICE (2018). Pirfenidone for treating idiopathic pulmonary fibrosis, see https://www.nice.org.uk/guidance/ta504/chapter/1-Recommendations.

[9] Lassenius, M. I., Toppila, I., Pöntynen, N., Kasslin, L., Kaunisto, J., Kilpeläinen, M., & Laitinen, T. (2020). Forced Vital Capacity (FVC) decline, mortality and healthcare resource utilization in idiopathic pulmonary fibrosis. European Clinical Respiratory Journal, 7(1), 1702618, see https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6968594/.

[10] O'Donnell, M. R., Tallman, M. S., Abboud, C. N., Altman, J. K., Appelbaum, F. R., Arber, D. A., Lancet, J. et al. (2013). Acute Myeloid Leukemia, Version 2.2013. Journal of the National Comprehensive Cancer Network, 11(9), 1047-1055, see https://jnccn.org/view/journals/jnccn/11/9/article-p1047.xml?print&print&print&print.

[11] National Health Care Institute, The Netherlands (2018). Gemtuzumab ozogamicine, see https://www.farmacotherapeutischkompas.nl/bladeren/preparaatteksten/g/gemtuzumab_ozogamicine (in Dutch)

[12] Lancet, J. E., Moseley, A., Komrokji, R. S., Coutre, S. E., DeAngelo, D. J., Tallman, M. S., Appelbaum, F. R., et al. (2016). ATRA, Arsenic Trioxide (ATO), and Gemtuzumab Ozogamicin (GO) Is Safe and Highly Effective in Patients with Previously Untreated High-Risk Acute Promyelocytic Leukemia (APL): Final Results of the SWOG/Alliance/ECOG S0535 Trial, see

https://ashpublications.org/blood/article/128/22/896/99048/ATRA-Arsenic-Trioxide-ATO-and-Gemtuzumab.

[13] In our second article in this series of articles on 'The way forward: value-based healthcare in partnerships', we describe how partnerships can create benefits by breaking down barriers.

[14] The Danish Medicines Council (2020). Medicinrådet anbefaler Luxturna som standardbehandling, see https://medicinraadet.dk/nyheder/2020/medicinradet-anbefaler-luxturna-som-standardbehandling (in Danish) and Baggrund for Medicinrådets anbefaling vedrørende voretigene neparvovec som mulig standardbehandling til behandling af arvelig RPE65-relateret nethindedystrofi, see https://medicinraadet.dk/media/kp0l4dv1/baggrund_for_medicinr%C3%A5dets_anbefaling_vedr_voretigene_til_arvelig_rpe65-relateret_nethindedystrofi-vers-_2-0_samt_bilag_adlegacy_123041.pdf (in Danish).

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