

FOREWORD

Under construction: roadmaps for HTA, pricing and reimbursement of cell and gene therapies



NEIL PALMER is Senior Strategic Adviser and President Emeritus of PDCI Market Access Inc., Canada's leading pricing and reimbursement consultancy that he co-founded in 1996. Prior to PDCI, Neil worked with the Patented Medicine Prices Review Board (PMPRB) where his responsibilities included policy development, overseeing the price review of patented medicines and conducting economic research. Prior to the PMPRB, he worked with the Health Division of Statistics Canada where he was responsible for economic and statistical analysis of health care costs and utilization. After completing his studies at the University of Western Ontario, Neil began his career in Montreal with the research group of the Kellogg Centre for Advanced Studies in Primary Care. He has presented extensively on pharmaceutical pricing and reimbursement issues and is a frequent speaker at conferences in North America and Europe.

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More than a dozen cell and gene therapies (CGT) are already on the market (e.g., LUX-TURNA[®], Kymriah[®], Yescarta[®], Zolgensma[®]) and there are several hundred cell and gene therapies in development [1]. McKinsey reports that “more than 750 trials of CGTs in almost 30,000 patients were underway as of June 2020”, representing a growing proportion of the pharmaceutical industry’s clinical and pre-clinical pipelines [2].

With the promise of significant and clinically meaningful advances in treatment, the early entrants are challenging national Health Technology Assessment (HTA), and pricing and reimbursement infrastructures around the world.

For traditional pharmaceuticals and biologics, the current HTA and market access roadmaps are generally clear, albeit often challenging. Analytical methods, standards and thresholds for assessing clinical and cost effectiveness are well established, limited primarily by gaps in clinical evidence than can sometimes be mitigated through risk sharing agreements with payers.

By comparison, the HTA and reimbursement roadmaps for CGT are still under construction, particularly in cases where there are unique or novel treatment modalities where there is no clear budget or funding mechanism within national or regional health care systems. Some CGTs are more akin to medical/surgical procedures than pharmacotherapy and require significant supporting medical care. And gene therapies for rare diseases may require cross-border travel to a specialized treatment centre (e.g., Strimvelis[®] in Milan) which raises logistics and reimbursement challenges [3].

This issue of *Cell and Gene Therapy Insights* addresses many of the important issues anticipated for HTA, pricing and reimbursement of cell and gene therapies.

Chaddah *et al.* report proceedings of their international workshop on the Challenges in the Adoption of Regenerative Medicine Therapies (CHART) [4]. The authors conclude that although current HTA methods are applicable to CGT, the dearth of long-term

evidence greatly increases uncertainty that CGT are clinically and cost effective. The authors recommend improvement in clinical trial design, establishment of incentives for real world evidence, engagement of multiple stakeholders including policy makers, improvements to patient and data management, and finally, addressing payment challenges for technologies with high upfront costs but uncertain long term benefits.

Dabbous *et al.* provide an informative overview of European multinational collaborations in HTA and procurement of health technologies. Although more than 30 European countries are actively involved in such collaborations, only two have published reviews or activities with respect to gene therapies, a number that will surely grow [5]. However, despite multinational HTA and pricing collaborations, distinct national and sub-national treatment and funding pathways will likely persist given the unique characteristics of the respective healthcare systems.

Hague and Price question whether the value assessment criteria employed by HTA agencies to chimeric antigen receptor T-cell (CAR-T) therapies are fit-for-purpose given CAR-T’s unique treatment characteristics and uncertainties in the evidence base. The authors recommend more systematic inclusion of evidence from patients and carers, a broader perspective of value to include productivity gains to address the limitations of cost-per-QALY value frameworks. They emphasize the important role of outcomes-based agreements to address uncertainty and the need for alignment on registries that will generate the evidence for the outcomes-based payment models [6]. Although, these concerns are not new to HTA agencies or payers as they face very similar challenges with highly specialized pharmaceutical technologies for rare diseases, the authors outline the specific concerns with respect to CAR-T.

The interview with Suzanne McGurn (President & CEO, CADTH) highlights the concerns of HTA agencies and payers that current and emerging CGT are novel and complex treatment technologies that need

to be integrated into the healthcare system. Moreover, CGTs are highly heterogeneous in nature so the HTA review process needs to be adaptable to the technology and its place in the healthcare system. To that end, McGurn describes CADTH's separate review process for CGT including the screening process by which sponsors provide information on the complexity of the CGT and the treatment modality – information that allows CADTH to inform and engage with provincial ministries of health that will be reimbursing/funding the CGT within their respective healthcare systems. The process also allows early engagement between CADTH and sponsors [7].

In his interview, Professor Mondher Toumi addresses how HTA and market access for CGTs will evolve in Europe. And like McGurn, he highlights the heterogeneity of CGT technologies and the challenges of decentralized health care systems. Importantly, he warns that most CGT companies are not headed in the right direction when it comes to HTA, perhaps clinging to the misbelief that being highly specialized, traditional HTA would not apply to their technologies [8]. And while there may be updated HTA processes for HTA of CGT, as McGurn describes, current HTA methods will be adapted to address the unique characteristics of a CGT only if standard drug review process is not appropriate.

The interview with Parag Meswani (SVP, Commercial Strategy & Operations, Axovant Gene Therapies) highlights key learnings from his time with Spark and the commercialization of LUXTURNA® for a rare inherited ophthalmic condition and from his new role where the target is the much larger Parkinson's disease patient population. For rare diseases, the challenge is finding patients; for

larger patient populations, it is identifying those patients who will benefit most from gene therapy and for whom the new technology offers greatest value compared to current treatments. In both cases, genetic testing programs will be important and clinical trial design needs to focus on safety and efficacy, but with HTA evidentiary requirements in mind. He discusses pricing, the importance of mapping pricing evidence requirements and stakeholder needs to support value communication. Finally, he stresses the need for flexibility in payment modalities across payers; to offer options for payers to assess price and to manage cash flow [9].

Janet Lambert (CEO Alliance for Regenerative Medicine) asserts that “payers, policymakers, and other stakeholders must implement the infrastructure necessary to ensure broad patient access and appropriate value-based reimbursement.” [10].

However, the development and implementation of national CGT infrastructures is more likely to be evolutionary than revolutionary. And that evolution is already underway; led by individual firms and their innovative technologies that are blazing new trails for CGT products. There is no doubt that political awareness and informed policy makers are critical to a supportive environment; but it is the early CGT technologies and their pioneering sponsors, in collaboration with HTA authorities and payers, that will have the greatest influence (as borne out by the CHART workshop).

AFFILIATION

W. Neil Palmer

Senior Strategic Adviser and President
Emeritus of PDCI Market Access Inc.

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