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CURATIVE THERAPIES

Uncertainty and Cures: Discontinuation, Irreversibility, and Outcomes-Based Payments: What Is Different About a One-Off Treatment?

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The development of treatments potentially offering “cure” has raised several challenges for healthcare systems, especially for payers. These challenges include 1) affordability of “curative” treatments, 2) degree of uncertainty in health gains, 3) impact on market dynamics, and 4) risk-sharing payment mechanisms and pricing. In order to facilitate unbiased decision making, the advent of cures requires an in-depth assessment of existing methods of economic evaluations and the interpretation of their findings.

Treatments achieving a cure can be delivered as one-off or as repeated-dose (ie, requiring repeated administration). This article outlines the criteria for managing decision uncertainties around these 2 types of curative treatments. Firstly, uncertainty about health gains when considering new adverse evidence (such as where the cure only lasts for 3 years). One-off treatment cannot be discontinued as it is irreversible; whereas, repeated-dose administration can be discontinued. Secondly, the value of collecting information on long-term health gains is a provision in coverage with evidence development/adoption

“only with research” (CED/OWR) schemes. One-off cures are irreversible; however, they can avoid widespread adoption. Lastly, payers and providers want to know about potential innovative payment models that can be used in risk-sharing.

The authors have presented a stylized example of managing decision uncertainty for curative treatments. An economic model was developed to assess the 2 deliveries of curative treatments compared to current standard of care (SoC). One-off and repeat-dose curative treatments are both assumed to be expensive and therapeutic, whereas the SoC is inexpensive but has no impact on mortality. The example is simplified by assuming that only the current prevalent population is treated; there is no incoming incident population. To alleviate the financial irreversibility of the one-off cost of curative therapy various payment mechanisms are proposed: an annual outcome-based “success” payment for each year for which the patient continues to benefit from treatment (ie, the patient is alive, and treatment continues to work), versus an annual annuity payment based on amortization, in which payment is made only for patients who are alive (ie, an payment scheme that is less sensitive to the treatment no longer working).

Cost-effectiveness and budget impact results are summarized, comparing uncertainties arising from one-off and repeat-dosage treatments and comparing the 2 payment mechanisms. The authors also present the cost-effectiveness acceptability curve (CEAC) and expected value of perfect information (EVPI) curve associated with one-off and repeat-dosage treatment. Generally, the degree of decision-making uncertainty (measured by EVPI) associated with one-off treatment is 4 times higher than that of repeat dosage (\$160 million compared to \$40 million, respectively) plus a probability of being cost-effective at a \$50,000 threshold is 86% for one-off dosage, compared to 100% with repeat-dose treatment. The results show that the only difference between the 2 treatments is the discontinuation effect (ie, the irreversibility of payment should

the one-off treatment stop working). The article concludes that prevalence and discrimination issues mean that the impact on the payer of an incorrect decision is greater with one-off treatment than a repeat therapy. With evidence collection, this risk diminishes over time (a form of CED or OWR). Financial arrangements or risk sharing can eliminate differences for the payer between one-off and repeat-dose therapy. Furthermore, market dynamics of the introduction of future competitive treatments can be used to pursue discounted prices that contribute to the affordability of treatments.

Even in the absence of a difference in uncertainty of outcomes, adverse payoffs differ. The greater financial risk associated with a cure is related to the issue of treatment discontinuation, driven by irreversibility. Pragmatic adjustments may need to be made to take account of cost-ineffective SoC comparators and of the potential impact of new entrants, which will change the price dynamics between the one-off and repeat forms of treatment.

In summary, this paper will be of interest to readers as it provides insight into how the results of economic evaluation one-off and repeat-dose potentially curative therapies will differ and what aspects warrant consideration in addition to traditional cost-effectiveness analyses. It outlines some criteria for managing decision uncertainty and provides a practical example to guide an unbiased economic evaluation for curative treatments. It also presents a new set of challenges related to irreversibility. The authors urge readers to look beyond the standard cost-effectiveness and budget impact results and delve deeper into the uncertainty around these treatments and potential ways to address them. Although both one-off and repeat-dose treatments could be cost-effective, the irreversibility of one-off treatments plays an important role in decision uncertainty. Collection of long-term data, introducing innovative payment models, and ensuring market dynamics can reduce the uncertainty and contribute to the affordability of these treatments. •