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Accessibility
Satisfaction Guaranteed — “Payment by Results” for Biologic Agents
Alan M. Garber, M.D., Ph.D., and Mark B. McClellan, M.D., Ph.D.

As increasing numbers of promising but expensive biologic agents are introduced for use as medical treatments, drug pricing has become a high-profile issue. Earlier this year, pricing practices took a new turn in Britain, when the National Institute for Health and Clinical Excellence (NICE), the evaluative agency that applies cost-effectiveness analysis in making recommendations concerning drug coverage, declined to support coverage of the proteasome inhibitor bortezomib (Velcade) by the British National Health Service (NHS) for the treatment of multiple myeloma. It concluded that the price was too high relative to NICE’s estimates of its average benefits for the population to be covered. Rather than reducing bortezomib’s price, its manufacturer, Johnson & Johnson, offered to forgo charges for patients who do not have an adequate response to the drug. Although many details remained to be negotiated — including the criteria defining a response — the proposal reflected the recognition that the time has come to consider new approaches to drug pricing.

Payment based on results, including “pay for performance,” has been touted as a way to avoid waste and increase value in health care. In a conventional pay-for-performance contract, a small part (typically, 1 to 10%) of the reimbursement to providers is tied to measures of the quality and cost...
of the care they give. Johnson & Johnson's proposal takes the concept of pay for performance to its logical extreme, offering a money-back guarantee that risks the loss of 100% of the drug price when the desired results are not achieved.

Furthermore, most performance incentives reward effort — often measured in terms of a provider's compliance with practice guidelines — more than outcomes. Providers have resisted payments based on outcomes, which are influenced by difficult-to-measure factors they cannot control, such as patient compliance and disease severity. In results-based payment, the manufacturer supplies an unvarying product, and the response to it depends heavily on the selection of patients — a decision made by physicians and patients, not the company. Why, then, might it make sense to accept payment by results rather than simply lowering the drug's price? And how broadly can this pricing model be applied?

In Britain, without a favorable determination by NICE, a costly new intervention is unlikely to be adopted by the NHS. Although NICE does not make decisions solely on the basis of cost-effectiveness, in the past it has indicated that it generally accepts interventions whose cost-effectiveness ratio it estimates to be below about £30,000 per quality-adjusted life-year for the intended population, though there have been exceptions.

For drug manufacturers, failure to obtain NICE's approval can mean the loss of a substantial market. For most patients in Britain, it means paying for the drug out of pocket or through the small but growing private-insurance market.

Replacing a per-unit price with an outcome- or results-based price shifts financial risk from the payer to the manufacturer. If NICE applied the definitions of response used in major clinical trials, and if response rates were similar to those in trials, bortezomib would sell at an effective discount rate of about 60% when used to treat relapsed multiple myeloma. However, the repercussions are different from those of a simple price cut. To maximize revenues, the manufacturer has a stronger incentive to maximize the number of patients with a response, not merely the number of patients treated or doses sold. A focus on responders might encourage redoubled efforts to address the undertreatment of indications for which a drug is effective. As a result, use of the drug may increase.

The fixed costs of bringing a pharmaceutical product to market can reach hundreds of millions of dollars, but the cost of producing each additional unit is very small in relation to the total cost and unit price. If the marginal cost of producing the drug is one tenth of the price, with payment by results, a manufacturer will profit by extending the treatment to any population of patients with a response rate of at least 10%.

Payment by results also represents an innovative approach to addressing one of the central dilemmas in the allocation of drugs to patients — the fact that a treatment's benefits vary greatly, often in predictable ways, from one patient to another. Survivors of myocardial infarction have larger short-term survival benefits from statins than do young women with hypercholesterolemia but with no other risk factors for heart disease. A much greater survival benefit of imatinib mesylate (Gleevec, Novartis) has been demonstrated among patients with gastrointestinal stromal tumors than among those with malignant glioma. Physicians may be aware of many other characteristics that determine whether a patient is likely to benefit more or less than the enrollees in a study. If the price of the compound is uniform, access is likely to be limited to patients in the population groups known to derive the greatest benefit (if the cost is paid by insurance) or willing to pay the most (if patients spend their own money). Patients in groups that are not expected to derive particularly large benefit are less likely to receive treatment, often because payers will create barriers to such use of the drug. In results-based payment, payers face much less financial risk from treating such groups.

Manufacturers with a monopoly often address variation in benefits by charging different patients different prices (price discrimination). Prices might be lower for low-income patients or for those not expected to receive large benefits. This approach makes the treatment available to more patients who might benefit while increasing sales and profits. However, in many circumstances, price discrimination is difficult to implement and unpopular, and both marketing considerations and political pressure limit its use.

Payment by results can extend access to drugs while avoiding some of these disadvantages. A manufacturer can earn more if nearly everyone in whom the performance goal might be achieved receives treatment. It's true that simply reducing the drug's price would also increase the number of patients for whom the cost-effectiveness ratio was favorable, but
the reduction would need to be deep to increase volumes by a similar amount, and it would not create similar incentives for ensuring that the patients likely to have high benefit received the drug.

Moreover, the payment-by-results approach obviates the need to calculate different cost-effectiveness ratios for different groups of patients: as long as benefit is captured well by the response measure, cost-effectiveness can be calculated the same way for everyone. In effect, payment by results creates a personalized rather than a population-based cost-effectiveness ratio, and the NHS need not restrict access for certain classes of patients to ensure that the cost-effectiveness test is met.

With such advantages over simple unit pricing, why has results-based pricing seldom been used? As the bortezomib negotiations suggest, there are many practical challenges. First, there must be a clearly defined, objective measure of results, and it must closely correspond to the desired treatment effect — that is, to a valid health outcome measure. Furthermore, the outcome measure must not be heavily confounded by patient characteristics or by other treatments. Survival, for example, is perhaps the most important outcome of treatment, but it is not usually a practical measure, because it is heavily influenced by underlying disease and by any other treatments given and because the timeline for observing changes in survival may be impractically long. The use of a surrogate measure, such as the monoclonal protein level in bortezomib’s case, will be most successful if it is a good biomarker or predictor of clinically meaningful outcomes and if it is not influenced by other treatments.

Johnson & Johnson proposed to accept payment by results for patients in whom at least one other treatment had failed — a policy that reduces the likelihood that the outcome measure would be confounded by other aspects of care. In such patients, the monoclonal protein level is an accepted measure of treatment response. Results-based pricing is most likely to be successful in other settings in which response can be defined with similar objectivity and reproducibility and among patients in whom other therapies have failed and whose condition is unlikely to improve if the compound is not used.

Any criterion used for payment should also be predictable, reliable, and difficult to manipulate. If a test result is highly variable or subjective, well-defined criteria and audits would be crucial to ensure that the measure worked as intended. For example, should a transient decrease in the monoclonal protein level be considered a response? Are multiple measures necessary? If there is room for judgment, how will disagreements over the interpretation of the performance criteria be adjudicated? If the performance measure is confounded by the underlying health of the patient, it could result in overpayments for healthier patients, creating incentives for focusing on lower-risk patients rather than on those most likely to benefit. Addressing this problem would require either a different price or different outcome measure for low-risk patients, either of which would complicate the approach.

Although Johnson & Johnson and NICE reached agreement on an indicator, they differ over the appropriate threshold for payment — whether an adequate response should be defined as a 50% or just a 25% reduction in the serum monoclonal protein level. In the United Kingdom, the cost-effectiveness standard will be determined by the NHS, not by competitive or other mechanisms.

Clearly, difficulties of implementation will limit the adoption of payment by results. Experience in overcoming the practical barriers, however, may well address both payer and industry concerns about pricing for potentially valuable drugs while increasing the number of patients who can receive effective treatments.

Dr. Garber is the associate director of the Center for Health Care Evaluation and a staff physician at the Veterans Affairs Palo Alto Health Care System — both in Palo Alto, CA; and a professor of medicine, economics, and health research and policy and director of the Center for Health Policy at Stanford University, Stanford, CA. Dr. McClellan is a senior fellow and director of the Engelberg Center for Health Care Reform at the Brookings Institution and a visiting scholar at the American Enterprise Institute — both in Washington, DC.


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