Satisfaction guaranteed — “payment by results” for biologic agents

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them to avoid such patients. Although this concern may be valid, the new rule only exacerbates an inherent side effect of prospective payment in the absence of perfect risk adjustment: to the extent that certain observable patient characteristics are associated with higher costs and are not accounted for in the payment formula, the DRG system already rewards hospitals for avoiding patients with these risk factors. On the other side of the issue, some stakeholders proposed substantial expansions of the list of nonreimbursable conditions, given the extent of injuries, the number of deaths, and the magnitude of the expense associated with patient-safety problems in hospitals; the approval of a much larger set of conditions would have ratcheted up the financial implications and made a more compelling case for more fundamental and comprehensive reform of inpatient care. In the end, however, CMS ruled out a number of candidate conditions, either because they could not be identified through existing DRG codes or because of a lack of proven strategies for preventing them.

In the same regulatory ruling, Medicare has also refined the DRG system to increase the extent of payment differentiation according to the severity of illness. Thus, along with emerging pay-for-performance initiatives, the new policy appears to be part of a larger reform of the Medicare payment scheme. The current reform rests on the following three principles: payers should pay more for the treatment of conditions that require more resources and that the provider could not reasonably have prevented; they should pay more when evidence-based or consensus-based best practices are followed; and they should pay less or not at all for low-quality care. Naturally, the last will be the most controversial.

The conditions for which Medicare will cease to pay hospitals as of next October have been shown to be within the control of hospitals, so there is a relatively compelling case that their costs should fall on the provider rather than the purchaser. It is unclear how Medicare will generalize the principle of refusal to pay for poor-quality care beyond this initial and largely symbolic effort. As inadequate as the store of evidence-based beneficial practices appears to advocates of pay for performance, there is even less empirical support or consensus for the identification of inappropriate or clearly contraindicated services and care patterns.

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Satisfaction Guaranteed — “Payment by Results” for Biologic Agents

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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

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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 simi-
lar amount, and it would not cre-
ate 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-effective-
ness ratios for different groups of
patients: as long as benefit is cap-
tured well by the response mea-
sure, cost-effectiveness can be cal-
culated the same way for everyone.
In effect, payment by results cre-
ates a personalized rather than a popula-
tion-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 sim-
ple 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 cor-
respond 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 treat-
ments. Survival, for example, is
perhaps the most important out-
come of treatment, but it is not
usually a practical measure, be-
cause it is heavily influenced by
underlying disease and by any
other treatments given and be-
cause the timeline for observing
changes in survival may be im-
practically long. The use of a sur-
rrogate measure, such as the mono-
clonal 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 oth-
er 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 mono-
clonal 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 com-
pound is not used.

Any criterion used for payment
should also be predictable, reli-
able, and difficult to manipulate.
If a test result is highly variable or
subjective, well-defined criteria
and audits would be crucial to en-
sure that the measure worked as
intended. For example, should a
transient decrease in the mono-
clonal protein level be considered
a response? Are multiple mea-
sures necessary? If there is room
for judgment, how will disagree-
ments over the interpretation of
the performance criteria be adju-
dicated? If the performance mea-
sure is confounded by the under-
lying health of the patient, it
could result in overpayments for
healthier patients, creating incen-
tives 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 out-
come criteria 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-effec-
tiveness standard will be deter-
dined by the NHS, not by com-
petitive or other mechanisms.

Clearly, difficulties of imple-
mentation will limit the adoption
of payment by results. Experience
in overcoming the practical barri-
ers, however, may well address
both payer and industry concerns
about pricing for potentially valu-
able drugs while increasing the
number of patients who can re-
ceive effective treatments.

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1. Institute of Medicine. Rewarding provider performance: aligning incentives in Medicare.
2. Devlin N, Parkin D. Does NICE have a cost-effectiveness threshold and what other factors influence its decisions? A binary
refractory myeloma. N Engl J Med 2003;348:
2609-17.
4. Richardson PG, Sonneveld P, Schuster
MW, et al. Bortezomib or high-dose dexa-
methasone for relapsed multiple myeloma.
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