

Assessing New Products in Diabetes: A Business Model in Support of Clinical Decision-Making

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Since 1990, more than 10 new drugs have been released for the treatment of diabetes, and there are currently 113 clinical trials on new treatment approaches listed with the Food and Drug Administration (FDA).¹ It is possible that the total number of new pharmaceutical products released between 1995 and 2005 will exceed the number of all pharmaceutical products released in the United States before then.

Trends in diabetes care suggest that drug treatments will often be used in combination.² Therefore, new products will be judged not only for their effectiveness when used alone, but also for their utility in combination with other therapies.

This makes the clinical decision-making process increasingly complex. It offers opportunities for better clinical results through more treatment options. However, it also expands the possibility of clinical error in treatment design or of sub-optimal treatment design from an economic and social standpoint. This brief review is intended to address the latter issues.

Social and economic issues may be important considerations in the process of selecting diabetes agents and designing diabetes treatment regimens. Such issues relate to factors that may influence patients' compliance with their treatment regimen. These include drug costs, dosing frequency, patient perceptions of the treatment, and difficulty of the treatment regimen.

Typically, these sorts of considerations are not included in clinical discussions of new therapies. For example, the

Table 1. Retail Costs of Commonly Used Drugs for the Treatment of Diabetes

Drug	Cost in Dollars/Month/30 tablets			
	Pharmacy 1	Pharmacy 2	Pharmacy 3	Pharmacy 4
Acarbose (Precose), 25 mg	23.97	21.95	20.72	23.29
Miglitol (Glyset), 25 mg	22.97	20.95	22.68	22.50
Pioglitazone (Actos), 30 mg	144.97	150.95	150.46	149.23
Rosiglitazone (Avandia), 8mg	144.97	150.95	144.62	149.39
Metformin (Glucophage), 500 mg	29.99	25.95	25.98	29.38
Metformin XR (Glucophage XR), 500 mg	26.97	25.95	23.98	26.70
Metformin-glyburide (Glucovance), 500/5 mg	29.29	28.95	26.92	30.49
Glipizide XL (Glucotrol), 10 mg	29.69	26.95	24.78	28.76
Glimiperide (Amaryl), 4 mg	30.97	28.95	27.84	30.33
Nateglinide (Starlix), 20 mg	35.97	34.95	32.78	35.80
Repaglinide (Prandin), 2 mg	31.97	29.95	29.72	40.00

Notes: Pharmacies surveyed included two major retail chains, an in-store pharmacy of a large, regional supermarket chain, and a local drug store. Prices/30 tablets/month should be recalculated for cost/month for usual recommended doses/day: for example, glimiperide is often given as one dose per day, so the monthly cost would be as shown; in contrast, nateglinide or repaglinide are recommended for three doses per day, so the monthly cost would be three times the amounts shown.

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latest Clinical Practice Recommendations from the American Diabetes Association³ do not include any description of such factors in their discussions of treatment guidelines. However, such factors can be relevant to the success of a treatment.

Social and Economic Issues in Drug Selection

The most important social or economic factor in drug selection is probably cost. As we noted in a previous issue of *Clinical Diabetes*,⁴ the monthly outlay patients may have to pay for treatment of their diabetes may represent a substantial portion of their total monthly income. Studies have shown that, in general, drug costs have a substantial impact on patient compliance when patients have to pay for prescription medications themselves.⁵ In addition, only one-third of physicians are knowledgeable about drug costs, and even those who are underestimate drug costs 40% of the time.⁵

Drug costs for diabetic patients are substantial (Table 1). This is especially true when patients are on combination therapies. In the absence of definitive head-to-head trials of the comparative efficacy of one drug to a similar drug in the same class, higher-cost drugs should not necessarily be considered more efficacious.⁶

A second important consideration in drug selection is dosing frequency. In general, drug regimens that require fewer doses per day are associated with higher rates of compliance.^{7,8} This holds true for diabetes.⁹ Moreover, when it comes to oral hypoglycemic agents, drugs requiring more frequent doses per day are not necessarily more effective than those requiring fewer doses per day.¹⁰

Patients' perceptions of treatments, as garnered from the media, may also influence compliance. Certainly this was seen with the use of troglitazone (Rezulin). As information in the lay press became negative, many providers experienced resistance from patients for

whom the drug was prescribed. Positive perceptions may also affect initial patient acceptance of therapy, as in the case of insulin pump therapy.¹¹

Overall, when these sorts of considerations are factored into the clinical decision-making process, they may alter therapeutic selections. Such influence was demonstrated in an excellent study by Schifferdecker et al.¹¹ on long-term therapy with insulin pumps. They demonstrated that only 79.6% of patients committed to insulin pump therapy remained on this therapy for more than 6 months, compared to 95% of patients on intensive insulin therapy with multiple injections of insulin. Complexity of use was identified as the most common cause of termination.

When the costs for initiation of pump therapy were factored into the overall costs for the 20.4% of patients who did not stay on pump therapy, the cost differential between pump therapy and multiple insulin injections rose. While not condemning pump therapy, the investigators recommended a more cautious, step-wise approach to initiating pump treatment.

A Model for Social and Economic Considerations in Assessing Diabetes Treatments

The information above suggests that providers may wish to employ additional considerations for evaluating new or existing diabetes treatments in addition to the traditional assessment of apparent

efficacy. Suggested additional considerations are summarized in Table 2.

The relative efficacy, and the relative cost compared to similar drugs are important considerations. For sulfonylureas, for example, the study by Noyes et al.⁶ demonstrates that two drugs in the class may have similar efficacy even though one costs less than the other. Differences in secondary failure rates between chlorpropramide and other sulfonylureas have been observed despite the fact that chlorpropramide costs less than the less-effective agents.¹²

Such differences are more convincing when they are shown in direct, head-to-head trials rather than inferred from data observed separately about one drug versus another. Differences that are not clearly related to or demonstrated to cause changes in clinical outcomes should be viewed with the most skepticism. For example, claims of differences in the hepatic metabolism of two drugs in the same class should be discounted unless they are clearly shown to cause a significant clinical effect.

Relative efficacy, then, should be considered in terms of relative pricing, both for drugs within the same class and for alternate forms of therapy. For example, sulfonylureas and sulfonylurea-like drugs may vary widely in average daily cost. The selection of the most expensive drugs in the class should be based on compelling evidence that those drugs offer clear clinical advantages over the less-expensive choices. Such clinical evidence is best shown in head-to-head trials. Because sulfonylureas and sulfonylurea-like drugs are often combined with metformin, the daily cost of the various combinations may also be considered. Drugs such as metformin-glyburide combinations may offer some relative cost advantages when considered in this way (Table 1).

Dosing frequency should also be considered. More complex oral therapies are associated with higher daily cost but may not be associated with clearly enhanced clinical efficacy. Until enhanced clinical efficacy is demonstrat-

Table 2. Suggested Considerations for Social and Economic Assessments of Diabetes Therapies

- Efficacy relative to similar drugs
- Cost relative to similar drugs
- Cost relative to other treatments
- Total cost of treatment if drug is often used as part of a combination of drugs
- Frequency of dosing
- Complexity of use
- Patients' perceptions of treatment

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ed, providers may wish to consider the existing evidence that more frequently dosed regimens have an adverse effect on patient compliance.

Finally, patient preference is important. These days, patients learn about therapy options in the lay press and on the Internet, and pharmaceutical companies advertise their products directly to patients through the mass media. If a physician opposes the preferences of the patient when there is no clear medical need to do so, there may be an adverse effect on outcomes.

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