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DESCRIPTIVE REPORT

Pharmacoeconomic Evaluations: Guidelines for Drug Purchasers

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OBJECTIVE:

To propose a set of guidelines for use by health care organizations in the United States that seek useful, comparative clinical information and economic analysis on pharmaceutical products to make sound drug purchasing decisions.

PRACTICE INNOVATION:

Based on a therapy intervention approach, the guidelines provide a structured framework to help managed care purchasers become more consistent in how they evaluate drug products for inclusion in the formulary. The guidelines factor in the need to examine the impact of new drug products on overall costs within the entire health system.

PRACTICE SETTING:

Intended for use by managed care organizations in the U.S. that purchase prescription drugs.

INTERVENTION:

Not applicable.

MAIN OUTCOME MEASURE:

Not applicable.

RESULTS:

The guidelines provide MCOs with a new systematic approach for identifying the overall cost and clinical outcomes impact of drug therapies. The guidelines are designed to take into account the characteristics of the patient population being treated and the fact that patients generally are redistributed among different treatment categories once a new drug product is introduced, thus offering MCOs an analysis model that extends beyond the traditional partial cost-outcomes approach. Emphasis is placed on looking at the cost-outcomes impact of a new drug or therapy within a systems or disease area framework in

which the redistribution of patients between therapy options is explicitly modelled. The guidelines specify that the following information elements be used in pharmacoeconomic analysis: product description, place in therapy, comparator products, therapy intervention framework, supporting clinical data, supporting pharmacoeconomic data, system impact assessments—costs—outcomes, overall assessment, and bibliography and supporting materials.

KEY WORDS:

Pharmacoeconomics, Managed care organizations, Pharmaceutical industry, New drugs, Formularies, Costs, Outcomes, Guidelines.

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Growing awareness of the need to evaluate pharmaceutical and other health care interventions in economic as well as clinical terms has led a number of drug purchasing agencies to recommend or, indeed, mandate that pharmaceutical manufacturers and other suppliers of health care products undertake pharmacoeconomic analyses to support the assessment and subsequent formulary listing or adoption of their products by health care systems.

For example, the Commonwealth Government of Australia, through the Department of Health, has mandated since January 1993 that all submissions to the Commonwealth for national formulary listing be supported by a pharmacoeconomic evaluation of the drug. The Australian *Guidelines* list a series of questions to which applicants

should respond and provides a framework for identifying and formatting the minimum necessary information to support an application for formulary listing and its subsequent assessment by a formulary review committee.¹ These information requirements are spelled out in even greater detail in the November 1995 revision of these *Guidelines*. Needless to say, the Australian guidelines have received considerable publicity and have proven to be a catalyst in the development of both guidelines and standards-related documents in countries such as Canada,² New Zealand,³ and the United Kingdom.⁴ However, none of the subsequent documents provides the same level of detail in specifying evidentiary requirements as the Australian *Guidelines*.

DEVELOPING GUIDELINES FOR THE UNITED STATES

Our purpose in this article is to propose a set of guidelines that U.S. health systems, as drug purchasers, can use to evaluate drug products for inclusion on the formulary.

While the terms “standards” and “guidelines” are often used interchangeably, there is an important distinction between them. The term “guidelines” is used typically to describe or proscribe evidentiary standards. Specifically, guidelines set the requirements or parameters for determining the type of pharmacoeconomic analysis that is needed or will be accepted in support of a formulary application. The information—driven in large part by the analytical requirements—that should accompany the analysis is usually also identified.

In the Australian *Guidelines*, for example, formulary submissions must meet strict evidentiary standards. These establish a clear hierarchy of data acceptability using evidence drawn from randomized clinical trials as the gold standard. Even though the modeling of drug interventions is recognized as legitimate by the Australian *Guidelines*, the data used and evidence presented must meet minimum standards to be considered.

Hence, the term “guidelines” can be interpreted in essentially evidentiary terms. The term “standards” refers to the techniques of analysis used to describe and assess cost–outcomes relations and the ways in which data can be assembled and presented for analysis. While there have been attempts to define “standards” of analysis, these are more appropriately seen as techniques accepted by practitioners in the area and used routinely in peer-reviewed and published papers.

Persons or organizations making submissions should be aware of the basic techniques of pharmacoeconomic and decision analysis and the extent to which there is a consensus in the use of these techniques. For example, the analyst should be aware of the need to separately identify units of resources from the application of the appropriate unit costs, use the appropriate surrogate of final outcome measure of therapy, consider alternative outcome measurement techniques, and use techniques such as discounting long-term therapy interventions and marginal or incremental assessments. A number of texts in this field provide a basic grounding in techniques of cost assessment and outcomes measurement.⁵

Ideally, guidelines should allow considerable latitude in the perspective to be adopted in the pharmacoeconomic analysis, the choice or type of economic analysis, data sources used, and the selection of alternative products in making comparative assessments. The standards to be applied in the analysis should be left to the discretion of the applicant. The issue of standards—and the extent to which there is agreement as to the appropriateness of particular methodologies or analytical techniques in pharmacoeconomic research—is important in what is seen as a rapidly evolving discipline. For example, awareness is growing that, from a purchaser's perspective, a health plan or system-wide frame of reference is essential. In adopting a system perspective—inevitable if a

purchaser is to take full account of the impact of adding or deleting a drug from the formulary—analysts are moving away from what can be described as the traditional approach to pharmacoeconomic assessments (i.e., simplistic drug A versus drug B comparisons) to an assessment of the overall costs and outcomes of a new therapy intervention. The proposed guidelines must permit this latitude as the field of pharmacoeconomics evolves.

Although considerable attention in the United States is being paid to the need for pharmacoeconomic analyses to support submissions to health care purchasers, guidelines to support formulary submissions are conspicuously absent. This position may seem paradoxical, given the release of the Pharmaceutical Research and Manufacturers of America (PhRMA) principles and the draft statement by the Food and Drug Administration's Division of Drug Marketing, Advertising and Promotion (DDMAQ) on substantiation of pharmacoeconomic claims.⁶ However, these documents are only a first step toward the formulation of more prescriptive statements of the informational and analytical needs of prospective drug purchasers—statements that need to be put in place if they are to support both the activities of pharmaceutical manufacturers and health care purchasers in assessing pharmaceutical and health care technology products.

While the guidelines presented in this article draw, inevitably, on those presently in place (or being developed) in other countries, principally Australia, Canada, and the United Kingdom, they differ in one important respect: the perspective taken is that of the individual health care system as a purchasing agency. In this context, the community- and economy-wide impacts of selecting and using alternative therapy options take second place. The focus is on the costs and outcomes of accepting or rejecting therapy options for the individual health care system. It is this system-perspective that dictates the form in which data should be presented, questions posed, and analytical techniques employed.

This is the first time guidelines for information assembly have been proposed for the U.S. market. However, these are not meant to be unduly prescriptive or static. Rather, they are intended to define what may be considered the current set of minimum information requirements necessary to support comprehensive assessments of both new and existing drugs within disease intervention or therapy areas. This is only the first version of these guidelines; no doubt, they will need regular updating as the informational and regulatory environment changes and new techniques for pharmacoeconomic assessment emerge.

PhRMA PRINCIPLES

The PhRMA principles (or industry code of practice) are not intended to be guidelines, but as a statement of principles to be followed in pharmacoeconomic studies. This industry initiative is used for both internal evaluation as part of strategic decisions on product development as well as applications

for reimbursement and formulary listing.

The PhRMA principles focus on five areas of pharmacoeconomic analysis: research design, reporting, report contents, data sources, and extrapolation of results. In the case of research design, the only principle proposed is that there be no restrictions placed on data sources. In the case of reporting results, the key principles are for a clear statement of study objectives and rationale for the outcome measure selected, together with a final report that describes assumptions, methods, and data sources. A total of 14 principles are identified for the content of pharmacoeconomic reports, all reflecting the traditional forms of pharmacoeconomic analysis: specification of study population, identification of alternative treatments, choice of relevant time horizons, statement of rationale for the analysis, and adopting standard approaches to the treatment of uncertainty.

For costs and resources to support therapy, authors need to identify the study perspective, recognize both average and marginal analyses, employ discounting when relevant, separate out resource units used from prices, and show how cost estimates are derived. The same principles apply in the case of outcomes. Data sources must be documented and their quality assessed. Finally, if necessary, extrapolation from one treatment environment to another, in terms of resource use and effectiveness, should be allowed.

Nothing in the PhRMA principles is inconsistent with the reporting structure proposed here. However, two key points should be made. First, the PhRMA principles are concerned with standards for analysis and reporting, not with the way in which assessments should be reported to prospective health care purchasers. Second—and more importantly—the PhRMA principles allow a range of analyses to be considered. These can range from the traditional drug A versus drug B to a systems approach based on a therapy intervention model framework. As explained below, it is this latter approach (or perspective) that underpins the guidelines we propose here.

ECONOMIC ANALYSIS OF PHARMACEUTICALS —

The ultimate objective of economic evaluations performed using our guidelines is to determine how introducing a particular drug product (or deleting it) from the formulary impacts the delivery of health care for a particular disease or therapy area. These effects can be considered both in terms of the impact of a particular therapy or treatment option on the costs to the entire health care system as well as the outcomes for the population being treated. These can be expressed in terms of clinical outcomes, measured health status, quality of life, and dollars saved.

Identifying the Proper Perspective

In taking a therapy or disease intervention approach, evaluations of formulary alternatives focus on the anticipated net or overall cost impacts for the health care system and the impact on the outcomes profile for patients treated within that disease or therapy area.⁷ Indirect cost impacts—while of po-

tential relevance—are generally secondary considerations for health care systems as drug purchasers.

In assessing the impact of introducing a new product to a formulary, a systems or global approach—described here as a therapy intervention or therapy modeling approach—is much needed. Once a therapy framework has been determined that identifies the relevant or principal treatment pathways, data are drawn from a variety of sources (together with assumptions and interpolations) to describe costs and outcomes (typically in probabilistic terms). While such an approach requires extensive and reliable data, it provides the framework within which existing formulary products and those proposed can be assessed. A therapy intervention approach identifies the following:

- ▲ Principal therapy interventions or options within disease or treatment areas

- ▲ Process of treatment within each intervention pathway

- ▲ Resources used to support each intervention pathway

- ▲ Outcomes of therapy in effectiveness—not efficacy—terms

For each pathway, these variables can be quantified: number and characteristics of patients, probabilities of achieving particular end-points of therapy, patterns of drug therapy, and costs of treatment. By expressing outcomes in probabilistic terms for each therapy pathway, the expected costs or treatment within disease areas can be estimated and related—in cost-effectiveness, cost-utility, or cost-benefit terms—to agreed end-points of interest to the health system.

Estimating Outcomes of Therapy

Once such a disease or therapy intervention framework for that health care system has been developed, system cost-outcomes relations can be specified. That is, it is possible—from retrospective medical and pharmaceutical claims data—to estimate therapy intervention costs using both the treatment pathway and the disease or intervention area as a whole, as well as the average cost and distribution of costs for patients who have been treated. These costs can be broken down by medical resource unit (drug costs, physician costs, laboratory costs, emergency room, and hospital costs) and the principal cost drivers identified.

While claims databases typically do not record outcomes of therapy (e.g., number of patients achieving a successful resolution of symptoms or stabilized within a given treatment timeframe), costs can be defined for predetermined treatment timeliness and supplementary patient surveys could be undertaken to identify the profile of therapy outcomes. In many cases, surveys are either too costly or not practical. What should be considered are attempts—as part of standard data-collection procedures—to develop outcome proxies. These might include, for particular interventions or disease states, reporting blood pressure level (in hypertension therapy), intraocular pressure (for glaucoma), cholesterol levels (for hypercholesterolemia), blood glucose levels (for diabetes), and peak flow rates (for asthma).

Defining an Equilibrium Change

The importance of prior identification of a disease or therapy intervention framework is that it forms the basis for evaluating the expected impact of either adding a new product or deleting an existing product from the formulary. Given estimates of the costs and outcomes associated with an existing or proposed therapy intervention, the impact of modifying a formulary listing can then be estimated. Such an impact assessment depends largely on projected patterns of drug substitution and the numbers of patients expected to switch therapy options.⁸ As patient-switching patterns take time to work themselves out, a plausible projection is needed for expected patterns of therapy switching and the resultant distribution of patients between therapy intervention areas. This impact assessment can be described in the language of the economist as a comparative static or equilibrium framework, in which a new equilibrium is achieved reflecting the new (or projected) distribution of patients between therapy or drug options in the disease area. The assessment of a new product—in cost and outcomes terms—is an exercise in contrasting an initial equilibrium in the distribution of patients by drug category with a projected equilibrium once patients have been reallocated between therapy options.

The assumption, all too often found in pharmacoeconomic analysis, that constant costs and outcomes obtain irrespective of the number or proportion of patients treated in a given population may not be appropriate in evaluating the impact of changing patterns of drug use. When a new drug is introduced to therapy, the patients not responsive to existing therapies are switched to the new therapy, affecting both average cost and outcomes relations. Average costs per outcome achieved may decline for existing therapies, which means that the new distribution of patients between drugs may result in quite different cost and outcomes profiles for each drug intervention within that therapy or disease area.⁹

To summarize this section, an overall assessment of the impact of adding a new product to existing therapy must, therefore, take a health plan or system perspective. The assessment should generate estimates of the overall impact of introducing the new product on the overall costs of therapy and the outcomes profile for patients treated in a disease area. Partial analyses (i.e., drug A versus drug B) that focus on comparing a new product with one presently on the formulary are unlikely to generate the necessary data for an overall assessment—unless it can be argued that product substitution is only expected to occur against a limited number, possibly only one, of the drugs presently on the formulary for that disease or treatment area and that constant costs and outcomes per patient treated obtain. Similarly, cost-outcomes assessments drawn from clinical or other small sample data sets are also likely to be misleading as a guide to overall system benefits. Again, it is up to the company or organization making the submission to make a case for using local or small sample (e.g., randomized clinical trial based) based cost-effectiveness, cost-utility, or cost-benefit ratios as predictors of overall sys-

tem impacts and the benefits from introducing new products, at the price sought, to the formulary.

TYPES AND USES OF AVAILABLE DATA

A final point concerns the role of clinical data in modeling therapy interventions and the relationship between resources used, costs, and therapy outcomes. Clinical data, while designed to generate estimates of therapeutic impact, are of limited use in assessing the real world, intention-to-treat impact of a drug in effectiveness terms. If clinical data are used to support a formulary application, the applicant must link clinical efficacy with therapeutic effectiveness. That is, factors such as comorbidities in the prospective treating population and potential lack of compliance in assessing cost-outcomes relationships should be considered.

This emphasis on effectiveness in modeling drug interventions does not mean that clinical data obtained from drug trials are not important in supporting a formulary application. Indeed, a key element in the proposed guidelines is the identification and summary of relevant clinical data with an overview of the therapeutic impact of the drug. Clearly, if a drug does not have an acceptable therapeutic impact (or one which is not statistically significant or clinically relevant at conventional decision levels), then any evaluation should question the basis of the submission unless a cost-minimization argument is being proposed. Clinical data may be describing the therapeutic impacts or outcomes of a drug against a placebo or other drugs presently on formulary. It is unlikely that clinical trial data will be available comparing most existing and prospective formulary alternatives, making necessary an assessment of likely impacts on outcomes profiles and modeling of the therapy interventions accordingly.

PREPARATION OF THE SUBMISSION

As in any marketing or promotional endeavor, the onus is on the supplier to convince the purchaser of the benefits of accepting a drug into a formulary. In the present case the presumption is that the proposal would be undertaken by the pharmaceutical company and that, while the prospective purchaser may provide data extracts from pharmacy and medical claim databases, the use of such data and the development of intervention models would be the responsibility of that company. This does not mean that the company should not, in the process of preparing the submission, confirm its choice (for example) or comparator products. But overall, the company is responsible for the form of the submission and the justification for formulary admission at the price sought.

PHARMACOECONOMIC SUBMISSION FORMAT

The following format and information requirements are proposed for pharmacoeconomic submissions to health plans as part of the formulary-approval process.

Part I: Product Description

A pharmacologic profile is needed of the product to be considered for formulary listing. This profile should include the following:

- ▲ Name, chemical composition, and therapeutic class
- ▲ Approved indications
- ▲ Principal pharmacologic action
- ▲ Course of treatment/regimen
- ▲ Any needed concomitant drugs
- ▲ Contraindications
- ▲ Adverse effects

Part II: Place in Therapy

The place of this product in therapy should be described as follows:

- ▲ Principal treatment options and practice patterns in the disease or therapy area
- ▲ Place of the proposed product in those treatment options
- ▲ Concomitantly prescribed drugs
- ▲ Brief pharmacological profile of principal drugs in disease or therapy area

Part III: Comparator Products

Principal comparator products (including those for which the proposed product is expected to be substituted) are then listed. In identifying the principal comparator products, information should be supplied about the following:

- ▲ Description and pharmacologic profile of comparator products
- ▲ Place of comparator products in therapy
- ▲ Concomitant drugs—if any
- ▲ Criteria for selecting comparator products
- ▲ Present distribution of comparator products (in unit and cost terms) within disease or therapy area
- ▲ Anticipated patterns of drug substitution of the new product for other comparator products

Part IV: Therapy Intervention Framework

Once the place of the proposed product in therapy has been identified, together with the principal comparator products, the framework for impact assessment—in terms of a therapy intervention model—should be detailed. Such a framework should define the following elements for the prospective health system as purchaser:

- ▲ Principal treatment options in that health system
- ▲ Processes of treatment
- ▲ Principal drug and medical resources consumed in therapy, by treatment pathway (retrospective analysis)
- ▲ Costs of resources consumed by treatment pathway
- ▲ Principal outcomes of therapy in clinical and health status terms (including utility measures and quality-adjusted life years)

Part V: Supporting Clinical Data

The anticipated clinical impact of the proposed product must be detailed. Clinical trial data are summarized, including

both pivotal clinical trials (to support safety and efficacy) and other trials considered important in identifying the place of the product in therapy (e.g., vis-a-vis comparator products). Key information requirements are the following:

- ▲ Justification of choice and applicability of clinical studies
- ▲ Summaries of clinical data (on a trial-by-trial basis)—location of trial, treating population, trial design and sample characteristics, comparators (including placebo), and outcomes

A clear statement of the statistical significance should be attached to the outcomes, particularly when a comparison involves the proposed therapy and those principal therapies for which it is expected to substitute in practice. If appropriate, a meta-analysis can be presented. The choice of study is to be justified by its relevance to the prospective population under treatment.

Part VI: Pharmacoeconomic Supporting Data

Any studies supporting or analyzing the impact of the proposed product in pharmacoeconomic terms should then be listed, described, and evaluated for the disease or therapy intervention area under consideration. The following should be included for each of the pharmacoeconomic studies cited:

- ▲ Justification for including the pharmacoeconomic study
- ▲ Description of the study and assessment framework
- ▲ Patient population to which the assessment relates
- ▲ Timeframe for the analysis
- ▲ Estimation of cost-outcomes relationships
- ▲ Relevance of the pharmacoeconomic study to the population under treatment

Part VII: System Impact Assessment-Costs

For the prospective purchasing organization, system impact costs for the proposed product should be assessed for the first three years of formulary listing or until the time at which a new equilibrium in the distribution of products has been established. To assess the cost impact, proposers must estimate and justify the rate of uptake of the new therapy, characteristics of the treating population (including comorbidities), patterns of substitution for other products, and resources used to support therapy. Cost estimates should include the cost of treating adverse events of therapy. The following are key information requirements (for agreed outcomes or end-points of therapy):

- ▲ Resources used to support therapy intervention before new product is introduced (by therapy intervention pathway, an agreed classification of drug and other direct medical inputs, and unit cost)
- ▲ Resources used to support therapy intervention after new product is introduced by therapy intervention pathway (by years 1 through 3 following product introduction)
- ▲ Net impact of new product on system resource use and costs (by comparator product—given assumptions as to patterns of drug substitution—for new product)

Table 1. Checklist for Formulary Submission

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- ▲ Has a comprehensive pharmacologic profile of the product been supplied?
 - ▲ Has the place of the product in therapy been described and justified for the managed care setting?
 - ▲ Has the proposal identified and justified the principal comparator product or products against which the proposed product is compared in the relevant managed care setting?
 - ▲ Has the proposal provided a pharmacologic profile and described the principal comparator products for the managed care setting?
 - ▲ Has the proposal identified, for the comparator products, those for which substitution is likely to occur and the timeframe and patterns of substitution in that managed care environment?
 - ▲ Has the proposal provided a comprehensive review of clinical data to support (1) the place of the proposed drug in therapy and (2) the clinical efficacy of the proposed product against the principal comparators identified?
 - ▲ Has the proposal described the outcomes of therapy considered relevant for the therapy intervention setting?
 - ▲ Has the proposal considered any constraints in an intention-to-treat environment that might modify, for the managed care setting, clinical outcome measures, and the assessment of the clinical impact of the proposed and comparator products in effectiveness terms?
 - ▲ Has the proposal opted for a particular type of pharmacoeconomic assessment?
 - ▲ Has the proposal justified the choice of type of pharmacoeconomic assessment?
 - ▲ Has the proposal detailed the structure of the pharmacoeconomic assessment, the characteristics of the treating population, and the time frame for the analysis in the managed care environment?
 - ▲ Has the proposal identified, for treatment and drug options, the resources used to support those interventions for the managed care environment?
 - ▲ Has the proposal costed resources used and generated (1) estimates of the cost of therapy interventions by treatment and drug options; (2) an estimate of the impact of introducing the new product on the costs of treatment for that managed care environment; and (3) an assessment of the impact of introducing the new product on the outcomes of therapy for that managed care environment?
 - ▲ How has the proposal related the overall net costs of therapy interventions in that disease area to the therapy outcomes profile for that managed care environment?
 - ▲ Has the proposal reviewed all possible outcome measures for this treatment area?
 - ▲ Has the proposal provided summary measures of cost–outcomes relations?
 - ▲ Has the proposal undertaken a sensitivity analysis of these cost–outcomes relations?
-

Part VIII: System Impact Assessment-Outcomes

The proposer must identify what are considered to be the appropriate outcomes of therapy for this intervention. These can be expressed as either intermediate or final outcomes. The outcomes must be expressed in effectiveness rather than efficacy terms and related to the anticipated treating population. Key informational requirements are the following:

- ▲ Choice and justification of outcomes
- ▲ Validity of measures used to generate outcomes
- ▲ Anticipated impact of new product (in net terms) on outcomes profile
- ▲ Justification of the assessment of impact of new product on outcomes profile
- ▲ Extent to which clinical trial results are expected to differ because of the treating environment and the characteristics of the prospective treating population (e.g., impact of comorbidities, compliance profiles)

Part IX: Costs and Outcomes—Overall Assessment

Finally, a statement is required of the estimated overall benefit for the treating population in the health care organization from bringing the product onto formulary. A number of techniques can be used in analyzing and summarizing cost–outcomes relationships, together with estimates of the robustness of these relationships. Key requirements are as follows:

- ▲ Concise description of application and analysis using the chosen therapy impact model
- ▲ Estimate of the overall costs of therapy interventions for the patient population treated
- ▲ Estimate of the overall impact of the new product on the final outcomes profile

- ▲ An evaluation of the robustness of the estimates to include the treatment of uncertainty (e.g., through a sensitivity analysis)

Part X: Bibliography and Supporting Materials

- ▲ Bibliography
- ▲ Modeling spreadsheets
- ▲ Copies of principal clinical and pharmacoeconomic papers

PHARMACOECONOMIC PROPOSAL CHECKLIST —

Table 1 describes a brief checklist that can be used for both companies submitting proposals to prospective drug purchasers as well as for those evaluating proposals. This is not the only checklist that can be developed, but it provides one basis for evaluating a proposal.

CONCLUSION —

In this paper, we propose guidelines for U.S. health systems to use in evaluating drug products for inclusion on the formulary. We have proposed a therapy intervention or systems approach under which drug manufacturers and suppliers are required to evaluate the net cost–outcomes impact on the disease or therapy area resulting from the introduction of that drug or health care product.

From a pharmacoeconomics perspective, these guidelines take a general, rather than partial approach to comparative evaluation. Rather than suggest the use of a narrow, clinically focused approach for evaluating cost–outcomes ratios, we propose using a system or equilibrium-to-equilibrium approach for evaluating drug impact. Such an approach—by taking into

account the shifting distribution of patients between different therapy options—assures that an appropriate cost-outcomes assessment is performed.

While this is more demanding in terms of both data and technical expertise than the traditional, partial approach, it is

more appropriate. Unless account is taken of the range of comparator products, anticipated patterns of drug substitution for the treating population, and their impact on the structure of costs and outcomes, any assessment of the impact of introducing a new drug remains incomplete. ■

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Editor's Note

The year 2020 marks the 25th anniversary of the *Journal of Managed Care & Specialty Pharmacy*. To commemorate this milestone, we are publishing a series of articles that document the changes to the journal and profession over the past 2 and a half decades. Each month we reprint an original article from a previous year, dating back to 1995. The reprinted articles feature topics of significance in our industry. Each reprinted article is accompanied by a contemporary reflection that will consider the historical significance of the topic, as well as the current and future state.

Laura E. Happe, PharmD, MPH
Editor-in-Chief