tive aspects of careers in the pharmaceutical industry.

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■ Shortcomings in Pharmacy Benefit Forecasting— Interferon Beta Products

Dear Editor,

I read with great interest the article by Meyer and colleagues in the March/April, 2003 issue of the *Journal*.¹ I am very concerned that the authors may not have used complete information and may have made inappropriate assumptions in their research. My concerns are as follows:

1. While the Evidence for Interferon Dose Effect: European-North American Comparative Efficacy (EVIDENCE) trial showed a 12% greater number of relapse-free patients for interferon beta-1a (Rebif—referred to as IB1a2 by the authors) versus Interferon beta-1a (Avonex—referred to as IB1a1 by the authors) at 24 weeks, the data showed a 1% greater number of relapse-free patients favoring IB1a1 at 48 weeks.² Inferring long-term clinical effectiveness, especially with a lifelong disease like multiple sclerosis, from short-term study findings can be fraught with difficulty.
2. No consideration is given by the authors to the costs of treating the increased number of side effects attributable to use of IB1a2 versus IB1a1 as demonstrated in the EVIDENCE trial.² These include higher frequency of occurrence of injection site disorders, liver abnormalities (including elevated ALT and AST), and white blood cell abnormalities (including leukopenia).
3. In estimating the incremental cost to a plan of adopting IB1a2, the authors deduct administrative costs related to managing multiple products on formulary. The assumption is that IB1a2 is adopted *in place of* other approved products, not *in addition to* these products. As such, the savings in question are attributable to the plan's decision to adopt an exclusive formulary, not to IB1a2 per se. Similar savings would accrue to the plan if exclusive status were awarded to IB1a1 or to *any other* approved product. The true incremental cost to a health plan of placing a new patient on IB1a2 versus other products in a nonexclusive formulary setting is therefore significantly higher than the \$.05 PMPM cited by the authors.
4. Incidence of neutralizing antibodies was much higher in IB1a2-treated versus IB1a1-treated subjects in EVIDENCE. In fact, at 48 weeks, 25% of IB1a2 patients had neutralizing antibody titers greater than or equal to 20 versus 2% of

IB1a1-treated patients.² While the clinical significance of antibodies has not been completely elucidated, many clinicians are now testing for neutralizing antibodies and discontinuing interferon beta therapy when the antibody titer increases to greater than 20.

5. IB1a1 is the only interferon beta product to have shown positive effects on brain atrophy³⁻⁵ and cognitive dysfunction⁶⁻⁸ in clinical trials. These findings may correlate to better long-term treatment success.
6. The claim in the article that assumes 80% of newly diagnosed multiple sclerosis patients would utilize IB1a2 appears to have no basis in fact. Market share in this category has not changed appreciably since IB1a2's entry. Due to mounting concern over neutralizing antibodies, it is highly doubtful that its market share will attain the projections reported by the authors.

In conclusion, pharmacoeconomic modeling is based upon certain assumptions, and the pharmacy-budget impact analysis in the article by Drs. Meyer, Phipps, Cooper, and Wright did not properly represent the known clinical evidence for the treatment of multiple sclerosis or common practices used in drug benefit administration.

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The Authors Respond

Dear Editor,

We appreciate Dr. Rich's careful review of our manuscript, which appeared in the March/April 2003 issue of *JMCP*.¹

As we clearly outlined in the introduction, our objective was to suggest a method for using administrative claims to evaluate potential direct population costs of pipeline therapies prior to the availability of full cost-effectiveness analyses. This analysis was undertaken before the launch of the product in order to provide preliminary information to those with direct responsibility for the pharmacy budget alone. The study was published after the drug was approved.

The majority of Dr. Rich's points (points 1, 2, 4, and 5) focus on costs related to clinical outcomes, side effects, and patient functioning that would be included in a full cost-effectiveness or budget impact analyses. These types of analyses are critically important to evaluate the true value of therapies, but formulary dossiers containing the information may not be available until after the drug is marketed.² However, payers frequently require customized proactive information prior to marketing to anticipate potential blockbuster drugs and possible cost-containment strategies. The proposed claims analysis is an attempt to bridge that early information gap.

When more information becomes available through detailed cost-effectiveness and completed phase III and IV studies, the true budget impact on both the pharmacy and medical budgets would indeed take precedent over preliminary assessments. For instance, the 63-week extension of the EVIDENCE study demonstrated a 17% reduction in relapse rates for 44 µg tiw interferon beta-1a (Rebif-IB1a2) compared to 36 µg cw interferon beta-1a (Avonex-IB1a1), indicating a sustained impact on relapse over time.³ With regard to side-effect management, a statistically significant higher rate of flu-like symptoms were also reported in the IB1a1 group (53.4%) compared to the IB1a2 group (44.8%).³ Information from the trial shows that neutralizing antibodies are not related to clinical impact on relapse rates; therefore, the influence of neutralizing antibodies is still unclear.³

We did include administrative costs of prior authorization related to costs that plans may incur by implementing a prior-authorization program (point 3). We assumed in the base analysis that the new product would compete with existing therapies and IB1a2 would be used in place of other similar products. The model is flexible to incorporate a variety of scenarios, but we chose a share-shift analysis approach in the base case where there was some decline from the other products.

The 80% share estimate in new users was indeed aggressively set forth by the manufacturer (point 6). We specifically performed sensitivity analysis around this estimate as presented

in the manuscript. However, a reduced market-share estimate would only reduce the anticipated impact of interferon beta-1b.

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■ Patient-Reported Utilization Patterns of Narcotic Drugs

Dear Editor,

I read the article on the above subject in the May/June 2003 issue of *JMCP*¹ with interest. A perhaps far more interesting topic could be explored by the authors: the topic of "the rest of the story," when patients choose to take themselves off of such medications. In the treatment of chronic nonmalignant pain, it is important to recognize that this category is a hodge-podge. We cannot assume that there is only one situation or pathophysiology involved. So, any commentary on the "group" needs to recognize that there will be variation in applicability.

However, with that said, it is fascinating to observe the patients with "chronic nonmalignant pain" who become fed up with taking all the pills (or patches) and simply take themselves off. They may go from high doses of very expensive medications to use of nothing more than ibuprofen. Yet, this may occur with no observable change in the underlying condition. The only thing that changes is their desires. This is a very, very revealing outcome when it happens.

Perhaps these authors would care to look at "the rest of the story." They must certainly have some patients who eventually go off of all the narcotics. When this happens, what leads to the outcome? What evidence exists that underlying pathology changed? Or is the change simply one of choice? If so, what do we learn from this?

Obviously, there are many countries in the world that do not