

## Tegaserod Treatment for IBS: A Model of Indirect Costs

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### Abstract

Irritable bowel syndrome (IBS) has been associated with substantial time lost from work (absenteeism) and reduced productivity at work (presenteeism), which are the indirect costs of illness. This article presents a productivity model demonstrating the indirect costs associated with IBS and the reduction in those costs for a cohort of female employees hypothetically treated with tegaserod, a new selective serotonin (5-hydroxytryptamine [5-HT]) type 4 (5-HT<sub>4</sub>) receptor agonist, which is approved by the US Food and Drug Administration for treating women with IBS-C. The model is based on economic and epidemiologic published literature and clinical trial results. In this model, tegaserod treatment resulted in \$1882 in avoided lost productivity per treated female employee. Considering only the benefits of decreased work loss and the costs of medical therapy, the model predicts a benefit/cost ratio of 3.75 in the base case. From an employer's perspective, medical therapy for IBS with tegaserod is cost-effective under a series of assumptions for the treatment of women with IBS with constipation.

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Estimates indicate that 75% of patients with irritable bowel syndrome (IBS) are between 25 and 64 years of age<sup>1</sup>; thus, most patients with IBS are of working age. IBS can have a negative impact on a patient's quality of life.<sup>2-4</sup> In addition, it imposes a substantial economic burden on patients and the rest of society.<sup>1,5</sup> The direct annual cost of IBS in the United States is estimated to be between \$1.7 billion and \$10 billion, excluding the cost of prescription and over-the-counter drugs.<sup>1,5</sup> In addition to direct costs, IBS has been associated with substantial indirect costs resulting from time lost from work (absenteeism) and reduced productivity at work (presenteeism), costs that are borne largely by the employer. In fact, indirect costs—estimated to be as high as \$20 bil-

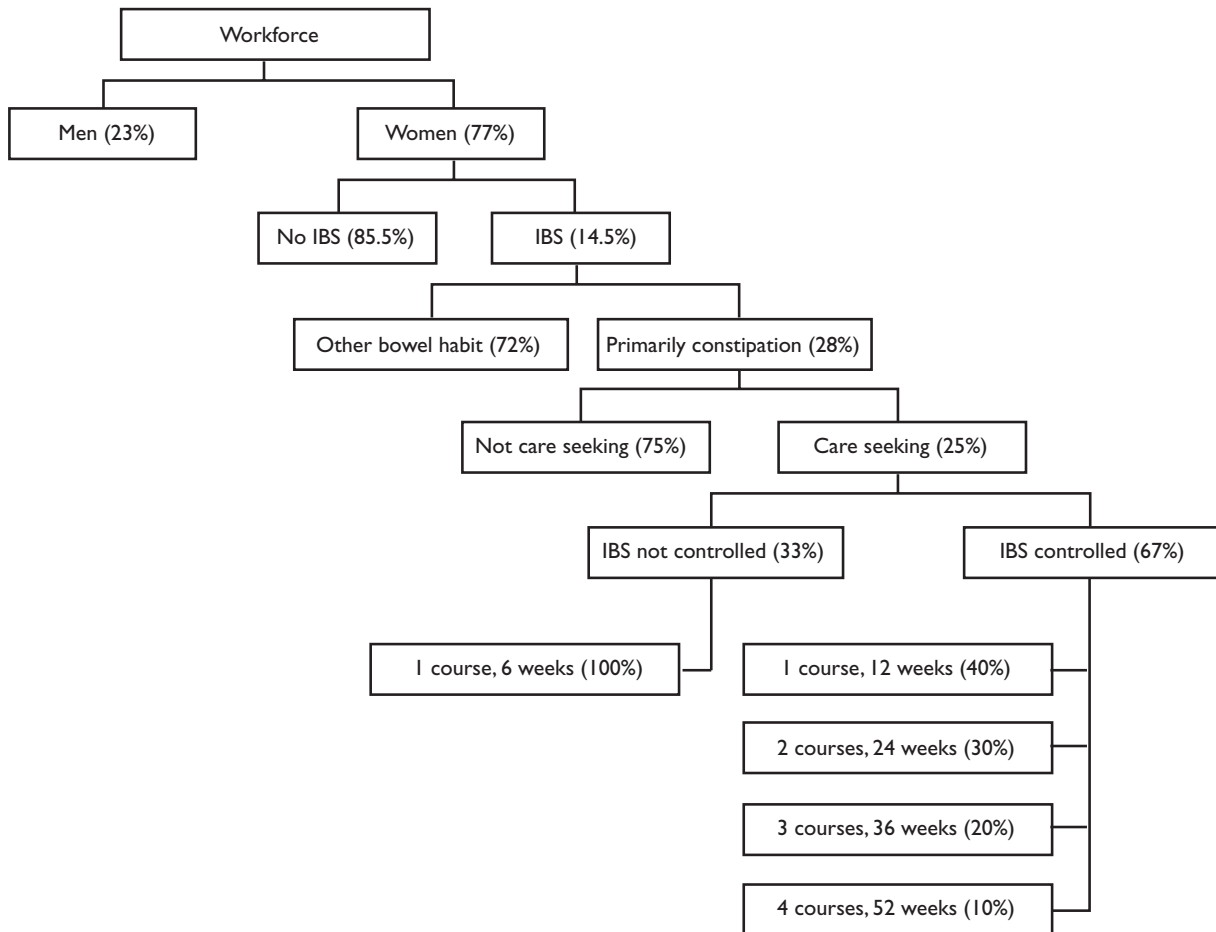
lion<sup>1</sup>—may account for the largest proportion of the total IBS economic burden.<sup>5</sup>

Patients with IBS are typically categorized into subtypes based on bowel dysfunction. The categories are IBS with constipation (IBS-C), IBS with diarrhea (IBS-D), and IBS that alternates between constipation and diarrhea (IBS-A),<sup>6</sup> which is also known as mixed-bowel IBS. Until recently, IBS treatment options consisted of single agents (ie, antispasmodics, fiber, laxatives, antidiarrheals, antidepressants) for specific individual symptoms (ie, abdominal pain, constipation, diarrhea) or various combinations of therapies aimed at alleviating multiple symptoms in individual patients. However, 2 agents are now available in the United States that address multiple IBS symptoms.

Since its reintroduction in 2002 under restricted conditions for use (after having been withdrawn in 2000), alosetron, a serotonin (5-hydroxytryptamine [5-HT]) type 3 (5-HT<sub>3</sub>) receptor antagonist, has been indicated for use in women with severe IBS-D that has not responded to conventional therapy. Tegaserod, a 5-HT<sub>4</sub> receptor agonist, has been indicated for use in women with IBS-C in the United States since 2002 and has recently been approved for men and women <65 years of age with chronic idiopathic constipation. In fact, tegaserod and alosetron were the only 2 agents to receive grade A recommendations from the American College of Gastroenterology Functional Gastrointestinal Disorder Task Force based on the high quality of published evidence supporting their global efficacy in IBS-C and IBS-D, respectively.<sup>6</sup>

This article presents an economic model of the indirect costs associated with IBS and the treatment of IBS with tegaserod. The

**Figure.** Diagram of the Productivity Model



IBS indicates irritable bowel syndrome.

purpose of the model is 2-fold: to demonstrate the impact that indirect costs associated with all IBS subtypes have on employers and to illustrate the potential costs and savings, in terms of indirect costs, associated with intervention for the treatment of patients with IBS-C using tegaserod as an example of cost-saving therapy. The workforce receiving the hypothetical treatment is that of Comerica Incorporated, a nationwide bank that offers personal, small business, and corporate banking services and that has major branches in Michigan, California, Texas, and Florida.

**Methods**

Data were obtained from a survey of the workforce at Comerica,<sup>7</sup> from literature on the epidemiology and treatment of IBS, and

from tegaserod clinical trial results. The model consists of several parameters that are specific for an employer and can be changed to customize the model results. Values based on the Comerica workforce are used as default values where possible in the model. The model can be used to analyze the indirect costs associated with IBS and the effect of treatment on these costs.

**The Model**

A representation of the workforce using demographics such as subpopulation sizes, sex, salaries, employment status (full-time vs part-time), illness (prevalence of IBS, incidence of IBS subtypes), and treatment (efficacy, costs) was constructed (**Figure**). Information on age and sex is based on data from the Comerica survey,<sup>7</sup> and default val-

ues for salary are based on data from the Bureau of Labor Statistics.<sup>8</sup> The proportions of male and female patients with IBS (default values of 7.7% [men] and 14.5% [women]) are based on data from the US Householder Survey.<sup>9</sup> The proportion of women with IBS-C (default value of 28%) is based on the literature.<sup>7</sup> The proportion of patients with IBS who seek medical care (default value of 25%) was also based on the literature.<sup>10</sup> A sample scenario was created in which women with IBS-C seeking medical attention were prescribed tegaserod. Sixty-seven percent of the women were assumed to have symptom control based on the highest efficacy value reported in the US tegaserod clinical trials,<sup>11</sup> which, in turn, affects the number of courses of treatment, from 6 weeks to 54 weeks as described in the "Treatment" section.

### Model Workforce

The workforce at Comerica has been examined for IBS prevalence and costs.<sup>7</sup> The workforce is composed of 11 806 employees aged 18 to 64 years; 90% are employed full-time, and 10% are employed part-time.<sup>7</sup> Although the age distribution of this workforce is typical, the percentage of women (77%) is greater than the norm (47%).<sup>8</sup> Wages for persons in this workforce were distributed by age and sex, according to the average distribution reported by the US Department of Labor, Bureau of Labor Statistics, and averaged \$19.82 per hour.<sup>8</sup>

### Epidemiologic Data Sources

The baseline percentage of persons with IBS was based on data from the US Householder Survey,<sup>9</sup> which surveyed a random sample of 8250 households in the National Family Opinion, Inc database. This survey was chosen because it provides data on IBS by age and sex.<sup>9</sup>

Percentages of patients with constipation (28%) and diarrhea (34%) as their primary altered bowel habit were based on the results of the Comerica survey.<sup>7</sup> Results of this survey are similar to those from studies in the published literature that report that the 3 IBS subtypes occur with approximately equal frequency.<sup>12,13</sup>

The percentage of patients with IBS seeking medical care (25%) was based on evi-

dence from the published literature.<sup>11</sup> This rate represents a conservative estimate of healthcare-seeking behavior. Other studies in US populations have found healthcare-seeking rates as high as 45%.<sup>9,14</sup>

### Productivity

The impact of symptoms and adverse effects from treatment on worker productivity has been documented for many well-known long-term conditions,<sup>15</sup> including diabetes,<sup>16,17</sup> asthma,<sup>18</sup> and migraine,<sup>19</sup> and for acute conditions, such as influenza.<sup>20</sup> One commonly used measure of productivity loss is the Work Productivity and Activity Impairment (WPAI) questionnaire. The WPAI is a productivity-based questionnaire that was developed as a general health measure, and it has been modified and validated for specific health conditions, including IBS.<sup>21</sup> It is designed to measure work impairment from absenteeism (time absent from work) and presenteeism (reduced productivity at work) and measure daily activity impairment, such as housework, shopping, childcare, and exercising, in the past 7 days.<sup>21</sup> WPAI outcomes are expressed as impairment percentages, with higher numbers indicating greater impairment and less productivity.

Default values for absenteeism per employee with IBS (1.7%) and presenteeism per employee with IBS (21.1%) were based on results from the Comerica survey.<sup>7</sup> Total lost productivity per employee with IBS (work productivity score [WPS]), which enumerates the reduced productivity attributed to IBS as a percentage of the potential total work productivity, was 21.1%, which is equivalent to working approximately 4 days of a 5-day work week) is also based on results of the Comerica survey.<sup>7</sup> WPS is defined as [(Hours absent from work + percentage of reduced productivity at work × hours actually worked)/(hours missed because of ill health + hours worked)] × 100.

With a 5-day week for 50 weeks per year, a WPS of 21.1% translates into a total annual loss of 50 days because of IBS per employee. Because the model uses the average absenteeism and presenteeism values from all employees included in the survey to calculate the WPS rather than from individual

employees (Comerica), an adjustment factor was applied to ensure that the model reflects the WPS for the Comerica workforce published in the literature.

### Treatment

Medications are prescribed for most (89%) patients with IBS.<sup>22</sup> This model enables an employer to calculate the costs and savings associated with a treatment option of their choice for a specific subpopulation of employees with IBS. The example used in this article is women with IBS-C who sought medical care and were treated with tegaserod, which is approved for this patient population.

The base value used in the model for the percentage of patients with satisfactory relief of IBS symptoms was 67%, which was based on the highest efficacy reported in the US tegaserod clinical trials.<sup>11</sup> A range of values from 37% (the lowest efficacy value reported in the tegaserod clinical trials)<sup>23</sup> to 67% are examined in the sensitivity analyses.

One assumption imposed to determine the treatment effect was that treatment with tegaserod permits 36% of lost productivity to be regained.<sup>24</sup> A second assumption related to the extent of treatment (the annual number of IBS symptom episodes that patients experience and the annual number of prescriptions for tegaserod written per year). US Food and Drug Administration–approved prescribing instructions, consistent with supporting clinical trials, recommend a dosage of 6 mg twice daily for 4 to 6 weeks with an additional 4- to 6-week course as needed if the patient responds to therapy.<sup>23,25</sup> Relief generally occurs within the first week of treatment for patients who respond, but symptoms may return after treatment has been stopped.<sup>11</sup> Relief of the symptoms of IBS occurs in 67% of patients; hence, 33% of patients may end therapy after the first prescription. It is not known how many patients who respond to therapy require treatment beyond the refill amount. Trials have shown that tegaserod is safe in patients receiving a 12-month course of therapy.<sup>26</sup>

### Outcome Measures

The outcomes of interest in this model are the treatment costs and success rates of therapy as measured by reductions in lost

productivity and costs to employers. Because treatment and productivity measures occur within the year, dollars are not discounted. For the purpose of this analysis, it was assumed the employer was self-insured or was experience-rated (ie, premiums are adjusted according to the number and size of claims made against the employer in previous years) for healthcare costs and thus bore the burden of the drug costs. Because treatment was only provided to patients who sought care, the incremental cost was solely that of the prescription cost. Costs associated with physician office visits and diagnostic testing were not considered in the model.

The cost to the employer of tegaserod 6 mg twice daily was assumed to be the wholesaler acquisition cost of \$4.30 per day.<sup>27</sup> Determining the cost more precisely would require information regarding the particular prescription drug benefit design offered by the employer directly or as part of a more comprehensive health plan. However, for the purposes of the model, assumptions were made based on common features of drug benefit designs, such as day supply limit per prescription (base case, 30 days) and patient cost sharing (base case, copayment per prescription). The model is easily varied with respect to day limits, mail order discounts, and copayment or coinsurance rates.

### Sensitivity Analyses

To determine whether the base values chosen for the model had a significant impact on findings, a series of sensitivity analyses was performed in which the effects of changing the value of the relevant assumptions were tested. Key assumptions tested were wage rates, absenteeism and presenteeism rates, medication price, efficacy of tegaserod, and productivity losses avoided because of successful treatment.

### Results

**Burden of IBS.** According to the base case scenario, the total cost of lost productivity attributed to IBS for the employer is \$12 508 421 per year, which was calculated by adding the cost of productivity loss by female employees with that lost by male

employees. For each sex, WPS (21.1%) was multiplied by an average working year in hours (2000 hours), average hourly compensation (\$18.52 for women, \$24.47 for men), firm workforce (11 800), sex distribution (78% women, 22% men), and IBS prevalence rate (14.5% for women, 7.7% for men).

When the number of weeks of therapy is taken into account, the average net cost per prescription to the employer per patient is \$119, and the average annual cost of treatment to the employer per patient is \$502. Each 30-day prescription entails a \$10 copay. Thus, a 1-month supply of tegaserod costs \$119 ( $\$4.30/\text{day} \times 30 \text{ days} - \$10 \text{ copay} = \$119$ ). At the start of treatment, all patients received 6 weeks of therapy, but only those with successful results continued. It is estimated that a decreasing percentage of patients obtained refills at each 12-week period. Thus, a year of treatment costs \$502 ( $\$4.30/\text{day} \times 7 \text{ days} \times [100\% \times 6 \text{ weeks} + 40\% \times 12 \text{ weeks} + 30\% \times 24 \text{ weeks} + 20\% \times 36 \text{ weeks} + 10\% \times 52 \text{ weeks}] - \$10 \text{ copay}$  each 30-day period).

#### **Benefits from Tegaserod Intervention.**

Tegaserod treatment in the base case scenario results in an annual savings of \$1882 in avoided lost productivity per treated female employee. At a cost of \$2.15 per dose ( $\$4.30$  per day for twice-daily dosing), the total costs of treatment are \$502 per year, resulting in a net savings cost to the employer of \$1381. Therefore, the benefit/cost ratio for the base case is 3.75 (\$1882 divided by \$502), indicating that the cost of treatment is offset by productivity regained nearly 4-fold (Table).

**Sensitivity Analyses.** This model is flexible. Inputs can be varied to meet the specific needs of individual employers. A number of model inputs affect the total amount of benefits and costs but not the results per patient. For example, per patient results do not change when the user alters the values for firm workforce size; sex distribution; proportion of employees with IBS; proportion of persons with IBS whose primary bowel habit is constipation, diarrhea, or alternating constipation and diarrhea; or the proportion of persons diagnosed with IBS who seek healthcare.

However, several model inputs do result in meaningful changes (ie, cost per patient) to benefits, costs, or both. For example, net savings are directly correlated with wage rates; lower wage rates result in lower net savings, whereas higher wage rates result in higher net savings. At an hourly wage rate of half the base case (\$10 per full-time female employee and \$5 per part-time female employee), the benefit/cost ratio is 1.92. Importantly, even though this ratio represents only half the ratio of the base case scenario, it still results in net savings to the employer. Adjusting medication price, medication supply limit per day, patient copayment per prescription, and patient coinsurance rate per prescription produces similar results. For example, doubling the medication price still leaves the benefit/cost ratio at 1.78. Additionally, reducing the rate of presenteeism (impairment while at work), which is the key to productivity lost because of IBS, from 20% to 10%, along with a 0% rate of absenteeism (reduced from 1.7% in the base case), leaves the benefit/cost ratio at 1.62.

One parameter that is obviously important to the benefit/cost ratio is the percentage of IBS patients who respond to tegaserod therapy. If the most conservative estimate of tegaserod efficacy (37%)<sup>23</sup> is used, the benefit/cost ratio is 2.98. Reducing effectiveness further to a net effectiveness (treatment effect less placebo effect) of 18% yields a benefit/cost ratio of 1.49. Although the benefits are substantially reduced when medication efficacy is decreased, medication costs are also reduced—that is, with a lower treatment effect, fewer patients are prescribed medication after the first 6- or 12-week supply. In addition, the benefit/cost ratio is also affected by the percentage of lost productivity

**Table.** Benefits and Costs of Treatment

	Per treated patient
Benefits: avoided annual lost productivity	\$1882
Costs: average annual cost of medication	\$502
Net savings (cost) to employer	\$1381
Benefit/cost ratio	3.75



regained because of symptom alleviation with tegaserod therapy. In the base case, a 36% regain rate in lost productivity was assumed<sup>25</sup>; however, if the actual rate for a given employer is only 25%, for example, the cost/benefit ratio will be similarly reduced (to 2.60).

Finally, in a worst case scenario that considers the combination of values in percent of time absent (0%), percent of time impaired (10%), satisfactory relief of IBS (37%), and productivity losses avoided (25%), costs (\$349) outweigh benefits (\$313), resulting in a benefit/cost ratio of 0.90. Thus, in this case, it is possible that employers would not realize savings from the inclusion of tegaserod in their formularies.

### Discussion

This IBS productivity economic model features a number of factors that distinguish it among other models of productivity. It is the first model on productivity to explicitly incorporate absenteeism and presenteeism as the components of indirect costs; most models just include absenteeism. Although it is true that presenteeism data are not often available, they are critical to the usefulness of this model because of the substantial role that presenteeism plays in productivity lost because of IBS.

This model takes advantage of the Worker Productivity Index (WPI), a tool that measures presenteeism (the actual decrease in productivity of employees while they are on the job), absenteeism, and disability. Using this tool in a study of 1039 employees of First Card, one of the largest credit card issuing companies in the United States, Burton and colleagues found that employees with digestive disorders had the lowest WPI rating compared with employees with mental health disorders, respiratory disorders, injuries, musculoskeletal disorders, and cancer, indicating that productivity loss from presenteeism is highest among employees with digestive disorders.<sup>16</sup> These results suggest that the absenteeism/presenteeism ratios reported in the previously mentioned studies may be low. The numbers used in the base case scenario in this model, therefore, may represent conservative estimates

of absenteeism/presenteeism attributed to IBS.

In addition, this model incorporates data from recent trials on the efficacy of a novel medication for the treatment of patients with IBS-C. Tegaserod has proven efficacy in providing global relief from the multiple symptoms of IBS in women with IBS-C and, more recently, from the multiple symptoms of chronic (idiopathic) constipation in men and women younger than 65 years of age. Although the total number of days lost per year per employee, calculated when the Comerica workforce data (50 days per year per employee) is applied to this model, may seem higher than that reported by other studies examining productivity lost, it is important to remember that this model includes days lost to absenteeism and presenteeism, whereas many studies evaluate absenteeism alone. For example, the US Householder Study found that patients with IBS (n = 629) were absent from work an average of 13.4 days per year compared with 4.9 days reported by persons not experiencing any functional gastrointestinal disorder.<sup>9</sup> Moreover, in a survey of 318 patients with IBS in the United States who had been medically diagnosed with IBS or who met diagnostic criteria, the average number of days affected by ill health leading to absenteeism was 6.4 compared with 3.0 days for persons without IBS.<sup>28</sup> However, a survey of 287 US members of the International Foundation for Functional Gastrointestinal Disorders<sup>29</sup> found that of the 30% of patients who reported missing some days of work because of their IBS symptoms, the average number of days absent from work (1.7 days in the 4-week period before the survey) translates into 22.1 days missed per patient per year, which, when added to the 39 days of reduced productivity reported by 46% of respondents (for a total of 61.1 days), actually exceeds the total number used in this model.

Other assumptions imposed on treatment outcomes merit review and verification in future studies. For example, data are sparse when it comes to verifying the assumption that symptom relief leads to 36% of lost pro-

ductivity regained.<sup>24</sup> Moreover, the model assumed full relief rather than incremental relief, which may or may not be appropriate. Full relief was used because of the high placebo response reported for IBS therapies, but incremental relief may be appropriate in some patients.

Finally, in this model, an assumption was made regarding the percentages of patients receiving multiple courses of treatment and the days they received them throughout the year. However, these percentages may not represent the correct distribution of days throughout the year and warrant further investigation.

### Conclusion

This model demonstrates that tegaserod is a cost-effective treatment for female employees with IBS-C. The costs of treating these employees with tegaserod are compensated fully by the regained productivity previously lost because of IBS symptoms. Although cost-effective services are common, actual cost-saving therapies are not.

In the base case scenario in this model, tegaserod saved the employer \$1381 per employee per year, for a benefit/cost ratio of 3.75. Even when changes are made to a variety of parameters (eg, reduction in hourly wage, increase in medication costs, reduction in productivity losses avoided), the sensitivity analysis shows cost savings/offsets or no additional costs to the employer. Therefore, covering tegaserod treatment is a cost-effective way for employers to reduce productivity losses from IBS among their female employees.

### REFERENCES

- American Gastroenterological Association.** *The Burden of Gastrointestinal Diseases.* Bethesda, Md: American Gastroenterological Association; 2001:1-86. Available at: <http://www.gastro.org/clinicalRes/pdf/burden-report.pdf>. Accessed November 16, 2004.
- Frank L, Kleinman L, Rentz A, Ciesla G, Kim JJ, Zacker C.** Health-related quality of life associated with irritable bowel syndrome: comparison with other chronic diseases. *Clin Ther.* 2002;24:675-689.
- Gralnek IM, Hays RD, Kilbourne A, Naliboff B, Mayer EA.** The impact of irritable bowel syndrome on health-related quality of life. *Gastroenterology.* 2000; 119:654-660.
- Koloski NA, Talley NJ, Boyce PM.** The impact of functional gastrointestinal disorders on quality of life. *Am J Gastroenterol.* 2000;95:67-71.
- Martin R, Barron JJ, Zacker C.** Irritable bowel syndrome: toward a cost-effective management approach. *Am J Manag Care.* 2001;7(suppl):S268-S275.
- Brandt LJ, Bjorkman D, Fennerty MB, et al.** Systematic review on the management of irritable bowel syndrome in North America. *Am J Gastroenterol.* 2002;97(suppl):S17-S26.
- Dean BB, Aguilar D, Barghout V, et al.** Impairment in work productivity and health-related quality of life in patients with irritable bowel syndrome. *Am J Manag Care.* 2005;11(suppl):S17-S26.
- US Department of Labor, Bureau of Labor Statistics.** Median weekly earnings of full-time wage and salary workers by union affiliation and selected characteristics. Available at: <http://www.bls.gov/cps/cpsaat41.pdf>. Accessed February 5, 2004.
- Drossman DA, Li Z, Andruzzi E, et al.** US household survey of functional gastrointestinal disorders: prevalence, sociodemography, and health impact. *Dig Dis Sci.* 1993;38:1569-1580.
- Drossman DA, Thompson WG.** The irritable bowel syndrome: review and a graduated multicomponent treatment approach. *Ann Intern Med.* 1992;116:1009-1016.
- Novick J, Miner P, Krause R, et al.** A randomized, double-blind, placebo-controlled trial of tegaserod in female patients suffering from irritable bowel syndrome with constipation. *Aliment Pharmacol Ther.* 2002;16: 1877-1888.
- Ringel Y, Drossman DA.** Toward a positive and comprehensive diagnosis of irritable bowel syndrome. *Medscape Gastroenterol.* 2000;2:1-10.
- Mayer EA.** Emerging disease model for functional gastrointestinal disorders. *Am J Med.* 1999;107(suppl):2S-19S.
- Talley NJ, Zinsmeister AR, Van Dyke C, Melton LJ 3rd.** Epidemiology of colonic symptoms and the irritable bowel syndrome. *Gastroenterology.* 1991;101:927-934.
- Druss BG, Marcus SC, Olsson M, Tanielian T, Elinson L, Pincus HA.** Comparing the national economic burden of five chronic conditions. *Health Aff (Millwood).* 2001;20:233-241.
- Burton WN, Conti DJ, Chen CY, Schultz AB, Edgington DW.** The role of health risk factors and disease on worker productivity. *J Occup Environ Med.* 1999;41:863-877.
- American Diabetes Association.** Economic consequences of diabetes mellitus in the US in 1997. *Diabetes Care.* 1998;21:296-309.
- Birnbaum HG, Berger WE, Greenberg PE, et al.** Direct and indirect costs of asthma to an employer. *J Allergy Clin Immunol.* 2002;109:264-270.
- Hu XH, Markson LE, Lipton RB, Stewart WF, Berger ML.** Burden of migraine in the United States: disability and economic costs. *Arch Intern Med.* 1999;159:813-818.
- Akazawa M, Sindelar JL, Paltiel AD.** Economic costs of influenza-related work absenteeism. *Value Health.* 2003;6:107-115.
- Reilly MC, Bracco A, Ricci JF, Santoro J, Stevens T.** The validity and accuracy of the Work Productivity and Activity Impairment questionnaire—irritable bowel syndrome version (WPAI:IBS). *Aliment Pharmacol Ther.* 2004;20:459-467.

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## REPORTS

22. **Shih YC, Barghout VE, Sandler RS, et al.** Resource utilization associated with irritable bowel syndrome in the United States 1987-1997. *Dig Dis Sci.* 2002;47:1705-1715.
23. **Zelnorm® (tegaserod maleate) tablets** [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; August 2004.
24. **Reilly MC, Barghout V, Ruegg P, Pecher E, Ricci J-F.** Tegaserod significantly reduces work productivity loss and daily activity impairment in patients with IBS with constipation [abstract]. *Am J Gastroenterol.* 2004; 99:S241.
25. **Rivkin A.** Tegaserod maleate in the treatment of irritable bowel syndrome: a clinical review. *Clin Ther.* 2003; 25:1952-1974.
26. **Tougas G, Snape WJ, Otten MH, et al.** Long-term safety of tegaserod in patients with constipation-predominant irritable bowel syndrome. *Aliment Pharmacol Ther.* 2002;16:1701-1708.
27. **Red Book: 2003 Drug Topics.** Montvale, NJ: Medical Economics Company; 2003.
28. **Hungin APS, Tack J, Mearin F, Whorwell PJ, Dennis E, Barghout V.** Irritable bowel syndrome (IBS): prevalence and impact in the USA—the truth in IBS (T-IBS) survey [abstract]. *Am J Gastroenterol.* 2002;97(suppl): S280-S281.
29. **Hahn BA, Yan S, Strassels S.** Impact of irritable bowel syndrome on quality of life and resource use in the United States and United Kingdom. *Digestion.* 1999;60:77-81.





