

# Some States Pass Disclosure Laws Ahead of Feds

BY JOYCE FRIEDEN

When it comes to public disclosure of drug company payments to doctors, how much your patients know depends on where you live—at least for now.

Although no federal law has yet been passed, “six states and the District of Columbia have already passed disclosure legislation,” Jennifer Colapietro, director of pharmaceutical and life sciences advisory services at PricewaterhouseCoopers, said during an audioconference sponsored by Harvard Health Policy Review and Rx Compliance Report.

Currently, California, Maine, Minnesota, Nevada, Vermont, and West Virginia all have disclosure laws in effect; Massachusetts recently passed a law that does not take effect until next year, she said.

State disclosure laws vary greatly, said Chris Armstrong, investigative counsel for the Senate Finance Committee, where Sen. Chuck Grassley (R-Iowa) is the ranking member. For example, only two states capture device payments, and only a few make the information collected available to the public, he said.

In addition to the laws already in effect, “there are 12 pieces of legislation filed so far, including 3 in Texas. This issue is gaining traction: Over the next few years, there will be a lot of growth in this area which will result in wide variety of rules.”

Maine state Rep. Sharon Anglin Treat (D-Hallowell) agreed that state disclosure laws vary, with only Minnesota’s law disaggregating the data so the public can see how much individual physicians are paid.

“States such as Maine and West Virginia also require reporting on [pharmaceutical] advertising and marketing, including direct-to-consumer television ads, whereas Vermont doesn’t collect that information,” said Ms. Treat, who is also executive director of the National Association on Prescription Drug Prices, a nonprofit organization formed by state legislators who were concerned about the cost of prescription drugs.

The answer to this problem, according to Mr. Armstrong, “is to have a single, clear, robust, and reasonable federal rule.” On that point, the Physician Payments Sunshine Act (S. 301) was introduced first in 2008 by Sen. Grassley and reintroduced this year. That measure would require drug companies to submit a report to the U.S. Health and Human Services secretary detailing any payments made to physicians, as well as any food, gifts, trips, rebates, admission to medical conferences, or any other compensation deemed appropriate. The reports would be available online.

Mr. Armstrong said that the federal legislation is not intended as a “floor” for state laws. “One person had the idea that if Iowa passed a law saying that companies had to disclose their payments twice a year—rather than once a year [as in] in our bill—that’s okay. But that’s not our intent. Any requirements that [necessitate] a duplication of that reporting on the state level are preempted.”

On the other hand, “that’s not to say Iowa couldn’t require reporting of payments to organizations or other prescribers,” Mr. Armstrong continued. “Because those are types of payments not in [the scope] of our bill, those aren’t preempted at all.”

Increased disclosure is not expected to discourage physicians from participating in medical education sponsored by drug companies, according to Mr. Armstrong.

“I certainly wouldn’t want a helpful activity like that to be lessened,” he said. “I have talked to a lot of physician groups, including the American Medical Association and others, and I haven’t heard a whole lot [of them suggesting that] that would happen.” In anticipation of a federal law, three pharmaceutical manufacturers—Pfizer Inc., Merck & Co., and Eli Lilly & Co.—have already announced plans to develop payment databases.

On another federal front, John T. Bentivoglio, a partner in the D.C. law firm King & Spalding LLP, noted that the HHS inspector general’s office has taken an increasing interest in making pharmaceutical companies disclose their physician payments, with Cephalon Inc. becoming the first company (in September 2008) to sign a corporate integrity agreement with the department that required disclosure of physician payments. ■

## IMPORTANT CORRECTION OF DRUG INFORMATION ABOUT BYSTOLIC® (NEBIVOLOL) TABLETS

An advertisement in professional journal publications for Bystolic® (nebivolol) tablets for the treatment of hypertension was the subject of a Warning Letter issued by the U.S. Food and Drug Administration (FDA) in August 2008.

Forest would like to take this opportunity to clarify the content of this advertisement.

### Indications and Usage

Bystolic is indicated for the treatment of hypertension. Bystolic may be used alone or in combination with other antihypertensive agents.

### Unsubstantiated Superiority and Mechanism of Action Claims

The FDA objected to claims that Bystolic was a novel and next generation beta blocker with a unique mechanism of action including cardioselective beta blockade and vasodilation. The FDA stated that these claims were misleading because they suggested that Bystolic is different from and superior to other  $\beta$ -adrenergic receptor blocking agents in the treatment of hypertension, when these implications have not been demonstrated by substantial evidence or substantial clinical experience. In extensive metabolizers (most of the population) and at doses  $\leq 10$  mg, Bystolic is preferentially  $\beta_1$  selective. The FDA also stated that the presentation of the mechanism of action implied that it had been established, when the package insert states that the mechanism of action of the antihypertensive response of Bystolic has not been definitively established.

### Omission and Minimization of Risk Information

The FDA stated that the advertisement did not disclose the following important safety information, which is contained in Bystolic’s full Prescribing Information:

**Warning:** In patients who have compensated congestive heart failure, Bystolic should be administered cautiously. If heart failure worsens, discontinuation of Bystolic should be considered.

**Precautions: CYP2D6 Inhibitors:** Use caution when Bystolic is co-administered with CYP2D6 inhibitors (quinidine, propafenone, fluoxetine, paroxetine, etc).

**Drug interactions:** Drugs that inhibit CYP2D6 can be expected to increase plasma levels of nebivolol. When Bystolic is co-administered with an inhibitor or an inducer of this enzyme, patients should be closely monitored and the nebivolol dose adjusted according to blood pressure response. Fluoxetine, a CYP2D6 inhibitor, administered at 20 mg per day for 21 days prior to a single 10 mg dose of nebivolol to 10 healthy adults, led to an 8-fold increase in the AUC and 3-fold increase in  $C_{max}$  for d-nebivolol.

The FDA objected to the claim, “Favorable tolerability profile with a low incidence of beta blocker-related side effects.” The FDA determined that this claim implied that the tolerability profile of Bystolic is better than the tolerability profile of other  $\beta$ -adrenergic receptor blocking agents, when this has not been demonstrated by substantial evidence or substantial clinical experience. The FDA also objected to the claim, “Favorable tolerability profile,” stating that it minimized the risks associated with Bystolic.

### Unsubstantiated Efficacy Claims

The FDA objected to the claim, “Efficacy demonstrated across a broad range of patients.” The FDA stated that the cited claim implied that efficacy was demonstrated within each subgroup (obese, poor metabolizers, and diabetic) presented in conjunction with this claim, when this has not been supported by substantial evidence or substantial clinical experience. None of the efficacy trials for Bystolic were specifically designed to evaluate effectiveness in patients who were obese, poor metabolizers, or diabetic. The FDA is not aware of any studies with Bystolic demonstrating efficacy in the above referenced subgroups. Effectiveness was established in black hypertensive patients and was similar in subgroups analyzed by age and sex.

### Important Safety Information

Patients being treated with Bystolic should be advised against abrupt discontinuation of therapy. Severe exacerbation of angina and the occurrence of myocardial infarction and ventricular arrhythmias have been reported following the abrupt cessation of therapy with beta blockers. When discontinuation is planned, the dosage should be reduced gradually over a 1- to 2-week period and the patient carefully monitored.

Bystolic is contraindicated in severe bradycardia, heart block greater than first degree, cardiogenic shock, decompensated cardiac failure, sick sinus syndrome (unless a permanent pacemaker is in place), severe hepatic impairment (Child-Pugh  $>B$ ), and in patients who are hypersensitive to any component of this product.

Bystolic should be used with caution in patients with peripheral vascular disease, thyrotoxicosis, in patients treated concomitantly with beta blockers and calcium channel blockers of the verapamil and diltiazem type (ECG and blood pressure should be monitored), severe renal impairment, and any degree of hepatic impairment or in patients undergoing major surgery. In patients who have compensated congestive heart failure, Bystolic should be administered cautiously. If heart failure worsens, discontinuation of Bystolic should be considered. Caution should also be used in diabetic patients as beta blockers may mask some of the manifestations of hypoglycemia, particularly tachycardia.

When Bystolic is administered with CYP2D6 inhibitors such as fluoxetine, significant increases in d-nebivolol may be observed (ie, an 8-fold increase in AUC).

In general, patients with bronchospastic disease should not receive beta blockers.

Bystolic should not be combined with other beta blockers.

The most common adverse events with Bystolic versus placebo (approximately  $\geq 1\%$  and greater than placebo) were headache, fatigue, dizziness, diarrhea, nausea, insomnia, chest pain, bradycardia, dyspnea, rash, and peripheral edema.

**Please see the accompanying brief summary of Prescribing Information for full risk information.**



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