In a high-stakes gamble, Abbott Laboratories is aggressively pitching its immensely popular thyroid drug Synthroid to doctors and patients, even though federal regulators are reviewing the drug and have asked Abbott to reduce Synthroid sales in the meantime.

The fifth-most prescribed medication in the U.S., Synthroid is a synthetic thyroid hormone intended for people whose thyroid gland falters, a condition called hypothyroidism. Thyroid insufficiency can cause tiredness, depression, dry skin and hair, constipation and elevated cholesterol. Perhaps as many as 15% of women over the age of 65 suffer from hypothyroidism, and women are roughly four times more likely than men to get it. In all, eight million U.S. patients now take Synthroid regularly.

Synthroid, first sold in 1955, and a few other prescription medicines are currently sold without the explicit approval of the U.S. Food and Drug Administration because they are decades old and slipped through the regulatory net. Over the years, in rare cases, patients taking Synthroid have suffered heart pain, palpitations and arrhythmia because of significant differences in the stability and potency of the pills, according to FDA documents. In 1997, the FDA finally decided that Synthroid and other thyroid hormone pills needed official approval.

In 2000, Abbott missed a deadline to file an application for approval. So on July 12, 2001, FDA officials ordered a gradual slowdown of Synthroid's distribution pending the agency's review "to make a reasonable transition" from Synthroid to pills approved by the agency. Right now, Abbott is allowed to sell only 60% of the quantities it was selling at this time last year. By late summer, Abbott must reduce shipments of Synthroid to 45% of those made from February through July of last year. Abbott is complying with these sales requirements. But instead of encouraging a gradual transition away from the pill, toward the possibility that approval is denied or delayed, Abbott is telling doctors that they can confidently continue to prescribe Synthroid even to new patients.

"We're going to get our [FDA approval] in six weeks or so," said an Abbott salesman at the Endocrine Society's annual meeting in San Francisco last month. "This is just a timing issue."

Reassured by Abbott, doctors are continuing to prescribe Synthroid for patients. "I guess you can call it brand loyalty," says Leonid Poretsky, an endocrinologist at Beth Israel Medical Center in New York City. "I've been prescribing Synthroid forever, and I don't have any problems with it."
But Mary J. Shomon, a patient advocate and author of "Living Well with Hypothyroidism," calls it unethical for Abbott to continue marketing Synthroid while the medicine's future is uncertain. "All I know is that the FDA has not approved their product," Ms. Shomon says. "Why are doctors still prescribing a drug that's not approved by the FDA when there are other options that are approved that are equally effective and are less expensive in most cases?"

Jennifer Smoter, an Abbott spokeswoman, says the FDA didn't mandate restrictions on Abbott's marketing of Synthroid. "Abbott's compliance with the FDA's phase-down doesn't really have a bearing on doctors writing prescriptions," she says, and she points out that Abbott's sales of Synthroid to wholesalers are being reduced, as required by the FDA order. "We are making sure that the Synthroid that we provide to the marketplace is a quality product."

She adds: "We have no reports of patients not being able to get their medication." Besides, she says, "approval is imminent."

An FDA spokeswoman says the agency "doesn't comment on unapproved products."

Abbott's marketing tactics could save its franchise if Synthroid does indeed win approval. But if the FDA doesn't approve Synthroid, millions of U.S. patients may suddenly find that their local pharmacy has run out of their medicine. There are two similar branded thyroid-hormone drugs that already have federal approval -- Unithroid, manufactured by Jerome Stevens Inc., and Levoxyl, made by King Pharmaceuticals Inc. Neither is an exact replica of Synthroid. Patients switching from Synthroid must visit their doctors to get a new prescription, and most physicians advise that they return a few weeks later for blood tests to determine whether the new pills are working as hoped.

If physicians are suddenly forced to switch most of their Synthroid patients to another medicine, endocrinologists say they will be swamped and some patients may have to do without their medicine for a time.

"It will be tremendously disruptive if Synthroid is taken off the market," says Paul Ladenson, professor and director of endocrinology at Johns Hopkins Medical Institutions in Baltimore.

An FDA decision is expected by the end of the summer. While Abbott expresses confidence that Synthroid will be approved, it is painfully aware that FDA actions are famously difficult to predict. In 1999, the company was forced to pay a $100 million fine and discontinue production of 125 products because of quality-control problems. After predicting that it would surmount those problems this year, Abbott recently admitted that the FDA still has concerns about its production standards and that a resolution is still a long way off.

Meantime, Abbott's 6,000 sales representatives are visiting doctors' offices and reassuring them that Synthroid will always be available. The salesmen are still stocking doctors' cabinets with free Synthroid samples, hoping to encourage physicians to start new patients on the medicine. And Abbott is attending physicians' conferences and assuring all comers that there won't be any interruption in Synthroid supplies.

At the Endocrine Society meeting, Abbott had an enormous booth festooned with Synthroid banners. The company handed out free espressos, so 20 or more doctors were frequently waiting for a cup and chatting with Abbott salesmen. Posters and handouts stated that "Synthroid is readily available and has extensive manufacturing quality control in place to assure reliability."

Demand for Synthroid remains strong at roughly 44 million prescriptions each year, according to data provided by NDCHealth, a health-care information-services company. Synthroid controls about two-thirds of the thyroid-hormone market. It brought in 11% of Abbott's drug sales in the first quarter, but the drug's relatively low price likely makes it less profitable than some other drugs the company sells.

Synthroid's sales to wholesalers roughly doubled last year when the FDA dismissed the last of Abbott's arguments against the drug undergoing the agency's approval process. Third-quarter sales were $206 million, compared with sales of just $65 million in the fourth quarter and $104 million in the first quarter of this year. Sales in 2000 were about $465 million. Full year 2001 and quarter-by-quarter 2000 sales aren't available.

"We had a tremendous amount of concern over inventory, and demand was incredible," Abbott's Ms. Smoter says.

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