

## ***Treating Allergies with Pills or Drops Instead of Shots***

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For much of her adult life, Shirley Hickey received two injections a week in an effort to tame severe allergies that caused frequent sore throats and sinus infections. Now she uses a less painful method.

“One drop under the tongue every morning, and that’s it,” said Ms. Hickey, 65, who lives in Beaver Falls, Pa. She is free of symptoms and sinus infections from her allergies to ragweed and tree pollens, she said.

Injections have been used to treat allergies from inhaled substances — often known as hay fever — for 100 years, and the basic formula has changed little. But an alternative is now emerging — liquids or tablets placed under the tongue.

Both Merck and [Stallergenes, a French company](#), are seeking marketing approval for tablets to treat grass pollen allergies. An advisory committee to the Food and Drug Administration will discuss the drugs next week.



Jennifer Maiolo’s allergy is treated with a liquid allergen extract, instead of an injection, as Dr. David P. Skoner watches. Dr. Skoner is excited about the allergen tablets that allergy sufferers can now take, replacing injections and decreasing office visits. Credit Jeff Swensen for The New York Times

The drugs are already available in Europe. If they are approved in the United States, they could make this type of therapy more broadly available, by allowing people to treat themselves at home rather than going for frequent shots. Children, who tend not to like

needles, might also find such treatment more acceptable. Approval would also deliver some extra credibility to this type of therapy, which aims to fundamentally alter the immune system.

“It’s hugely important,” said Dr. Linda S. Cox, president of the American Academy of Allergy, Asthma and Immunology. But there are drawbacks. The shots can be tailored to match the patient’s allergies while the liquid drops and tablets are standardized.

An estimated 30 million to 60 million Americans, including up to 40 percent of children and 10 to 30 percent of adults, suffer nasal congestion, runny nose, sneezing, itchy eyes or other symptoms from allergies to something they inhale.

The typical treatments are antihistamines or nasal steroids. But those drugs merely alleviate symptoms.

Immunotherapy, as allergy shots and under-the-tongue treatments are called, involves giving controlled doses of the allergen to teach the immune system to tolerate it. That can lead to longer-lasting relief.

Some studies have shown that three years of immunotherapy provides substantial relief for two years after treatment is stopped, in some cases for longer. Some studies also suggest that immunotherapy can reduce the risk of developing asthma.

But only a small percentage of people with respiratory allergies get the shots.

One reason is that people have to visit the doctor for shots at frequencies ranging from twice a week to once a month for several years. Another is that immunotherapy, while now broadly accepted as studies have accumulated, has had its doubters.

“Allergists always had a bad rap,” said Dr. David P. Skoner, chief of allergy, asthma and immunology at Allegheny Health Network in Pittsburgh. “We were called quacks and shot doctors. The reason was the science wasn’t there.”

The allergen extracts used for the shots are approved by the F.D.A. on the basis of their safety, purity and potency. But because immunotherapy has been around for so long, extracts generally do not go through clinical trials to prove they can actually help tame allergies.

Merck and Stallergenes, by contrast, have done controlled clinical trials and are seeking approval on the same basis as any other drug. That could enhance the credibility of the treatments.

In Merck’s biggest trial, involving 1,500 adults and children who are allergic to Timothy grass, those who took the tablets had a 20 percent reduction in symptoms during one allergy season compared with those who received a placebo. They also used antihistamines or other symptom-relieving drugs less often. Stallergenes’ results were in the same ballpark.

Still, not all allergists will welcome the tablets. That is because they make money giving shots, while the tablets would be prescribed like other pills.

“The allergists in the United States are frightened by this, concerned about it, a little paranoid about it,” said Dr. Skoner, who is also a professor at Temple University and West Virginia University and a consultant to Merck.

The sublingual tablets are kept under the tongue for about a minute, allowing them to dissolve, pass through the mucous membranes and be taken up by immune system cells.

Stallergenes’ product, called Oralair, contains extracts from five grass pollens. If approved, it would be marketed by Greer Laboratories, an allergen extract manufacturer based in North Carolina.

Merck’s product, which the company proposes to call Grastek, contains extract only from Timothy grass. Merck licensed its product from a Danish company, ALK-Abello, which sells it in Europe [under the name Grazax](#).

Oralair is meant to be taken for about six months a year, starting four months before the grass pollen season and extending through the season. Merck’s drug is meant to be taken year-round.

Merck has also applied for approval of a tablet, also licensed from ALK-Abello, to treat ragweed allergy. Greer is developing a liquid sublingual product for ragweed. Sublingual therapy for dust mite allergy might come after that.

Grazax and Oralair have been available in Europe for several years. A variety of factors, including the time needed to do American clinical trials, explain why it has taken so long for the drugs to reach the United States.

Some American doctors have not waited. A survey in 2011 found that 11 percent of allergists were using the extracts approved for injection as off-label sublingual treatments. That is the treatment Ms. Hickey is using.

Shots have to be given in a doctor’s office because they can, though only rarely, provoke potentially fatal immune system reactions, called anaphylaxis. Also, to avoid such reactions, the dose used is started low and gradually increased over several months.

The sublingual treatments can cause throat irritation as well as itching and swelling in the mouth, but almost never anaphylaxis. So it is expected that, except for the initial dose, the treatments can be taken at home. And patients can start at the full dose immediately or almost immediately.

Still, some studies suggest that the sublingual therapy may not be quite as effective as injections. Also, the tablets contain only specific allergens, such as for grass; shots are customized by allergists to contain multiple extracts, such as for weeds, dust mites and so on, to match a patient’s allergies.

“It’s rare that somebody comes in and they are just allergic to one grass,” said Dr. Rohit K. Katial, professor of medicine at National Jewish Health in Denver. “Generally, people who are allergic tend to be allergic to multiple things.”

The companies have not said how much the drugs will cost, but some doctors think it will be about \$150 a month. Oralair sells for about that much in Canada. Shots cost about \$25 each, higher if they contain more allergens, according to Dr. Cox, who has been a consultant to Stallergenes and other companies.

Mark Schoenebaum, an analyst at ISI Group, projects that Merck’s tablets for grass and ragweed will have peak annual sales of about \$350 million combined. That is not much for a giant like Merck, but it bolsters the company’s allergy and asthma business, which is suffering from generic competition to the blockbuster pill Singulair.

Another issue is whether patients will continue taking the daily tablets long enough to achieve lasting changes in their immune systems.

A recently published study from the Netherlands, which analyzed pharmacy records, found that only 7 percent of those getting sublingual immunotherapy completed the recommended three years of treatment. That was even worse than the 23 percent of patients getting allergy shots.

New approaches might help. “What we need is something that is very quick, a very short course, that has a long duration of effect,” said Dr. Mark Larché, a professor of medicine at McMaster University in Canada.

Dr. Larché is a co-founder of Circassia, a British company that is developing a therapy that would require as few as four monthly injections. It is now in the final phase of clinical trials as a treatment for cat allergies.

Another short-duration treatment that has shown promise consists of three monthly injections of the allergen into the lymph nodes in the groin.

Other treatments are being developed, but some have fallen by the wayside. The immune system is complex, as is nature. Some clinical trials have failed because the allergy season turned out to be so mild that even those getting the placebo had few symptoms.

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