



News Release



FOR IMMEDIATE RELEASE

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FDA Approves Merck's GRASTEK[®] (Timothy Grass Pollen Allergen Extract) Sublingual Tablet as Immunotherapy to Treat Grass Pollen-Induced Allergic Rhinitis with or without Conjunctivitis in Children and Adults

GRASTEK is the Only FDA Approved Sublingual Allergy Immunotherapy Tablet Indicated for Children as Young as 5 Years of Age

WHITEHOUSE STATION, N.J., April 14, 2014 – Merck (NYSE: MRK), known as MSD outside the United States and Canada, today announced that the U.S. Food and Drug Administration (FDA) has approved GRASTEK[®] (Timothy Grass Pollen Allergen Extract) Tablet for Sublingual Use [2800 Bioequivalent Allergy Units (BAU)]. GRASTEK is an allergen extract indicated as immunotherapy for the treatment of grass pollen-induced allergic rhinitis with or without conjunctivitis confirmed by positive skin test or *in vitro* testing for pollen-specific IgE antibodies for Timothy grass or cross-reactive grass pollens. GRASTEK is approved for use in persons 5 through 65 years of age. GRASTEK is not indicated for the immediate relief of allergic symptoms.

The prescribing information for GRASTEK includes a boxed warning regarding severe allergic reactions. GRASTEK is contraindicated in patients with severe, unstable or uncontrolled asthma; a history of any severe systemic allergic reaction; a history of any severe local reaction after taking any sublingual allergen immunotherapy; a history of eosinophilic esophagitis; or hypersensitivity to any of the inactive ingredients contained in the product.

“Every grass pollen season, many patients with moderate to severe allergic rhinitis experience nasal and ocular allergy symptoms at their worst while taking symptom-relieving medication,” said Dr. David Bernstein, professor of medicine and environmental health, Division of Immunology, Allergy and Rheumatology, University of Cincinnati College of Medicine. “These patients often have multiple sensitivities. Some of these patients may be candidates for

GRASTEK[®] is a registered trademark of Merck & Co., Inc., Whitehouse Station, N.J., USA.

immunotherapy, but decline allergy shots. With the FDA approval of GRASTEK, allergy specialists now have a new sublingual approach to offer these patients for their grass allergies.”

Symptoms of grass pollen-induced allergic rhinitis with or without conjunctivitis may include sneezing, runny or itchy nose, stuffy or congested nose, or itchy and watery eyes, and typically intensify during the grass pollen season.

“The FDA approval of GRASTEK brings an important new sublingual tablet for allergy specialists treating adults and children with allergic rhinitis with or without conjunctivitis caused by Timothy or cross-reactive grass pollens,” said Dr. Sean Curtis, vice president, Respiratory and Immunology, Merck Research Laboratories. “This important milestone marks another opportunity for Merck to build on our respiratory heritage with allergy specialists.”

About Timothy grass allergy

Timothy grass is one of the most common grasses in the United States and has been demonstrated to be cross-reactive with other grasses, including sweet vernal, orchard (also known as cocksfoot), perennial rye, Kentucky blue (also known as June grass), meadow fescue and redtop. Timing of the grass pollen season varies regionally across the United States.

Dosing and administration of GRASTEK (Timothy Grass Pollen Allergen Extract)

The recommended dose of GRASTEK is one tablet daily to be placed under the tongue, where it will dissolve.

The first dose of GRASTEK should be administered in a healthcare setting under the supervision of a physician with experience in the diagnosis and treatment of allergic diseases. The physician should observe the patient for at least 30 minutes after receiving the first dose of GRASTEK to monitor for signs or symptoms of a severe systemic or a severe local allergic reaction. If the patient tolerates the first dose, the patient may take subsequent doses at home. The physician should prescribe auto-injectable epinephrine, and instruct and train the patient on its appropriate use. Children must take GRASTEK under adult supervision.

Initiate GRASTEK at least 12 weeks before the expected onset of each grass pollen season and continue treatment throughout the season. The safety and efficacy of in-season initiation have not been established.

For sustained effectiveness for one grass pollen season after cessation of treatment, GRASTEK may be taken daily for three consecutive years (including the intervals between the grass pollen seasons). The safety and efficacy of in-season initiation have not been established.

GRASTEK will be available in U.S. pharmacies in late April.

About the clinical study program for GRASTEK (Timothy Grass Pollen Allergen Extract)

The efficacy of GRASTEK was supported by two studies of approximately 24 weeks treatment duration over one grass season each in patients 5 through 65 years of age, and one 5-year grass pollen season study in patients 18 through 65 years of age. In all three randomized, double-blind, parallel-group, multi-center studies:

- Patients had a history of grass pollen-induced allergic rhinitis with or without conjunctivitis, and sensitivity to grass confirmed by positive skin test or *in vitro* testing for pollen-specific IgE antibodies for Timothy grass;
- Patients with non-grass sensitivities were included as long as the patients did not require treatment as a result of symptoms from those non-grass allergies during the grass season;
- GRASTEK or placebo was administered as a sublingual tablet and initiated approximately 12 weeks before the start of the grass pollen season;
- Patients in both arms of the study were allowed to take symptom-relieving medications (including systemic and topical antihistamines, and topical and oral corticosteroids) as needed;
- Efficacy was established by self-reporting of rhinoconjunctivitis daily symptom scores (DSS) and daily medication scores (DMS), the sums of which were combined into the total combined scores (TCS);
- Daily rhinoconjunctivitis symptoms included four nasal symptoms (runny nose, stuffy nose, sneezing and itchy nose), and two ocular symptoms (gritty/itchy eyes and watery eyes).

The FDA criteria for clinically relevant efficacy of allergen immunotherapy is based on the TCS, which must have an average difference relative to placebo of less than or equal to -15 percent, and the upper bound of the 95 percent confidence interval (CI) must be less than or equal to -10 percent.

First season efficacy in adults and children

One study compared GRASTEK to placebo in 1,501 patients 5 through 65 years of age, of whom approximately 25 percent had mild, intermittent asthma and 85 percent were sensitized to other allergens in addition to grass. Patients treated with GRASTEK had significant reduction of nasal and ocular symptoms, and reduction in use of symptom-relieving allergy medication, as measured by a decrease in the TCS for the entire grass pollen season, compared to placebo;

difference for GRASTEK (Timothy Grass Pollen Allergen Extract) (n=629) relative to placebo (n=672) was -23 percent (95% CI: -36.0%; -13.0%).

A second study compared GRASTEK to placebo in 344 patients 5 through 17 years of age, of whom 26 percent had mild, intermittent asthma and 89 percent were sensitized to other allergens in addition to grass. Patients treated with GRASTEK had significant reduction of nasal and ocular symptoms, and reduction in use of symptom-relieving allergy medication, as measured by a decrease in the TCS for the entire grass pollen season, compared to placebo; difference for GRASTEK (n=149) relative to placebo (n=158) was -26 percent (95% CI: -38.2%; -10.1%).

Sustained effect

In one 5-year study, 634 patients 18 through 65 years of age received GRASTEK or placebo for three consecutive years and were then observed for two years during which they did not receive study drug. Patients treated with GRASTEK had a decrease in TCS throughout the grass pollen season during the three years of active treatment. This effect was sustained during the grass pollen season in the first year after discontinuation of GRASTEK, but not in the second year.

TCS difference (GRASTEK relative to placebo) per year:

- Year 1: -34% (95% CI: -42.0%;-26.3%); (n=568*)
- Year 2: -41% (95% CI: -51.8%;-29.5%); (n=316*)
- Year 3: -34%;(95% CI: -45.5%;-21.4%); (n=287*)
- Post Treatment Year 1: -27% (95% CI: -39.9%;-12.4%); (n=257*)

*Number of patients in analysis in both treatment groups (GRASTEK and placebo).

About allergic rhinitis due to Timothy and cross-reactive grasses

It is estimated that approximately 7.5 million U.S. children and adults ages 5 to 64 have been diagnosed with moderate to severe allergic rhinitis and are sensitized to Timothy and cross-reactive grass pollens.

Selected safety information about GRASTEK (Timothy Grass Pollen Allergen Extract)

WARNING: SEVERE ALLERGIC REACTIONS

GRASTEK can cause life-threatening allergic reactions such as anaphylaxis and severe laryngopharyngeal restriction. Do not administer GRASTEK to patients with severe, unstable or uncontrolled asthma. Observe patients in the office for at least 30 minutes following the initial dose. Prescribe auto-injectable epinephrine, instruct and train patients on its appropriate use, and instruct patients to seek immediate medical care upon its use. GRASTEK may not be suitable for patients with certain underlying medical conditions that may reduce their ability to survive a serious allergic reaction. GRASTEK may not be suitable for patients who may be unresponsive to epinephrine or inhaled bronchodilators, such as those taking beta-blockers.

GRASTEK is contraindicated in patients with severe, unstable, or uncontrolled asthma; a history of any severe systemic allergic reaction; a history of any severe local reaction after taking sublingual allergen immunotherapy; a history of eosinophilic esophagitis; or hypersensitivity to any of the inactive ingredients (gelatin, mannitol and sodium hydroxide) contained in the product.

GRASTEK can cause systemic allergic reactions including anaphylaxis which may be life-threatening. In addition, GRASTEK can cause severe local reactions, including laryngopharyngeal swelling, which can compromise breathing and be life-threatening. Educate patients to recognize the signs and symptoms of these allergic reactions and instruct them to seek immediate medical care and discontinue therapy should any of these occur. Allergic reactions may require treatment with epinephrine. Prescribe auto-injectable epinephrine to patients receiving GRASTEK. Instruct patients to recognize the signs and symptoms of a severe allergic reaction, and in the proper use of emergency auto-injectable epinephrine. Instruct patients to seek immediate medical care upon use of auto-injectable epinephrine and to stop treatment with GRASTEK. Review the epinephrine package insert for complete information.

Administer the initial dose of GRASTEK in a healthcare setting under the supervision of a physician with experience in the diagnosis and treatment of allergic diseases, and prepared to manage a life-threatening systemic or local allergic reaction. Observe patients in the office for at least 30 minutes following the initial dose of GRASTEK.

GRASTEK can cause local reactions in the mouth or throat that could compromise the upper airway. Consider discontinuation of GRASTEK in patients who experience persistent and escalating adverse reactions in the mouth or throat.

Eosinophilic esophagitis has been reported in association with sublingual tablet immunotherapy. Discontinue GRASTEK (Timothy Grass Pollen Allergen Extract) and consider a diagnosis of eosinophilic esophagitis in patients who experience severe or persistent gastro-esophageal symptoms including dysphagia or chest pain.

GRASTEK has not been studied in patients with moderate or severe asthma or any patients who required daily medication to treat asthma. Withhold immunotherapy with GRASTEK if the patient is experiencing an acute asthma exacerbation.

GRASTEK has not been studied in patients who are receiving concomitant allergen immunotherapy. Concomitant dosing with other allergen immunotherapy may increase the likelihood of local or systemic adverse reactions to either subcutaneous or sublingual allergen immunotherapy.

Stop treatment with GRASTEK to allow complete healing of the oral cavity in patients with oral inflammation (e.g., oral lichen planus, mouth ulcers or thrush) or oral wounds, such as those following oral surgery or dental extraction.

The most common adverse reactions reported in clinical studies for patients 18 through 65 years of age with Timothy grass pollen-induced allergic rhinitis with or without conjunctivitis and treated with GRASTEK vs. placebo included oral pruritus (26.7% vs. 3.5%), throat irritation (22.6% vs. 2.8%), ear pruritus (12.5% vs. 1.1%) and mouth edema (11.1% vs. 0.8%).

The most common adverse reactions for GRASTEK vs. placebo in clinical studies for pediatric patients between 5 and 17 years of age with grass pollen-induced allergic rhinitis with or without conjunctivitis included oral pruritus (24.4% vs. 2.1%), throat irritation (21.3% vs. 2.5%), and mouth edema (9.8% vs. 0.2%).

Because systemic and local adverse reactions with immunotherapy may be poorly tolerated during pregnancy, GRASTEK should be used during pregnancy only if clearly needed.

Find an allergy specialist

To find an allergy specialist, please visit the websites of the [American Academy of Allergy, Asthma, and Immunology \(AAAAI\)](#); the [American College of Allergy, Asthma & Immunology \(ACAAI\)](#); or the [American Academy of Otolaryngic Allergy \(AAOA\)](#).

About Merck

Today's Merck is a global healthcare leader working to help the world be well. Merck is known as MSD outside the United States and Canada. Through our prescription medicines, vaccines, biologic therapies, and consumer care and animal health products, we work with customers and operate in more than 140 countries to deliver innovative health solutions. We also demonstrate our commitment to increasing access to healthcare through far-reaching policies,

programs and partnerships. For more information, visit www.merck.com and connect with us on [Twitter](#), [Facebook](#) and [YouTube](#).

Forward-Looking Statement

This news release includes “forward-looking statements” within the meaning of the safe harbor provisions of the United States Private Securities Litigation Reform Act of 1995. These statements are based upon the current beliefs and expectations of Merck’s management and are subject to significant risks and uncertainties. If underlying assumptions prove inaccurate or risks or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements.

Risks and uncertainties include but are not limited to, general industry conditions and competition; general economic factors, including interest rate and currency exchange rate fluctuations; the impact of pharmaceutical industry regulation and health care legislation in the United States and internationally; global trends toward health care cost containment; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approval; Merck’s ability to accurately predict future market conditions; manufacturing difficulties or delays; financial instability of international economies and sovereign risk; dependence on the effectiveness of Merck’s patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions.

Merck undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise. Additional factors that could cause results to differ materially from those described in the forward-looking statements can be found in Merck’s 2013 Annual Report on Form 10-K and the company’s other filings with the Securities and Exchange Commission (SEC) available at the SEC’s Internet site (www.sec.gov).

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Please see Prescribing Information, including Boxed Warning, for GRASTEK (Timothy Grass Pollen Allergen Extract) Tablet for Sublingual Use at http://www.merck.com/product/usa/pi_circulars/g/grastek/grastek_pi.pdf and Medication Guide for GRASTEK at http://www.merck.com/product/usa/pi_circulars/g/grastek/grastek_mg.pdf.