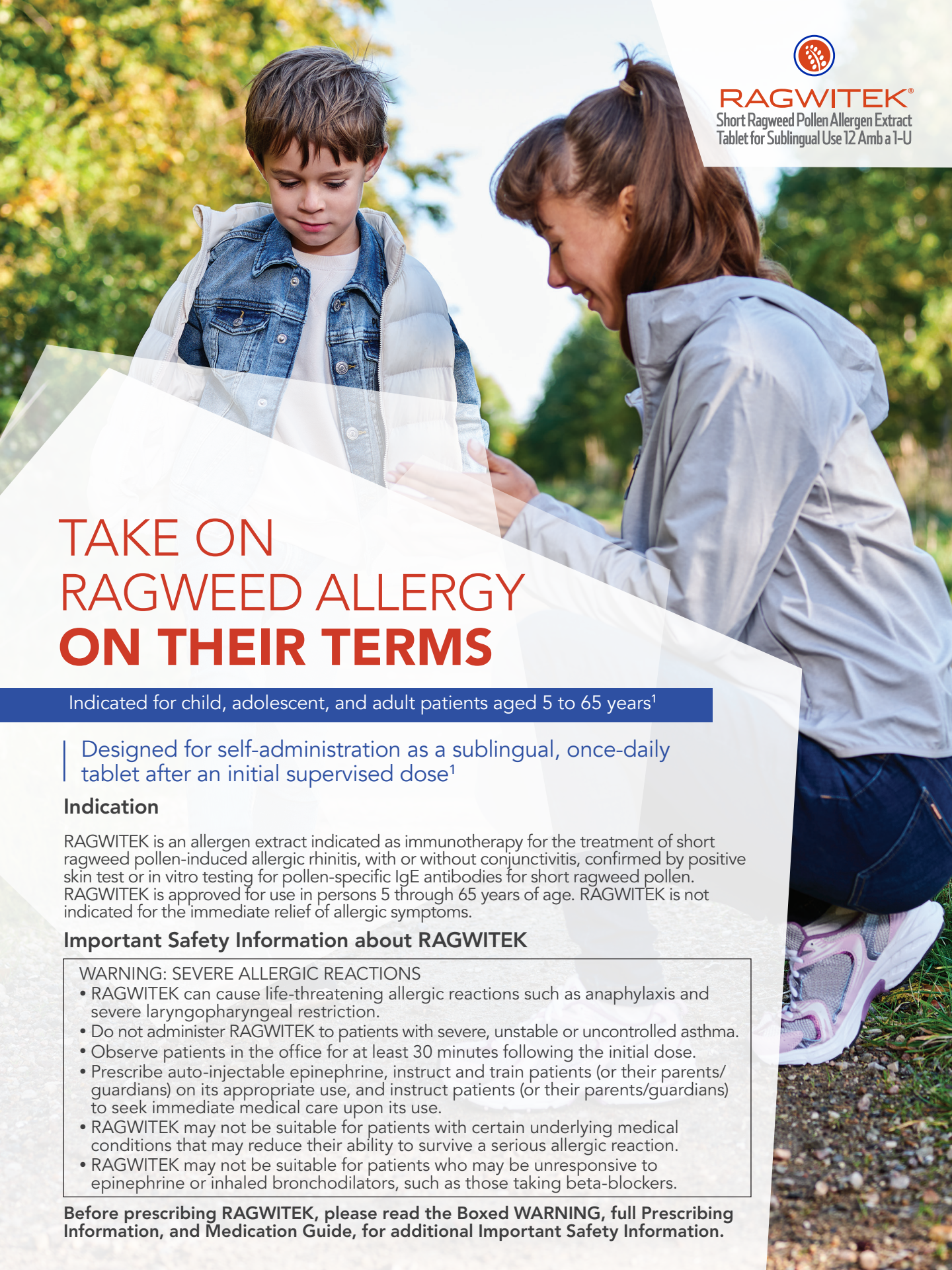
RAGWITEK®
Short Ragweed Pollen Allergen Extract
Tablet for Sublingual Use 12 Amb a 1-U



TAKE ON RAGWEED ALLERGY **ON THEIR TERMS**

Indicated for child, adolescent, and adult patients aged 5 to 65 years[1]

Designed for self-administration as a sublingual, once-daily tablet after an initial supervised dose[1]

Indication

RAGWITEK is an allergen extract indicated as immunotherapy for the treatment of short ragweed pollen-induced allergic rhinitis, with or without conjunctivitis, confirmed by positive skin test or in vitro testing for pollen-specific IgE antibodies for short ragweed pollen. RAGWITEK is approved for use in persons 5 through 65 years of age. RAGWITEK is not indicated for the immediate relief of allergic symptoms.

Important Safety Information about RAGWITEK

WARNING: SEVERE ALLERGIC REACTIONS

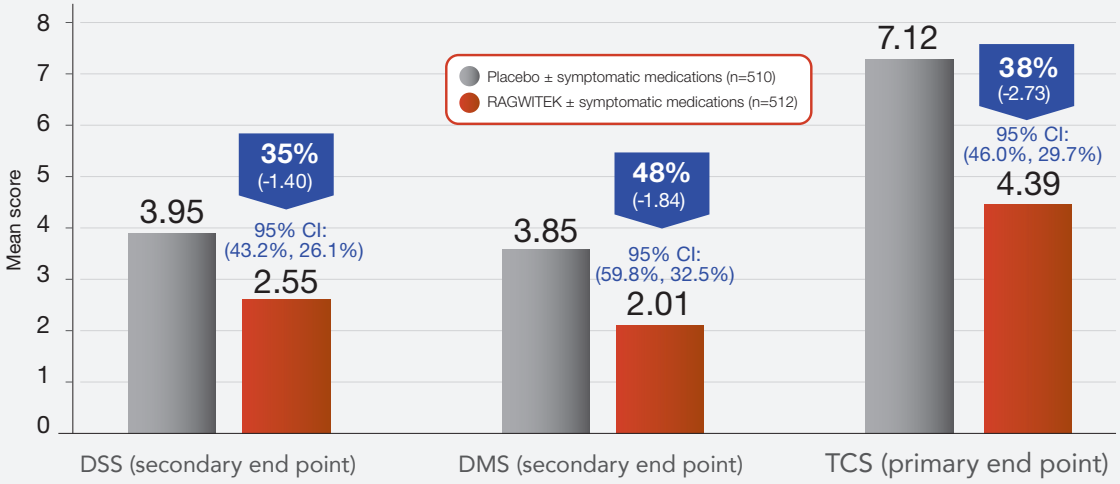
- RAGWITEK can cause life-threatening allergic reactions such as anaphylaxis and severe laryngopharyngeal restriction.
- Do not administer RAGWITEK to patients with severe, unstable or uncontrolled asthma.
- Observe patients in the office for at least 30 minutes following the initial dose.
- Prescribe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

Before prescribing RAGWITEK, please read the Boxed WARNING, full Prescribing Information, and Medication Guide, for additional Important Safety Information.

In the largest pediatric SLIT-tablet trial to date[2]

SIGNIFICANT RELIEF IN PATIENTS AS YOUNG AS AGE 5

RAGWITEK demonstrated a 38% reduction in TCS during peak ragweed season[1,*,†]



Total Combined Score (TCS) = Daily Symptom Score (DSS) + Daily Medication Score (DMS)

- Throughout the entire ragweed pollen season, **RAGWITEK reduced TCS by 32%** relative to placebo (3.88 vs 5.75, respectively [95% CI: -40.7%, -23.3%])[1]
- **58.5%** of patients receiving RAGWITEK did not use any symptomatic therapies during peak ragweed pollen season (vs 42.7% receiving placebo)[2]

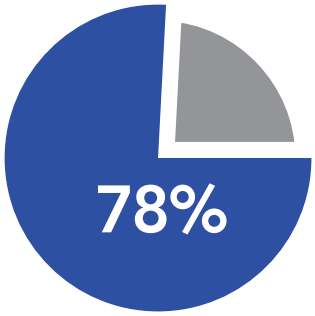
*An approximately 28-week, randomized, double-blind, parallel-group, multicenter clinical trial (N=1022, 5 to 17 years of age), with a history of ragweed-induced allergic rhinitis (with or without conjunctivitis and with or without asthma) and sensitivity to short ragweed as determined by specific IgE testing against *Ambrosia artemisiifolia* (class ≥2; ≥0.7 kU/L). Patients were randomized across the 2016, 2017, and 2018 ragweed pollen seasons to be treated with RAGWITEK (n=512) or placebo (n=510) administered as a daily sublingual tablet. The primary end point was the average TCS during the peak ragweed season. Secondary end points included the average DSS and the average DMS during the peak ragweed season. Daily rhinoconjunctivitis symptoms included 4 nasal symptoms (runny nose, stuffy nose, sneezing, and itchy nose) and 2 ocular symptoms (gritty/itchy eyes and watery eyes). The rhinoconjunctivitis symptoms were measured on a scale of 0 (none) to 3 (severe). The DMS measured the use of standard open-label allergy medications, including oral antihistamines, ocular antihistamine drops, and intranasal corticosteroids. Predefined values were assigned to each class of medication to represent the symptomatic relief provided by the rescue medication.[1,2]

†Peak ragweed pollen season was defined as maximum 15 days with the highest moving average pollen counts during the entire ragweed season.[1]

Important Safety Information about RAGWITEK (continued)

- RAGWITEK 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
  - Hypersensitivity to any of the inactive ingredients [gelatin, mannitol and sodium hydroxide] contained in this product

Before prescribing RAGWITEK, please read the Boxed WARNING, full Prescribing Information, and Medication Guide, for additional Important Safety Information.



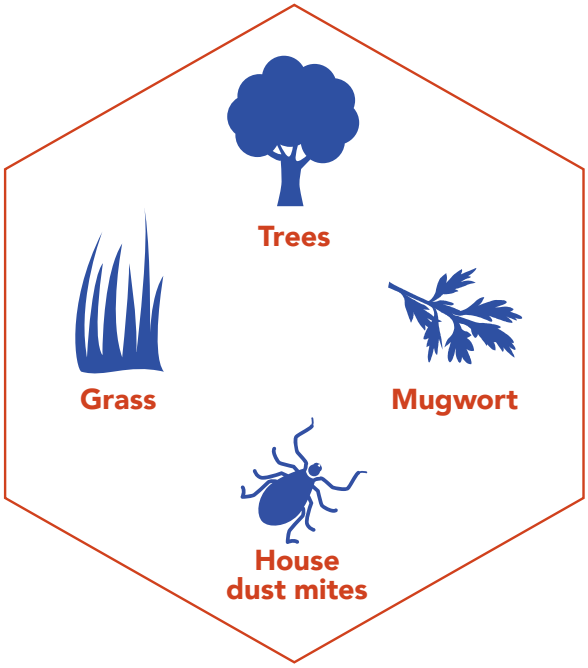
In this study of children and adolescents[2]:

78% of patients were polysensitized[2]

43% of patients had controlled asthma[2,‡]

‡RAGWITEK is not indicated for the treatment of asthma.[1]

Polysensitized patients were defined as those who were sensitized to allergens in addition to ragweed. In this study, those allergens included[2]



IgE=immunoglobulin E; SLIT=sublingual immunotherapy.

Important Safety Information about RAGWITEK (continued)

- RAGWITEK can cause systemic allergic reactions including anaphylaxis which may be life-threatening and severe local reactions, including laryngopharyngeal swelling, which can compromise breathing and be life-threatening. Educate patients (or their parents/guardians) 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.

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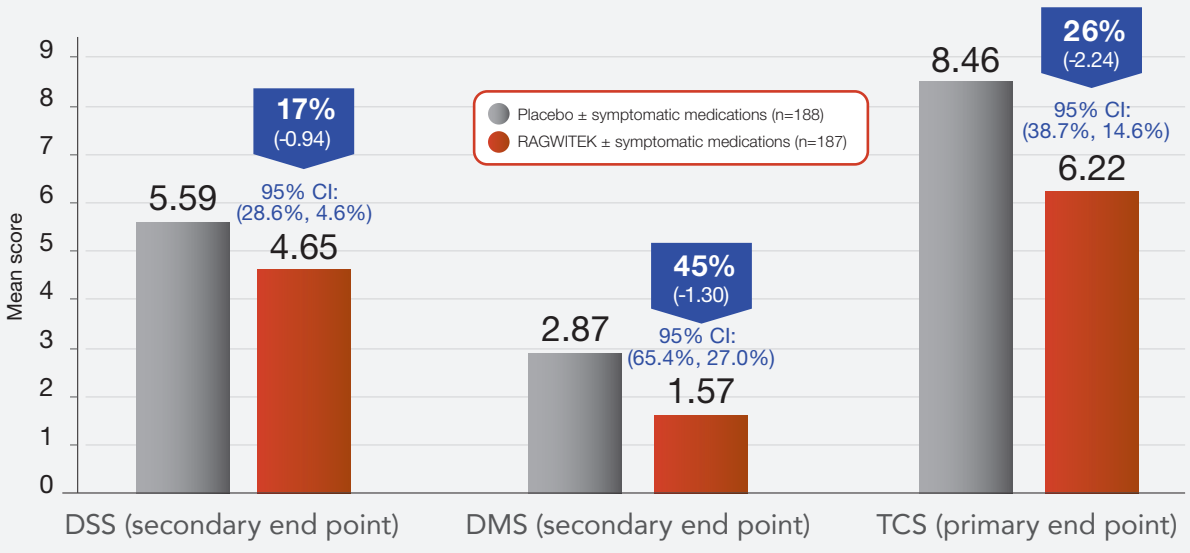
REDUCED SYMPTOMS AND MEDICATION USE IN MULTIPLE TRIALS

In North America, RAGWITEK demonstrated efficacy in DSS, DMS, and TCS vs placebo during peak ragweed pollen season[1,*,†]



Total Combined Score (TCS) = Daily Symptom Score (DSS) + Daily Medication Score (DMS)

- Throughout the entire ragweed pollen season, **RAGWITEK reduced TCS by 26%** relative to placebo (5.21 vs 7.01, respectively [95% CI: -37.6%, -13.5%])[1]

*Approximately 52-week, North American, randomized, multicenter, parallel-group, double-blind, placebo-controlled trial (N=565 patients, 18 to 50 years of age), with a history of ragweed-induced allergic rhinoconjunctivitis (with or without asthma) for at least 2 years and sensitivity to short ragweed as determined by a positive skin prick test (wheal diameter [≥5 mm]) and specific IgE testing against *Ambrosia artemisiifolia* (class ≥2; ≥0.7 kU/L). Patients were randomized in a 1:1:1 ratio to be treated with RAGWITEK 12 Amb a 1-U (n=187), 6 Amb a 1-U (n=190), or placebo (n=188) administered as a daily sublingual tablet. The primary end point was the TCS during the peak ragweed season. Secondary end points included the rhinoconjunctivitis DSS and DMS during the peak ragweed season. Daily rhinoconjunctivitis symptoms included 4 nasal symptoms (runny nose, stuffy nose, sneezing, and itchy nose) and 2 ocular symptoms (gritty/itchy eyes and watery eyes). The rhinoconjunctivitis symptoms were measured on a scale of 0 (none) to 3 (severe). The DMS measured the use of standard open-label allergy medications, including systemic and topical antihistamines and topical and oral corticosteroids. Predefined values were assigned to each class of medication to represent the symptomatic relief provided by the rescue medication.[1,3]

†Peak ragweed pollen season was defined as maximum 15 days with the highest moving average pollen counts during the entire ragweed season.[1]

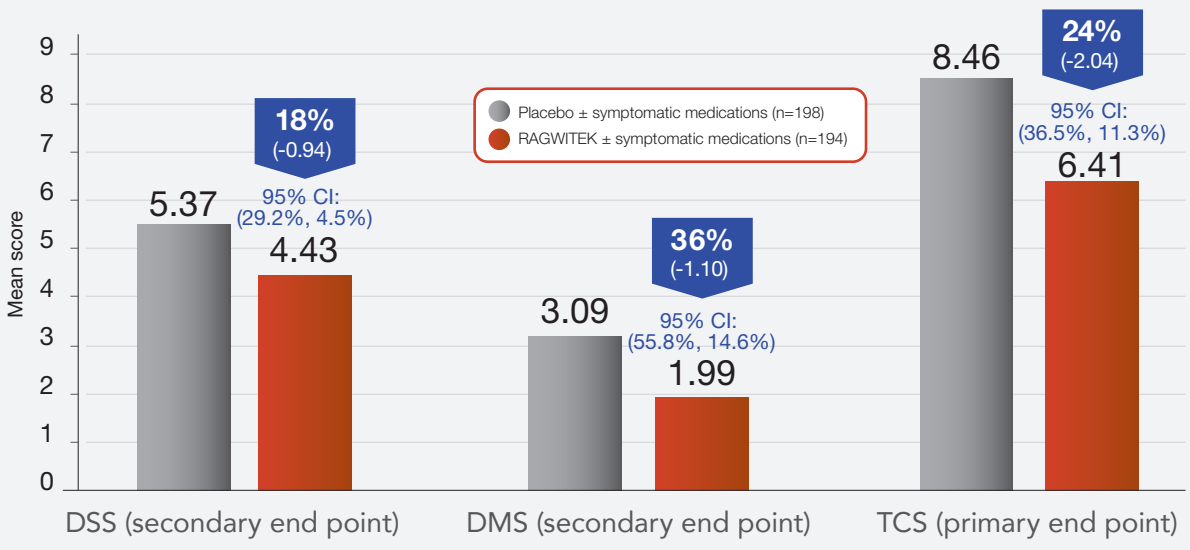
Important Safety Information about RAGWITEK (continued)

- Prescribe auto-injectable epinephrine to patients receiving RAGWITEK. Instruct patients (or their parents/guardians) to recognize the signs and symptoms of a severe allergic reaction and in the proper use of emergency auto-injectable epinephrine. Instruct patients (or their parents/guardians) to seek immediate medical care upon use of auto-injectable epinephrine and to stop treatment with RAGWITEK. Review the epinephrine package insert for complete information.

Before prescribing RAGWITEK, please read the Boxed WARNING, full Prescribing Information, and Medication Guide, for additional Important Safety Information.

In adults

Results were consistent in a second trial across North America and Europe[1,‡,§]



Total Combined Score (TCS) = Daily Symptom Score (DSS) + Daily Medication Score (DMS)

- Throughout the entire ragweed pollen season, **RAGWITEK reduced TCS by 27%** relative to placebo (5.18 vs 7.09, respectively [95% CI: -38.8%, -14.1%])[1]

IgE=immunoglobulin E.

‡Approximately 52-week, North American and European, multicenter, double-blind, randomized, placebo-controlled, parallel group, dose-ranging trial (N=784 patients, 18 to 50 years of age), with a history of ragweed-induced allergic rhinoconjunctivitis (with or without asthma) for at least 2 years and sensitivity to short ragweed as determined by a positive skin prick test (wheal diameter ≥5 mm) and specific IgE testing against *Ambrosia artemisiifolia* (class ≥2; ≥0.7 kU/L). Patients were randomized in a 1:1:1:1 ratio to be treated with RAGWITEK 12 Amb a 1-U (n=194), 6 Amb 1-U (n=195), 1.5 Amb 1-U (n=197), or placebo (n=198) administered as a daily sublingual tablet. Patients in clinical trials were allowed to take symptom-relieving medications, including systemic and topical antihistamines and topical and oral corticosteroids, as needed.[1,4]

§Peak ragweed pollen season was defined as maximum 15 days with the highest moving average pollen counts during the entire ragweed season.[1,4]

Important Safety Information about RAGWITEK (continued)

- Administer the initial dose of RAGWITEK 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 RAGWITEK.

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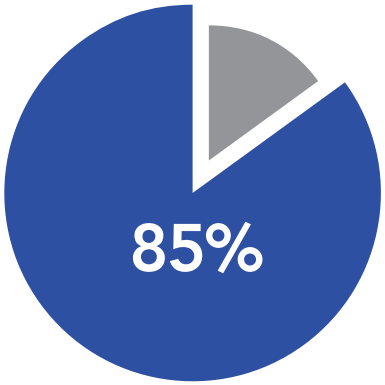
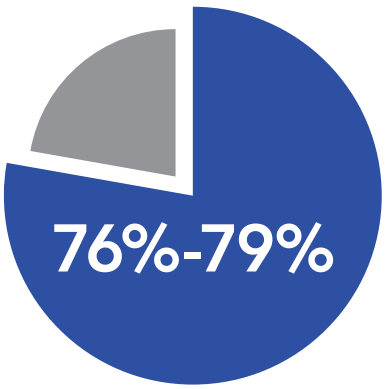
PROVEN IN POLYSENSITIZED PATIENTS[3,4]



In a pivotal trial with North American adults[3]:

85% of patients were polysensitized[3]

23% of patients had controlled asthma[3,*]



In a pivotal trial with North American and European adults[4]:

76%-79% of patients were polysensitized[4]

16%-19% of patients had controlled asthma[4,*]

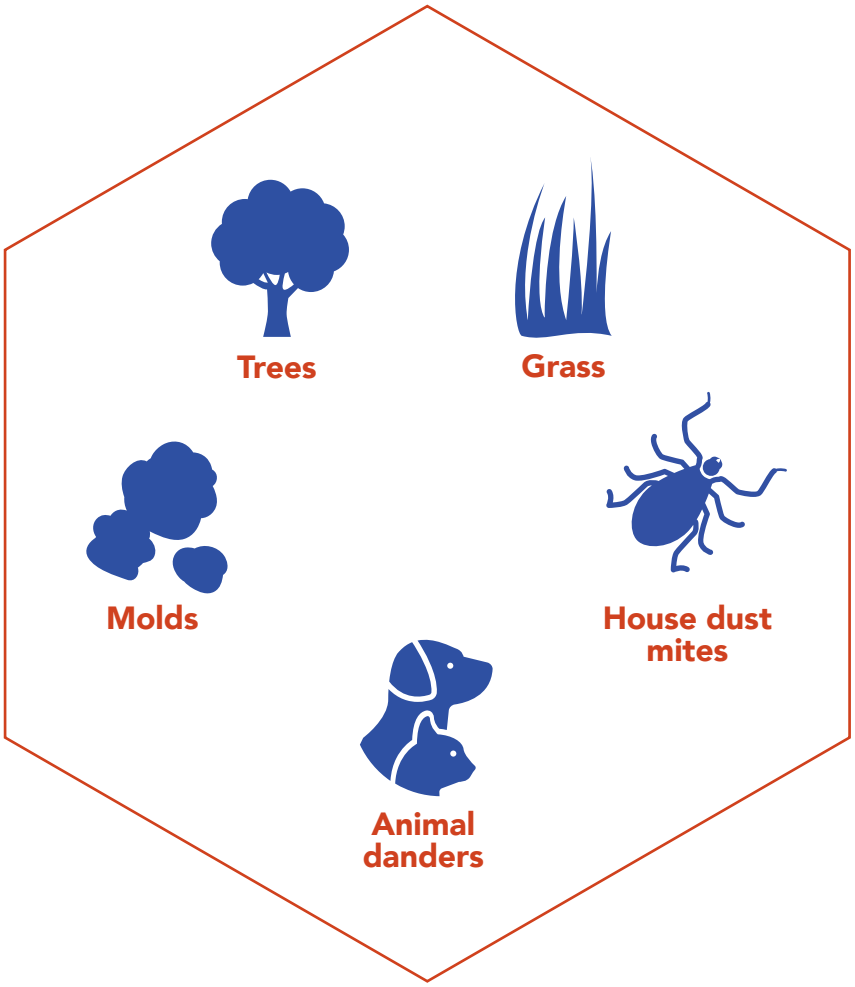
*RAGWITEK is not indicated for the treatment of asthma.[1]

Important Safety Information about RAGWITEK (continued)

- Patients who have persistent and escalating adverse reactions in the mouth or throat should be considered for discontinuation of RAGWITEK. Eosinophilic esophagitis has been reported in association with sublingual tablet immunotherapy. Discontinue RAGWITEK and consider a diagnosis of eosinophilic esophagitis in patients who experience severe or persistent gastro-esophageal symptoms including dysphagia or chest pain.
- RAGWITEK has not been studied in subjects with severe asthma. Immunotherapy with RAGWITEK should be withheld if the patient is experiencing an acute asthma exacerbation.

Before prescribing RAGWITEK, please read the Boxed WARNING, full Prescribing Information, and Medication Guide, for additional Important Safety Information.

Polysensitized patients were defined as those who were sensitized to allergens in addition to ragweed. In these trials, those allergens included[3,4]



Important Safety Information about RAGWITEK (continued)

- RAGWITEK has not been studied in subjects 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.

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SAFETY PROFILE IN CHILDREN, ADOLESCENTS, AND ADULTS

Common adverse reactions in adults[1]

Adverse reactions reported in ≥10% of adult subjects treated with RAGWITEK (28-day pooled analysis)		
Adverse reaction	**RAGWITEK (n=1057),%**	**Placebo (n=757),%**
Throat irritation	16.6	3.3
Oral pruritus	10.9	2.0
Ear pruritus	10.4	1.1
Oral paraesthesia	10.0	4.0

The overall safety profile beyond Day 28 in the two 52-week trials was similar to that observed in the 28-day pooled analysis.[1]

Children and adolescents

- Adverse reactions reported in ≥5% of children and adolescents 5 through 17 years of age were: throat irritation, oral pruritus, ear pruritus, lip swelling, glossodynia, nausea, oral pain, pharyngeal edema, swollen tongue, abdominal pain upper, stomatitis, and enlarged uvula[1]
- The percentage of subjects who discontinued from the clinical trial because of an adverse reaction while exposed to RAGWITEK or placebo was 3.9% and 1.0%, respectively. The most common adverse reaction that led to study discontinuation in subjects who were exposed to RAGWITEK was throat irritation[1]
- The overall safety profile was similar in patients with or without a history of asthma[2]
- Local allergic reactions were early (median day of onset ranged from 1 to 10 days), brief (median duration ranged from 10.5 to 25 minutes on day 1), and were limited in recurrence (median duration of days patients experienced reactions ranged from 1 to 2.5 days)[2]

Important Safety Information about RAGWITEK (continued)

- Stop treatment with RAGWITEK 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.

Before prescribing RAGWITEK, please read the Boxed WARNING, full Prescribing Information, and Medication Guide, for additional Important Safety Information.

Systemic allergic reactions

- Systemic allergic reactions, including anaphylactic reactions and severe local allergic reactions, have occurred in clinical trial patients treated with RAGWITEK[1]

  — Prescribe auto-injectable epinephrine, instruct and train patients or their parents/guardians on its appropriate use, and instruct patients or their parents/guardians to seek immediate medical care upon its use[1]

  — One adult subject (1/1057; 0.1%) who received RAGWITEK experienced a treatment-related severe systemic allergic reaction that led to discontinuation of RAGWITEK. The subject fully recovered after treatment with epinephrine (self-administered), antihistamines, and oral corticosteroids[1]

  — Three child or adolescent subjects (0.6%) treated with RAGWITEK and one child or adolescent subject (0.2%) treated with placebo experienced treatment-related systemic allergic reactions[1]

    - There were no instances of eosinophilic esophagitis[2]
    - Three adverse events were considered severe (oral pruritus, laryngitis, and eczema); all others were mild or moderate[2]
    - No child or adolescent patients required intramuscular epinephrine[2]

- Immediately discontinue RAGWITEK in any patient developing clinical evidence of a severe systemic or severe local allergic reaction. In such cases, consider discontinuing treatment with RAGWITEK permanently[1]

  — Patients or their parents/guardians should be informed and educated about the symptoms of a severe allergic reaction, instructed to discontinue RAGWITEK, and told to seek immediate medical care and contact their physician should any of these symptoms occur after taking RAGWITEK

  — Signs and symptoms that may be associated with a systemic allergic reaction include syncope, dizziness, hypotension, tachycardia, dyspnea, wheezing, bronchospasm, chest discomfort, cough, abdominal pain, vomiting, diarrhea, rash, pruritus, flushing, and urticaria

Important Safety Information about RAGWITEK (continued)

- The most common adverse reactions reported in adults treated with RAGWITEK vs placebo included throat irritation (16.6% vs 3.3%), oral pruritus (10.9% vs 2.0%), ear pruritus (10.4% vs 1.1%), oral paraesthesia (10.0% vs 4.0%), mouth edema (6.1% vs 0.5%), and tongue pruritus (5.1% vs 0.5%).

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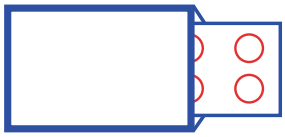
A TABLET SOLUTION TO MEET TODAY'S AIT CHALLENGES

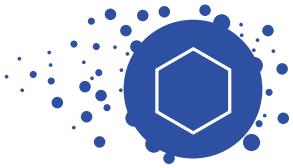
Fewer appointments

Allows patients to receive AIT even if they can't make frequent office visits



Same dose for children, adolescents, and adults[1]

Once-daily standardized dosing with no titration or updosing



Sublingual administration[1]

Gives patients a needle-free AIT option that dissolves under their tongue

RAGWITEK tablets should be placed under the tongue with dry fingers. Swallowing should be avoided for 1 minute, and drinking and eating should be avoided for the following 5 minutes[1]

Important Safety Information about RAGWITEK (continued)

- The most common solicited adverse reactions reported in children and adolescents 5 through 17 years of age treated with RAGWITEK vs placebo included throat irritation/tickle (48.3% vs 17.7%), itching in the mouth (47.8% vs 11.2%), itching in the ear (33.9% vs 6.3%), mouth pain (18.9% vs 4.5%), swelling of the lips (13.8% vs 1.2%), nausea (11.5% vs 3.3%), swelling of the tongue (11.3% vs 0.8%), throat swelling (10.7% vs 1.6%), and stomach pain (10.1% vs 4.5%).

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START EARLY TO SET YOUR PATIENTS UP FOR SUCCESS

RAGWITEK can be easily added on to symptomatic therapies to enhance symptom relief without burdening your patients or practice

After confirming a ragweed allergy, administer the first dose in your office at least 12 weeks before the expected start of the season[1]

30-minute observation time[1]

If tolerated, subsequent doses can be taken at home and maintained throughout the season[1]

Flexible follow-up opportunities: Schedule in-person or remote appointments

AE and adherence check-in

Efficacy check-in

AE=adverse event; AIT=allergy immunotherapy.

Important Safety Information about RAGWITEK (continued)

- The most common unsolicited adverse reactions reported in children and adolescents 5 through 17 years of age treated with RAGWITEK vs placebo included oral pruritus (7.8% vs 1.0%), throat irritation (7.6% vs 1.6%), ear pruritus (4.5% vs 0.2%), and tongue pruritus (4.5% vs 0.4%).

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RAGWEED ALLERGY IMMUNOTHERAPY DESIGNED TO FIT THEIR LIVES

Start early to set your patients up for success throughout ragweed season, using these 3 simple steps:

IDENTIFY

Determine which appropriate child, adolescent, and adult patients in your practice may benefit from adding RAGWITEK on to their symptomatic therapies

PLAN

Schedule in-person appointments at least 12 weeks prior to the expected start of ragweed season for patients' initial doses

FOLLOW UP

Regularly check in with your patients to make sure they are adhering to therapy

References: 1. RAGWITEK. Prescribing information. ALK-Abelló A/S; Rev. 2021. **2.** Nolte H, Bernstein DI, Nelson HS, Ellis AK, Kleine-Tebbe J, Lu S. Efficacy and safety of ragweed SLIT-tablet in children with allergic rhinoconjunctivitis in a randomized, placebo-controlled trial. *J Allergy Clin Immunol Pract.* 2020;8(7):2322-2331.e5. doi:10.1016/j.jaip.2020.03.041 **3.** Nolte H, Hébert J, Berman G, et al. Randomized controlled trial of ragweed allergy immunotherapy tablet efficacy and safety in North American adults. *Ann Allergy Asthma Immunol.* 2013;110(6):450-456.e4. doi:10.1016/j.anai.2013.03.013 **4.** Creticos PS, Maloney J, Bernstein DI, et al. Randomized controlled trial of ragweed allergy immunotherapy tablet in North American and European adults. *J Allergy Clin Immunol.* 2013;131(5):1342-1349.e6. doi:10.1016/j.jaci.2013.03.019

Important Safety Information about RAGWITEK (continued)

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

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