ODACTRA- dermatophagoides pteronyssinus and dermatophagoides farinae tablet
ALK-Abello A S

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use ODACTRA safely and effectively. See full prescribing information for ODACTRA.

ODACTRA™ House Dust Mite (*Dermatophagoides farinae* and *Dermatophagoides pteronyssinus*) Allergen Extract
Tablet for Sublingual Use
Initial U.S. Approval: 2017

WARNING: SEVERE ALLERGIC REACTIONS

See full prescribing information for complete boxed warning.

- **ODACTRA can cause life-threatening allergic reactions such as anaphylaxis and severe laryngopharyngeal restriction. (5.1)**
- **Do not administer ODACTRA to patients with severe, unstable or uncontrolled asthma. (4)**
- **Observe patients in the office for at least 30 minutes following the initial dose. (5.1)**
- **Prescribe epinephrine, instruct and train patients or parents/guardians on its appropriate use, and instruct patients or parents/guardians to seek immediate medical care upon its use. (5.1)**
- **ODACTRA may not be suitable for patients with certain underlying medical conditions that may reduce their ability to survive a serious allergic reaction. (5.1)**
- **ODACTRA may not be suitable for patients who may be unresponsive to epinephrine or inhaled bronchodilators, such as those taking beta-blockers. (5.1)**

RECENT MAJOR CHANGES

Indications and Usage (1) 02/2025

INDICATIONS AND USAGE

ODACTRA is an allergen extract indicated as immunotherapy for the treatment of house dust mite (HDM)-induced allergic rhinitis, with or without conjunctivitis, confirmed by positive *in vitro* testing for IgE antibodies to *Dermatophagoides farinae* or *Dermatophagoides pteronyssinus* house dust mites or by positive skin testing to licensed house dust mite allergen extracts. ODACTRA is approved for use in individuals 5 through 65 years of age. (1)

DOSAGE AND ADMINISTRATION

For sublingual use only. (2)

- One tablet daily. (2.1)
- Place the tablet immediately under the tongue where it will dissolve within 10 seconds. Allow it to remain there until completely dissolved. Do not swallow for at least 1 minute. (2.2)
- Administer the first dose of ODACTRA under the supervision of a healthcare professional with experience in the diagnosis and treatment of allergic diseases. Observe patients in the office for at least 30 minutes following the initial dose. (2.2)

DOSAGE FORMS AND STRENGTHS

- Tablet, 12 SQ-HDM. (3)

CONTRAINDICATIONS

- Severe, unstable or uncontrolled asthma. (4)
- History of any severe systemic allergic reaction or any severe local reaction to sublingual allergen immunotherapy. (4)
- A history of eosinophilic esophagitis. (4)
- Hypersensitivity to any of the inactive ingredients contained in this product. (4)

WARNINGS AND PRECAUTIONS

- Inform patients or parents/guardians of the signs and symptoms of serious allergic reactions and instruct them to seek immediate medical care and discontinue therapy should any of these occur. (5.1)
- In case of oral inflammation or wounds, stop treatment with ODACTRA to allow complete healing of the oral cavity. (5.6)

ADVERSE REACTIONS

- The most common solicited adverse reactions reported in ≥10% of adult participants (18 through 65 years of age) treated with ODACTRA were: throat irritation/tickle, itching in the mouth, itching in the ear, swelling of the uvula/back of the mouth, swelling of the lips, swelling of the tongue, tongue pain, nausea, throat swelling, stomach pain, tongue ulcer/sore on the tongue, mouth ulcer/sore in the mouth, and food tastes different. (6.1)
- The most common solicited adverse reactions reported in ≥10% of adolescent participants (12 through 17 years of age) treated with ODACTRA were: throat irritation/tickle, itching in the mouth, itching in the ear, tongue pain, stomach pain, swelling of the uvula/back of the mouth, swelling of the lips, swelling of the tongue, throat swelling, nausea, tongue ulcer/sore on the tongue, and mouth ulcer/sore in the mouth, and diarrhea. (6.1)
- The most common solicited adverse reactions reported in ≥10% of pediatric participants (5 through 11 years of age) treated with ODACTRA were: itching in the mouth, throat irritation/tickle, itching in the ear, stomach pain, swelling of the lips, tongue pain, food tastes different, nausea (feel like throwing up), swelling in the back of the mouth, swelling of the tongue, and mouth ulcer. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact ALK-Abelló Inc., a subsidiary of ALK-Abelló A/S, at 1-855-216-6497 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.
See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 2/2025

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FULL PRESCRIBING INFORMATION

WARNING: SEVERE ALLERGIC REACTIONS

- **ODACTRA can cause life-threatening allergic reactions such as anaphylaxis and severe laryngopharyngeal restriction. (5.1)**
- **Do not administer ODACTRA to patients with severe, unstable or uncontrolled asthma. (4)**
- **Observe patients in the office for at least 30 minutes following the initial dose. (5.1)**
- **Prescribe epinephrine, instruct and train patients or parents/guardians on its appropriate use, and instruct patients or parents/guardians to seek immediate medical care upon its use. (5.1)**
- **ODACTRA may not be suitable for patients with certain underlying medical conditions that may reduce their ability to survive a serious allergic reaction. (5.1)**
- **ODACTRA may not be suitable for patients who may be unresponsive to epinephrine or inhaled bronchodilators, such as those taking beta-blockers. (5.1)**

1 INDICATIONS AND USAGE

ODACTRA™ is an allergen extract indicated as immunotherapy for the treatment of house dust mite (HDM)-induced allergic rhinitis, with or without conjunctivitis, confirmed by positive *in vitro* testing for IgE antibodies to *Dermatophagoides farinae* or *Dermatophagoides pteronyssinus* house dust mites, or by positive skin testing to licensed house dust mite allergen extracts. ODACTRA is approved for use in individuals 5 through 65 years of age.

ODACTRA is not indicated for the immediate relief of allergic symptoms.

2 DOSAGE AND ADMINISTRATION

For sublingual use only.

2.1 Dose

One ODACTRA tablet daily.

2.2 Administration

Administer the first dose of ODACTRA in a healthcare setting under the supervision of a healthcare professional with experience in the diagnosis and treatment of allergic diseases. After receiving the first dose of ODACTRA, observe the patient for at least 30 minutes 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 patient should administer ODACTRA as follows:

- Take the tablet from the blister unit after carefully removing the foil with dry hands.
- Place the tablet immediately under the tongue where it will dissolve within 10 seconds. Do not swallow for at least 1 minute.
- Wash hands after handling the tablet.
- Do not take the tablet with food or beverage. Food or beverage should not be taken for 5 minutes after taking the tablet.

Data regarding the safety of restarting treatment after missing a dose of ODACTRA are limited. In the clinical studies, treatment interruptions for up to seven days were allowed. Prescribe epinephrine to patients prescribed ODACTRA and instruct patients (or their parents/guardians) in the proper use of epinephrine *[see Warnings and Precautions (5.1)]*.

3 DOSAGE FORMS AND STRENGTHS

ODACTRA is available as 12 SQ-HDM* tablets that are white to off-white, circular with a debossed pentagon detail on one side.

*SQ-HDM is the dose unit for ODACTRA. SQ is a method of standardization of biological potency, major allergen content and complexity of the allergen extract. HDM is an abbreviation for house dust mite.

4 CONTRAINDICATIONS

ODACTRA 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 contained in this product *[see Description (11)]*

5 WARNINGS AND PRECAUTIONS

5.1 Severe Allergic Reactions

ODACTRA can cause systemic allergic reactions including anaphylaxis which may be life-

threatening. In addition, ODACTRA can cause severe local reactions, including laryngopharyngeal swelling, which can compromise breathing and be life-threatening.

Allergic reactions may require treatment with epinephrine. Prescribe epinephrine to patients receiving ODACTRA. Instruct patients or their parents/guardians to recognize the signs and symptoms of a severe allergic reaction and in the proper use of emergency epinephrine. Instruct patients or their parents/guardians to seek immediate medical care and to stop treatment with ODACTRA upon use of epinephrine [see *Patient Counseling Information (17)*]. See Prescribing Information for epinephrine for complete information.

ODACTRA may not be suitable for patients with certain medical conditions that may reduce the ability to survive a serious allergic reaction or that may increase the risk of adverse reactions after epinephrine administration. Examples of these medical conditions include but are not limited to: markedly compromised lung function (either chronic or acute); severe mast cell disorder; or cardiovascular disease including unstable angina, recent myocardial infarction, significant arrhythmia, and uncontrolled hypertension. In addition, ODACTRA may not be suitable for patients who are taking medications that can potentiate or inhibit the effects of epinephrine (see Prescribing Information for epinephrine for information on drug interactions).

Administer the initial dose of ODACTRA in a healthcare setting under the supervision of a healthcare professional 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 ODACTRA.

5.2 Upper Airway Compromise

ODACTRA can cause local reactions in the mouth or throat that could compromise the upper airway *[see Adverse Reactions (6.1)]*. Consider discontinuation of ODACTRA in patients who experience persistent and escalating adverse reactions in the mouth or throat.

5.3 Eosinophilic Esophagitis

Eosinophilic esophagitis has been reported in association with sublingual tablet immunotherapy *[see Contraindications (4)]*. Discontinue ODACTRA and consider a diagnosis of eosinophilic esophagitis in patients who experience severe or persistent gastroesophageal symptoms including dysphagia or chest pain.

5.4 Asthma

Withhold immunotherapy with ODACTRA if the patient is experiencing an acute asthma exacerbation. Re-evaluate patients who have recurrent asthma exacerbations and consider discontinuation of ODACTRA.

5.5 Concomitant Allergen Immunotherapy

ODACTRA has not been studied in participants 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.

5.6 Oral Conditions

Stop treatment with ODACTRA 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, tooth loss or dental extraction.

6 ADVERSE REACTIONS

The most common solicited adverse reactions reported in ≥10% of adult participants (18 through 65 years of age) treated with ODACTRA were: throat irritation/tickle, itching in the mouth, itching in the ear, swelling of the uvula/back of the mouth, swelling of the lips, swelling of the tongue, tongue pain, nausea, throat swelling, stomach pain, tongue ulcer/sore on the tongue, mouth ulcer/sore in the mouth, and food tastes different.

The most common solicited adverse reactions reported in ≥10% of adolescent participants (12 through 17 years of age) treated with ODACTRA were: throat irritation/tickle, itching in the mouth, itching in the ear, tongue pain, stomach pain, swelling of the uvula/back of the mouth, swelling of the lips, swelling of the tongue, throat swelling, nausea, tongue ulcer/sore on the tongue, and mouth ulcer/sore in the mouth, and diarrhea.

The most common solicited adverse reactions reported in ≥10% of pediatric participants (5 through 11 years of age) treated with ODACTRA were itching in the mouth, throat irritation/tickle, itching in the ear, stomach pain, swelling of the lips, tongue pain, food tastes different, nausea (feel like throwing up), swelling in the back of the mouth, swelling of the tongue, and mouth ulcer.

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

Adults (18 through 65 years of age)

In four double-blind, placebo-controlled, randomized clinical studies, a total of 1279 participants with house dust mite-induced allergic rhinitis, with or without conjunctivitis, 18 through 65 years of age was treated with at least one dose of ODACTRA 12 SQ-HDM. Of participants treated with ODACTRA in the four studies, 50% had mild to moderate asthma and 71% were polysensitized to other allergens in addition to HDM, including trees, grasses, weeds, molds, and animal danders. The study population was 88% White, 6% African American, 4% Asian and 55% female.

Study 1 (NCT01700192) was a randomized, double-blind, placebo-controlled study conducted in the US and Canada evaluating ODACTRA in 1482 participants 12 years of age and older with house dust mite-induced allergic rhinitis with or without conjunctivitis. Of the 1482 participants, 640 participants 18 through 65 years of age received at least one dose of ODACTRA, with a median treatment duration of 267 days (range 1 to 368 days). 631 participants received placebo. Placebo tablets contained the same inactive ingredients as ODACTRA without allergen extract and were packaged identically so that treatment blind/masking was maintained. Participants were monitored for unsolicited adverse events and serious adverse events (SAEs) for the duration of therapy (up to 52 weeks). Participants were monitored for solicited adverse reactions for the first 28 days

following treatment initiation.

Study participants were provided side effect report cards in which they recorded the occurrence of specific solicited adverse reactions daily for the first 28 days following treatment initiation with ODACTRA or placebo. In Study 1, the most common solicited adverse reactions reported in ≥10% of participants treated with ODACTRA were: throat irritation/tickle (67.0% vs. 20.8% placebo), itching in the mouth (61.3% vs. 14.1%), itching in the ear (51.7% vs. 11.7%), swelling of the uvula/back of the mouth (19.8% vs. 2.4%), swelling of the lips (18.0% vs. 2.7%), swelling of the tongue (15.8% vs. 2.1%), nausea (14.2% vs. 7.1%), tongue pain (14.2% vs. 3.0%), throat swelling (13.6% vs. 2.4%), tongue ulcer/sore on the tongue (11.6% vs. 2.1%), stomach pain (11.3% vs. 5.2%), mouth ulcer/sore in the mouth (10.3% vs. 2.9%), and taste alteration/food tastes different (10.0% vs. 3.6%). Table 1 summarizes all solicited adverse reactions reported within the first 28 days of treatment initiation in participants 18 through 65 years of age using the patient-friendly term.

Table 1: Solicited* Adverse Reactions Occurring Within 28 Days After Initiation of Treatment with ODACTRA or Placebo (Study 1, Safety Analysis Set) in Participants 18 through 65 Years of Age

Adverse Reaction	**Any Intensity**		**Severe†**	
	ODACTRA (N=640)	Placebo (N=631)	ODACTRA (N=640)	Placebo (N=631)
Ear and labyrinth disorders				
Itching in the ear	51.7%	11.7%	0.3%	-
Gastrointestinal disorders				
Itching in the mouth	61.3%	14.1%	0.2%	-
Swelling of the uvula/back of the mouth‡	19.8%	2.4%	-	-
Swelling of the lips	18.0%	2.7%	-	-
Swelling of the tongue	15.8%	2.1%	-	-
Nausea	14.2%	7.1%	-	-
Tongue pain	14.2%	3.0%	-	-
Tongue ulcer/sore on the tongue	11.6%	2.1%	-	-
Stomach pain	11.3%	5.2%	0.2%	-
Mouth ulcer/sore in the mouth	10.3%	2.9%	-	-
Diarrhea	6.9%	3.6%	-	-
Vomiting	2.5%	1.4%	-	-
Nervous system disorders				
Taste alteration/food tastes different	10.0%	3.6%	-	-
Respiratory, thoracic				

and mediastinal disorders				
Throat irritation/tickle	67.0%	20.8%	0.3%	-
Throat swelling	13.6%	2.4%	0.2%	-

In Table 1, the dashes represent no participants.

*Solicited adverse reactions (modified from World Allergy Organization [WAO] list of local side effects of sublingual immunotherapy [SLIT]) were those reported by participants within the first 28 days after treatment initiation.

†Severe adverse reactions were those assessed by the investigator as severe in intensity, which is defined as incapacitating with inability to work or do usual activity.

‡The percentage of participants reported for the patient-friendly term of "swelling of the uvula/back of the mouth" includes participants with an enlarged uvula, palatal swelling/edema, and/or mouth swelling/edema (which can be anywhere in the mouth, not specifically back of the mouth).

In Study 1, the timing of the adverse reaction relative to exposure to ODACTRA was evaluated for 7 solicited adverse reactions (itching in the ear, itching in the mouth, swelling of the uvula/back of the mouth, swelling of the lips, swelling of the tongue, throat irritation/tickle, and throat swelling). The median time to onset of these adverse reactions following initiation of treatment with ODACTRA varied from 1 to 7 days. The median duration of these adverse reactions that occurred on the first day of treatment initiation varied from 30 to 60 minutes. These adverse reactions recurred for a median of 2 to 12 days.

In Study 1, the following unsolicited adverse events were reported in numerically more participants treated with ODACTRA than with placebo and occurred in ≥1% of participants 18 through 65 years of age within 28 days after initiation of treatment with ODACTRA: paresthesia oral (9.2% vs. 3.2%), tongue pruritus (4.7% vs. 1.1%), oral pain (2.7% vs. 0.6%), stomatitis (2.5% vs. 1.1%), dyspepsia (2.2% vs. 0.0%), pharyngeal erythema (2.0% vs. 0.3%), eye pruritus (1.7% vs. 1.4%), oral mucosal erythema (1.7% vs. 0.2%), upper respiratory tract infection (1.6% vs. 1.1%), sneezing (1.6% vs. 0.3%), lip pruritus (1.4% vs. 0.3%), dysphagia (1.4% vs. 0.0%), fatigue (1.3% vs. 1.0%), hypoesthesia oral (1.3% vs. 1.0%), oropharyngeal pain (1.3% vs. 0.6%), chest discomfort (1.3% vs. 0.3%), dry throat (1.3% vs. 0.3%), pruritus (1.1% vs. 1.0%), and urticaria (1.1% vs. 0.3%).

Studies 2 (NCT01454544) and 3 (NCT01644617) were randomized, double-blind, placebo-controlled studies of participants 18 years of age and older with house dust mite-induced allergic rhinitis with or without conjunctivitis, and with or without asthma. Study 4 (NCT01433523) was a randomized, double-blind placebo-controlled study that included participants 18 years of age and older with house dust mite-induced asthma and allergic rhinitis, with or without conjunctivitis.

Across the four clinical studies, 1279 participants received at least one dose of ODACTRA, of whom 1104 (86%) completed at least 4 months of therapy.

The percentages of participants in these studies who discontinued treatment because of an adverse reaction while exposed to ODACTRA or placebo were 8.1% and 3.0%, respectively. The most common adverse reactions (≥1.0%) that led to study

discontinuation in participants who received ODACTRA were throat irritation (1.5%), oral pruritus (1.3%), ear pruritus (1.1%), and mouth swelling (1.0%).

Serious adverse events were reported, 16/1279 (1.3%) among ODACTRA recipients and 23/1277 (1.8%) among placebo recipients. No deaths were reported.

Epinephrine use was reported in 5/1279 (0.4%) participants who received ODACTRA compared to 3/1277 (0.2%) of participants who received placebo. Of these participants, 1 ODACTRA recipient reported a systemic allergic reaction and used epinephrine on the day of treatment initiation compared to 2 placebo recipients who reported anaphylaxis and used epinephrine 6 and 25 days after treatment initiation, respectively.

Of 1279 participants who received ODACTRA, 34 (2.7%) reported dyspepsia compared to 0/1277 (0%) of participants who received placebo. Twenty participants who received ODACTRA (1.6%) reported symptoms of gastroesophageal reflux disease (GERD) compared to 3/1277 (0.2%) of participants who received placebo.

Adolescents (12 through 17 years of age)

In two clinical studies, a total of 347 adolescent participants were treated with at least one dose of ODACTRA. Study 1 (NCT01700192) was a double-blind, placebo-controlled, randomized clinical study. Study 5 (NCT04541004) was a single arm, open-label safety study. Because the study design and safety data presentation differ in the studies, adverse reaction rates cannot be directly compared. Overall, the safety profile in adolescents was consistent with the safety profile in adults.

Study 1 was a randomized, double-blind, placebo-controlled study conducted in the US and Canada evaluating ODACTRA in 1482 participants 12 years of age and older with house dust mite-induced allergic rhinitis with or without conjunctivitis. Of the 1482 participants, 94 participants 12 through 17 years of age received at least one dose of ODACTRA, with a median treatment duration of 279 days (range 1 to 353 days). 95 participants received placebo. Of the adolescent participants treated with ODACTRA, 53% were male, 39% had asthma, and 72% were polysensitized to other allergens in addition to HDM. The adolescent participant population was 69% White, 13% Black or African American, 10% multiple race, 5% Asian, and 3% American Indian or Alaska Native. Participant demographics in placebo-treated participants were similar to the active treatment group.

In Study 1, study participants were provided side effect report cards in which they recorded the occurrence of specific solicited adverse reactions daily for the first 28 days following treatment initiation with ODACTRA or placebo. The solicited adverse reactions reported in adolescent participants 12 through 17 years of age are summarized in Table 2.

Table 2: Solicited* Adverse Reactions Occurring Within 28 Days After Initiation of Treatment with ODACTRA or Placebo (Study 1, Safety Analysis Set) in Participants 12 through 17 Years of Age

Adverse Reaction (Any Intensity‡)	**ODACTRA (N=94)**	**Placebo (N=95)**
Ear and labyrinth disorders		

Itching in the ear	50.0%	11.6%
Gastrointestinal disorders		
Itching in the mouth‡	73.4%	14.7%
Tongue pain	24.5%	4.2%
Stomach pain	23.4%	15.8%
Swelling of the uvula/back of the mouth†	20.2%	3.2%
Swelling of the lips	20.2%	1.1%
Swelling of the tongue	19.1%	3.2%
Nausea‡	17.0%	9.5%
Tongue ulcer/sore on the tongue	12.8%	4.2%
Mouth ulcer/sore in the mouth	10.6%	3.2%
Diarrhea	7.7%	2.1%
Vomiting‡	4.3%	-
Nervous system disorders		
Taste alteration/food tastes different	4.3%	4.2%
Respiratory, thoracic and mediastinal disorders		
Throat irritation/tickle‡	73.4%	35.8%
Throat swelling	18.1%	8.4%

In Table 2, the dashes represent no participants.

*Solicited adverse reactions (modified from World Allergy Organization [WAO] list of local side effects of sublingual immunotherapy [SLIT]) were those reported by participants within the first 28 days after treatment initiation.

†The percentage of participants reported for the patient-friendly term of "swelling of the uvula/back of the mouth" includes participants with an enlarged uvula, palatal swelling, and/or mouth swelling/edema (which can be anywhere in the mouth, not specifically back of the mouth).

‡Of those participants reporting any intensity of: itching in the mouth, nausea, throat irritation/tickle, or vomiting in the ODACTRA group, 1 participant (1.1%) reported severe intensity of the reaction. Adverse reactions were categorized as severe according to the definition ‘incapacitating with inability to work or do usual activity’, as assessed by the investigator.

In Study 1, participants were monitored for unsolicited adverse events and serious adverse events (SAEs) for the duration of treatment (up to 52 weeks). Unsolicited adverse events that were reported in numerically more participants treated with ODACTRA than with placebo and occurred in ≥1% of participants 12 through 17 years of age within 28 days after initiation of treatment with ODACTRA are summarized in Table 3.

In Study 1, 94 adolescent participants received at least one dose of ODACTRA, of whom 81 (86%) completed at least 4 months of treatment.

The percentage of adolescent participants who discontinued from the study because of an adverse reaction while exposed to ODACTRA or placebo was 10% and 1%, respectively. The most common adverse reaction that led to study discontinuation in adolescent participants who were exposed to ODACTRA were throat irritation (4%), swollen tongue (2%) and nausea (2%).

No adolescent participants treated with ODACTRA in Study 1 reported serious adverse events, treatment-related systemic allergic reactions, or adverse reactions treated with epinephrine.

Table 3: Unsolicited Adverse Reactions Occurring During the Entire Trial After Initiation of Treatment with ODACTRA or Placebo (Study 1, Safety Analysis Set) Reported in ≥1% of Participants 12 through 17 Years of Age

Adverse Reaction	ODACTRA (N=94)†	Placebo (N=95)†
Ear and labyrinth disorders		
Ear discomfort	1.1%	-
Ear pain	1.1%	-
Eye disorders		
Eye pruritus	1.1%	-
Eye swelling	1.1%	-
Gastrointestinal disorders		
Paraesthesia oral	5.3%	-
Oral pain	4.3%	-
Tongue pruritus	3.2%	-
Stomatitis	2.1%	1.1%
Aphthous ulcer	1.1%	-
Dysphagia	1.1%	-
Eosinophilic esophagitis	1.1%	-
Salivary gland enlargement	1.1%	-
Tongue discomfort	1.1%	-
General disorders and administration site conditions		
Chest discomfort	2.1%	-
Chest pain	1.1%	-
Non-cardiac chest pain	1.1%	-
Infections and infestations		
Acute sinusitis	1.1%	-

Musculoskeletal and connective tissue disorders		
Arthralgia	1.1%	-
Neck pain	1.1%	-
Respiratory, thoracic and mediastinal disorders		
Oropharyngeal pain	1.1%	-
Rhinorrhea	1.1%	-
Throat tightness	1.1%	-
Tonsillar hypertrophy	1.1%	-
Skin and subcutaneous tissue disorders		
Pruritus	2.1%	1.1%
Vascular disorders		
Flushing	1.1%	-

In Table 3, the dashes represent no participants.

† Due to the population size (ODACTRA; N=94; and placebo; N=95), 1.1% represents one participant.

Study 5 (NCT04541004) was a single-arm, open label study conducted in Europe, and exposed 253 participants 12 through 17 years of age with house dust mite-induced allergic rhinitis with or without conjunctivitis and with or without asthma to at least one dose of ODACTRA. The median treatment duration was 28 days (range 11 to 32 days). Of the participants, 60% were male, 43% had asthma, and 56% were polysensitized to other allergens in addition to HDM. The participant population was 99.6% White and 0.4% Native Hawaiian or Other Pacific Islander.

Study participants were provided side effect report cards in which they recorded the occurrence of specific solicited adverse reactions daily for the first 28 days following treatment initiation with ODACTRA or placebo. Participants were monitored for unsolicited adverse events and serious adverse events (SAEs) for the duration of the study.

In Study 5, the proportions of participants reporting solicited adverse reactions during the first 28 days following initiation of treatment with ODACTRA were comparable to those reported during the first 28 days following initiation of treatment with ODACTRA in Study 1.

In Study 5, the following unsolicited adverse reactions occurred in ≥1% of participants 12 through 17 years of age during the entire study [median treatment duration 28 days (range 11 to 32 days)] after initiation of treatment with ODACTRA: oral pain (3.2%), oral pruritus (2.8%), throat irritation (1.6%), ear pruritus (1.2%), and mouth ulceration (1.2%).

In Study 5, 253 adolescent participants received at least one dose of ODACTRA, of whom 248 (98%) completed 28 days of treatment. The percentage of participants who discontinued from the study because of an adverse reaction while exposed to ODACTRA

was 1%.

No adolescent participants in Study 5 reported serious adverse events, treatment-related systemic allergic reactions, or adverse reactions treated with epinephrine.

Children (5 through 11 years of age)

Study 6 (NCT04145219) was a randomized, double-blind, placebo-controlled study conducted in Europe, US and Canada evaluating ODACTRA in 1458 participants 5 through 11 years of age with house dust mite-induced allergic rhinitis/rhinoconjunctivitis with or without asthma. Of the 1458 participants, 727 participants received at least one dose of ODACTRA, with a median treatment duration of 378 days (range 1 to 486 days) and 731 participants received placebo, with a median treatment duration of 379 days (range 1 to 449 days). Placebo tablets contained the same inactive ingredients as ODACTRA without allergen extract. Of the participants treated with ODACTRA, mean age was 8 years, 67% were male, 99% White, <1% Black or African American, <1% multiple race, <1% Asian, and <1% American Indian or Alaska Native. Participant demographics in the placebo group were similar to the ODACTRA group. In the ODACTRA group, 37% of participants had asthma and 54% were sensitized to other allergens in addition to HDM; the treatment groups were similar with respect to these baseline characteristics.

In Study 6, participants were provided an eDiary in which they recorded the occurrence of specific solicited adverse reactions daily for the first 28 days following treatment initiation with ODACTRA or placebo.The investigator reviewed the symptoms with the participant and determined if they were possibly related to the study treatment. The solicited adverse reactions reported in pediatric participants 5 through 11 years of age are summarized in Table 4.

Table 4: Solicited Adverse Reactions* Occurring Within 28 Days After Initiation of Treatment with ODACTRA or Placebo (Study 6, Safety Analysis Set) in Participants 5 through 11 Years of Age

Adverse Reaction	**Any Intensity**		**Severe†**	
	ODACTRA (N=727)	Placebo (N=731)	ODACTRA (N=727)	Placebo (N=731)
Ear and labyrinth disorders				
Itching in the ear	32.7%	17.0%	0.1%	-
Gastrointestinal disorders				
Itching in the mouth	57.1%	23.9%	0.1%	-
Stomach pain	28.2%	15.7%	0.1%	-
Swelling of the lips	20.5%	4.9%	0.3%	-
Tongue pain	19.4%	5.2%	0.1%	-
Nausea (feel like throwing up)	15.7%	9.0%	-	-
Swelling in the back of the mouth	13.5%	3.3%	-	-
Swelling of the tongue	13.5%	2.6%	-	-
Mouth ulcer	10.0%	6.4%	-	-

Diarrhea	8.0%	5.9%	-	-
Tongue ulcer	6.3%	3.4%	-	-
Vomiting	4.5%	2.2%	-	-
Nervous system disorders				
Food tastes different	16.0%	14.5%	-	-
Respiratory, thoracic and mediastinal disorders				
Throat irritation/tickle	55.2%	31.5%	-	-
Throat swelling	9.2%	2.9%	-	-

In Table 4, the dashes represent no participants.

*Solicited adverse reactions (modified from World Allergy Organization [WAO] list of local side effects of sublingual immunotherapy [SLIT]) were those reported by participants within the first 28 days after treatment initiation and determined by the investigator to be possibly related to the study treatment.

†Severe adverse reactions were those assessed by the investigator as severe in intensity, which is defined as incapacitating with inability to work or do usual activity.

In Study 6, participants 5 through 11 years of age were monitored for unsolicited adverse events and SAEs for the entire duration of treatment (approximately 12 months). Unsolicited adverse reactions that were commonly reported (≥1%) and for which the rate for ODACTRA exceeded the rate for placebo are presented in Table 5.

Table 5: Unsolicited Adverse Reactions Occurring During the Entire Trial After Initiation of Treatment with ODACTRA or Placebo (Study 6, Safety Analysis Set) Reported in ≥1% of Participants 5 through 11 Years of Age

Adverse Reaction	ODACTRA (N=727)	Placebo (N=731)
Ear and labyrinth disorders		
Ear pruritus	1.5%	0.4%
Gastrointestinal disorders		
Oral pruritus	5.4%	1.1%
Abdominal pain upper	1.5%	0.7%
Nausea	1.1%	0.3%
Respiratory, thoracic and mediastinal disorders		
Throat irritation	3.4%	1.4%

In Table 5, the events are presented by SOC and PT.

In Study 6, 727 participants received at least one dose of ODACTRA, of whom 702 (97%) completed at least 3 months of treatment.

The percentage of participants who discontinued the study treatment because of an adverse reaction while exposed to ODACTRA or placebo was 1.8% and 1.0%, respectively. The most common adverse reactions that led to study discontinuation in participants who were exposed to ODACTRA were nausea (0.6%), lip swelling (0.4%) and throat irritation (0.4%).

No participants treated with ODACTRA in Study 6 reported treatment-related serious adverse events, treatment-related anaphylaxis, or adverse reactions treated with epinephrine.

Across twelve clinical studies in which individuals 5 through 85 years of age received ODACTRA or tablets containing different quantities of the same house dust mite allergen extracts and inactive ingredients as ODACTRA, eosinophilic esophagitis was reported in 3/4614 (0.07%) participants; no cases of eosinophilic esophagitis were reported among 2949 (0%) participants who received placebo. The three cases of eosinophilic esophagitis were assessed as related to study treatment. One case, which was reported as an SAE, occurred in a 10 year old participant on Day 31 of treatment. The other cases occurred in a 13 year old participant and a 34 year old participant on Day 204 and Day 99 of treatment, respectively.

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of ODACTRA. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

- *Gastrointestinal disorder*: esophageal irritation
- *General Disorders and Administration Site Conditions:* sensation of foreign body
- *Immune System Disorders:* serious systemic allergic reactions, including anaphylaxis
- *Respiratory, Thoracic and Mediastinal Disorders:* asthma exacerbations, cough, dysphonia
- *Skin and Subcutaneous Tissue Disorders:* angioedema, erythema.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on ODACTRA administered to pregnant women are insufficient to inform associated risks in pregnancy.

In an embryo/fetal developmental toxicity study performed in mice, administration of ODACTRA during gestation did not reveal adverse developmental outcomes in fetuses [*see Data (8.1)*].

Data

Animal Data

In a developmental toxicity study, the effect of ODACTRA on embryo/fetal development was evaluated in mice. Animals were administered ODACTRA subcutaneously daily from day 6 to day 17 of the gestation period at doses up to 5 times the human sublingual dose. There were no ODACTRA-related post-implantation losses, fetal malformations or variations.

8.2 Lactation

Risk Summary

It is not known whether ODACTRA is excreted in human milk. Data are not available to assess the effects of ODACTRA on the breastfed child or on milk production and excretion in the nursing woman. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for ODACTRA and any potential adverse effects on the breastfed child from ODACTRA or from the underlying maternal condition.

8.4 Pediatric Use

The safety and effectiveness of ODACTRA have been established in individuals 5 through 17 years of age with HDM-induced allergic rhinitis, with or without conjunctivitis. *[see Adverse Reactions (6.1) and Clinical Studies (14)]*.

The safety and effectiveness have not been established in individuals below 5 years of age.

8.5 Geriatric Use

Safety and effectiveness have not been established in individuals older than 65 years of age.

10 OVERDOSAGE

Symptoms of overdose may include hypersensitivity reactions such as systemic allergic reactions or severe local allergic reactions *[see Warnings and Precautions (5.1)]*. In case of severe adverse reactions such as angioedema, difficulty in swallowing, difficulty in breathing, changes in voice, or feeling of fullness in the throat, immediate medical evaluation is needed. These reactions should be treated as medically indicated, including the use of epinephrine as appropriate *[see Warnings and Precautions (5.1)]*.

11 DESCRIPTION

ODACTRA tablets contain house dust mite allergen extract from *Dermatophagoides farinae* and *Dermatophagoides pteronyssinus*. ODACTRA is a sublingual tablet that dissolves within 10 seconds.

ODACTRA is available as a tablet of 12 SQ-HDM [6 SQ-HDM *D. farinae* and 6 SQ-HDM *D. pteronyssinus*]. Each tablet contains a 1:1:1:1 potency ratio of *D. farinae* group 1 allergen, *D. farinae* group 2 allergen, *D. pteronyssinus* group 1 allergen, and *D. pteronyssinus* group 2 allergen.

Inactive ingredients: gelatin NF (fish source), mannitol USP, and sodium hydroxide NF.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The precise mechanisms of action of allergen immunotherapy have not been fully established.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

ODACTRA has not been evaluated for carcinogenic potential or impairment of fertility in animals. Two *in vitro* chromosome aberration assays, an *in vitro* bacterial mutagenesis assay and a combined *in vivo* Comet and micronucleus assay for mutagenicity in rats were performed using HDM (*D. farinae* and *D. pteronyssinus*) allergen extracts. One *in vitro* chromosome aberration assay was positive. Based on the aggregated results, the weight of evidence indicates that this finding is unlikely to be of clinical relevance.

14 CLINICAL STUDIES

The efficacy of ODACTRA for the treatment of HDM-induced allergic rhinitis was investigated in three double-blind, placebo-controlled, randomized clinical field efficacy studies (Studies 1, 2, and 6) and one environmental exposure chamber (EEC) study (Study 3).

Adolescents and Adults

Study 1 (North American Field Efficacy Study)

Study 1 was a double-blind, placebo-controlled, randomized field efficacy study conducted in the United States and Canada for a duration of up to 12 months, that compared the efficacy of ODACTRA (N=741) compared to placebo (N=741) in the treatment of HDM-induced allergic rhinitis. Participants 12 through 85 years of age were enrolled if they had a history of symptomatic allergic rhinitis and were sensitized to *D. farinae* and/or *D. pteronyssinus* as determined by house dust mite specific IgE. Participants were required to be symptomatic and were not taking symptom-relieving allergy medications at enrollment.

Participants with mild to moderate asthma, defined as asthma of a severity that required, at most, a daily medium dose of an inhaled corticosteroid, were enrolled in the study.

In this study, 31% of participants had asthma, 48% had conjunctivitis, and 76% were polysensitized to other allergens in addition to HDM, including trees, grasses, weed, animal danders and molds. The participant population was 76% White, 11% African American, 7% Asian, and 59% female. The mean age of participants was 35 years.

The efficacy of ODACTRA in the treatment of HDM-induced allergic rhinitis was assessed through self-reporting of symptoms and medication use. Based on these self-assessments, the Total Combined Rhinitis Score (TCRS), daily symptom scores (DSS)

and daily medication scores (DMS) for rhinoconjunctivitis were calculated. Daily symptoms included four nasal symptoms (runny nose, stuffy nose, sneezing, and itchy nose) and two ocular symptoms (gritty/itchy eyes and watery eyes). Each of these rhinoconjunctivitis symptoms was individually graded by participants daily on a scale of 0 (none) to 3 (severe) and then summed. Participants in active and placebo arms of this study were allowed to take symptom-relieving allergy medications (including oral and ocular antihistamines and nasal corticosteroids) during the study as needed. The DMS measured the use of these standard symptom-relieving allergy medications. Predefined daily maximum scores were assigned to each class of rhinitis and conjunctivitis medication as 0=none, 6=oral antihistamine, 6=ocular antihistamine, and 8=nasal corticosteroid.

The primary endpoint was the difference between the treatment and placebo groups in the average TCRS during approximately the last 8 weeks of treatment. The TCRS represents the sum of the daily rhinitis DSS and the rhinitis DMS. Other secondary endpoints in this study included the average rhinitis DSS, the average rhinitis DMS, and the Total Combined Score (TCS). The TCS represents the sum of the rhinoconjunctivitis DSS and the rhinoconjunctivitis DMS, which was then averaged during approximately the last 8 weeks of treatment.

Participants in this study were required to stop taking symptom-relieving allergy medication during the baseline period. The mean rhinitis DSS at baseline was 7.94 out of 12 total points in both the treatment arm and in the placebo arm. The results of this study are shown in Table 6. Consistent results across age groups were observed, supporting a similar treatment effect in adolescent and adult subgroups.

Table 6: Total Combined Rhinitis Score (TCRS), Rhinitis Daily Symptom Score (DSS), Rhinitis Daily Medication Score (DMS), and Total Combined Score (TCS) During the Last 8 Weeks of Treatment with ODACTRA in Participants 12 Years of Age and Older (Study 1, Field Efficacy Study)

Endpoint*	ODACTRA (n=566)† Score‡	Placebo (n=620)† Score‡	Treatment Difference (ODACTRA-Placebo)	Difference Relative to Placebo§ Estimate (95% CI)
Primary Endpoint				
TCRS¶	4.10	4.95	-0.80	-17.2% (-25.0%, -9.7%)
Secondary Endpoints				
Rhinitis DSS	3.55	4.20	-0.60	-15.5% (-24.4%, -7.3%)
Rhinitis DMS	0.65	0.79	-0.15	-18.4% (-41.0%, 4.3%)
TCS	5.50	6.60	-1.10	-16.7% (-24.6%, -4.0%)

TCRS=Total Combined Rhinitis Score (Rhinitis DSS + Rhinitis DMS); TCS=Total Combined Score (Rhinoconjunctivitis DSS + Rhinoconjunctivitis DMS); CI=Confidence Interval

Analyses were based on the full analysis set (FAS), which included all randomized and treated participants. Participants were analyzed according to the treatment group to which they were randomized.

*Non-parametric analysis for TCRS, Rhinitis DSS, and TCS endpoints; Parametric analysis using zero-inflated log-normal model for Rhinitis DMS endpoint.

†Number of participants in analyses.

‡For TCRS, Rhinitis DSS, and TCS endpoints, the estimated group medians are reported. Treatment difference and that relative to placebo is based on estimated group medians. For Rhinitis DMS, the estimated group means are reported. Treatment difference and that relative to placebo is based on estimated group means.

§Difference relative to placebo computed as: (ODACTRA – placebo)/placebo x 100.

¶The pre-specified criteria for demonstration of efficacy was defined as a TCRS difference relative to placebo less than or equal to -15 percent, and the upper bound of the 95 percent confidence interval (CI) of TCRS difference relative to placebo less than or equal to -10 percent.

Adults

Study 2 (European Field Efficacy Study)

This double-blind, placebo-controlled, randomized field efficacy study evaluated adult participants 18 through 66 years of age comparing ODACTRA (N=318) and placebo (N=338) administered as a sublingual tablet daily for a duration of approximately 12 months. Participants in this study had a history of symptomatic allergic rhinitis when exposed to house dust and were sensitized to *D. farinae* and/or *D. pteronyssinus* as determined by house dust mite specific IgE testing. At study entry, participants were required to be symptomatic despite taking symptom-relieving allergy medications during the baseline period.

In this study, 46% of participants had asthma, 97% had conjunctivitis and 67% were polysensitized to other allergens in addition to HDM, including trees, grass, weeds, animal danders and molds. The study population was 98% White, <1% African American, and <1% Asian; 50% of participants were female. The mean age of participants in this study was 32 years. The primary efficacy endpoint was the difference relative to placebo in the average TCRS during the last 8 weeks of treatment. The mean Rhinitis DSS at baseline was 7.95 out of 12 for the treatment arm and 8.00 out of 12 total points for the placebo arm. The results of this study are shown in Table 7.

Table 7: Total Combined Rhinitis Score (TCRS), Rhinitis Daily Symptom Score (DSS), Rhinitis Daily Medication Score (DMS), and Total Combined Score (TCS) During the Last 8 Weeks of Treatment with ODACTRA in Participants 18 Years of Age and Older (Study 2, European Field Efficacy Study)

Endpoint*	ODACTRA (n)† Score‡	Placebo (n)† Score‡	Treatment Difference (ODACTRA - Placebo)	Difference Relative to Placebo§ Estimate (95% CI)
Primary Endpoint				

TCRS¶	(318) 5.71	(338) 6.81	-1.09	-16.1% (-25.8%, -5.7%)
Secondary Endpoints				
Rhinitis DSS¶	(318) 2.84	(338) 3.31	-0.47	-14.1% (-23.8%, -3.9%)
Rhinitis DMS¶	(318) 2.32	(338) 2.86	-0.54	-18.9% (-34.7%, -1.3%)
TCS#	(241) 7.91	(257) 9.12	-1.21	-13.2% (-23.7%, -1.5%)

TCRS=Total Combined Rhinitis Score (Rhinitis DSS + Rhinitis DMS); TCS=Total Combined Score (Rhinoconjunctivitis DSS + Rhinoconjunctivitis DMS); CI=Confidence Interval

*Parametric analysis using analysis of covariance model for all endpoints.

†Number of participants in analyses.

‡The estimated group least squares means are reported. Treatment difference and that relative to placebo is based on estimated group least squares means.

§Difference relative to placebo computed as: (ODACTRA – placebo)/placebo x 100.

¶Analysis based on FAS-MI: full analysis set with multiple imputations. The analysis treats participants who discontinued the study before the efficacy assessment period as placebo participants. For the primary analysis (FAS-MI) only the absolute difference was pre-specified. Additional analyses describing the corresponding pre-specified relative differences to placebo for the full analysis set (FAS): TCRS: -18.1% (-27.6%, -7.7%); rhinitis DSS: -16.2% (-25.7%, -5.8%); and rhinitis DMS: -21.4% (-36.6%, -3.2%).

#Participants from Serbia and Croatia were excluded from the analysis of TCS because the preferred formulations of antihistamine eyedrops were not available in these countries at the time the study was conducted. The TCS analysis is based on the full analysis set (FAS). All available data used to its full extent, i.e. participants who provided data during the efficacy assessment period.

Study 3 (Environmental Exposure Chamber Study)

This double-blind, placebo-controlled, randomized EEC study evaluated adult participants 18 through 58 years of age comparing ODACTRA (N=42) and placebo (N=41) administered as a sublingual tablet daily for approximately 24 weeks. Participants had a history of symptomatic allergic rhinitis and were sensitized to *D. farinae* and/or *D. pteronyssinus* as determined by HDM specific IgE. In this study, 23% of participants had asthma, 87% had conjunctivitis, and 84% were polysensitized to other allergens in addition to HDM, including tree, grass, weed, animal danders and molds. The participant population was 90% White, <1% African American, 8% Asian, and 43% female. The mean age of participants was 27 years.

The primary endpoint was the difference relative to placebo in the average TNSS at Week 24. The Total Nasal Symptom Score (TNSS) represents the sum of 4 nasal symptoms (runny nose, stuffy nose, sneezing, and itchy nose). Secondary endpoints were the differences relative to placebo in the average TNSS at Weeks 8 and 16 and average Total Symptom Score (TSS) at Week 24, which represents the sum of TNSS plus 2 ocular

symptoms (gritty/itchy eyes and watery eyes). Baseline TNSS following house dust mite EEC challenge prior to treatment was 7.74 out of 12 total points for ODACTRA and 7.32 out of 12 total points for placebo. The results of this study are shown in Table 8.

Table 8: Total Nasal Symptom Score (TNSS) and Total Symptom Score (TSS) During HDM-Allergen Challenge (Study 3, Environmental Exposure Chamber Study)

Endpoint*	ODACTRA (n)† Score‡	Placebo (n)† Score‡	Treatment Difference (ODACTRA - Placebo)	Difference Relative to Placebo§ Estimate (95% CI)
Primary Endpoint				
TNSS – Week 24	(36) 3.83	(34) 7.45	-3.62	-48.6% (-60.2%, -35.3%)
Secondary Endpoints				
TNSS – Week 8	(40) 5.34	(39) 6.71	-1.37	-20.4% (-33.3%, -6.8%)
TNSS – Week 16	(39) 4.82	(38) 6.90	-2.08	-30.1% (-42.3%, -16.8%)
TSS – Week 24	(36) 4.43	(34) 9.27	-4.84	-52.2% (-65.0%, -37.0%)

TNSS=Total Nasal Symptom Score; TSS=Total Symptom Score (TNSS + total ocular symptom score); CI=Confidence Interval

*Parametric analysis using analysis of covariance for all endpoints.

†Number of participants in analyses.

‡The estimated group least squares means are reported. Treatment difference and that relative to placebo is based on estimated group least squares means.

§Difference relative to placebo computed as: (ODACTRA – placebo)/placebo x 100.

Children

Study 6 (European and North American Field Efficacy Study)

Study 6 was a double-blind, placebo-controlled, randomized field efficacy study conducted in Europe, the United States and Canada for a duration of approximately 12 months, that compared the efficacy of ODACTRA (N=693) to placebo (N=706) in the treatment of HDM allergic rhinitis/rhinoconjunctivitis with or without asthma in children 5 through 11 years of age.

Participants were enrolled if they, during the previous year prior to screening, had a history of HDM allergic rhinitis/ rhinoconjunctivitis with symptoms despite having received symptom-relieving medication and were sensitized to *D. farinae* and/or *D. pteronyssinus* as determined by house dust mite specific IgE testing. At study entry, participants were required to be symptomatic despite taking symptom-relieving allergy medications at enrollment.

Of the participants treated with ODACTRA, mean age was 8 years, 67% were male, 99% White, <1% Black or African American, <1% multiple race, <1% Asian, and <1% American Indian or Alaska Native. Participant demographics in the placebo group were similar to the ODACTRA group. In the ODACTRA group, 37% of participants had asthma and 54% were sensitized to other allergens in addition to HDM; the treatment groups were similar with respect to these baseline characteristics.

Together with the parents/caregivers, participants recorded their symptoms and medication use daily in an eDiary for 21 days prior to randomization (baseline) to determine eligibility for the study. Symptoms and medication use were recorded daily during specified eDiary periods during the study. The primary efficacy assessment period was the last 8 weeks of the 1 year treatment period. Based on the data recorded in the eDiaries, the Total Combined Rhinitis Score (TCRS), daily symptom scores (DSS) and daily medication scores (DMS) for rhinitis were calculated. Daily symptoms included four nasal symptoms (runny nose, stuffy nose, sneezing, and itchy nose) and two ocular symptoms (gritty/itchy eyes and watery eyes). Each of these symptoms was individually graded by participants on a scale of 0 (none) to 3 (severe) and then summed. Participants in active and placebo arms of this study were provided with and allowed to take symptom-relieving allergy medications (including oral and ocular antihistamines and nasal corticosteroids) during the study as needed. The DMS measured the use of these standard symptom-relieving allergy medications. Predefined daily maximum scores were assigned to each class of rhinitis and conjunctivitis medication as 0=none, 6=oral antihistamine, 6=ocular antihistamine, and 8=nasal corticosteroid.

The primary endpoint was the difference between the treatment and placebo groups in the average TCRS during the last approximately 8 weeks of treatment. The TCRS represents the sum of the rhinitis DSS and the rhinitis DMS. Other secondary endpoints in this study included the rhinitis DSS, the rhinitis DMS, and Total Combined Score (TCS). The TCS is the sum of the rhinoconjunctivitis DSS and rhinoconjunctivitis DMS, assessed during the last 8 weeks of treatment.

The baseline mean TCRS was approximately 18 in both treatment groups (on a scale of 0-24) and the mean rhinitis DSS and rhinitis DMS were approximately 8 and 10, respectively, in both treatment groups (on a scale of 0-12).

The results of this study are shown in Table 9.

Table 9: Total Combined Rhinitis Score (TCRS), Rhinitis Daily Symptom Score (DSS), Rhinitis Daily Medication Score (DMS), and Total Combined Score (TCS) During the Last 8 Weeks of Treatment with ODACTRA in Participants 5 through 11 Years of Age (Study 6, European and North American Field Efficacy Study)

Endpoint*	ODACTRA (n)† Score‡	Placebo (n)† Score‡	Treatment Difference (ODACTRA - Placebo)	Difference Relative to Placebo§ Estimate (95% CI)
Primary Endpoint¶				
TCRS	(693) 3.4	(706) 4.4	-1.0	-22.0% (-31.1; -12.0)

Secondary Endpoints				
Rhinitis DSS	(693) 1.5	(706) 1.9	-0.4	-22.2% (-30.8; -12.8)
Rhinitis DMS	(693) 1.4	(706) 1.9	-0.5	-25.3% (-38.3; -10.5)
TCS	(693) 4.0	(706) 5.2	-1.1	-22.2% (-31.5; -12.0)

TCRS=Total Combined Rhinitis Score (Rhinitis DSS + Rhinitis DMS); TCS=Total Combined Score (Rhinoconjunctivitis DSS + Rhinoconjunctivitis DMS); CI=Confidence Interval.

*Primary analysis using mixed model analysis of covariance.

†n: number of participants with observations contributing to the analysis.

Analysis based on full analysis set, which included all randomized and treated participants. Participants were analyzed according to the treatment group to which they were randomized.

‡The estimated group least squares means are reported. Treatment difference and that relative to placebo is based on estimated group least squares means.

§Difference relative to placebo computed as: (ODACTRA – placebo)/placebo x 100, 95 CI.

¶The pre-specified criteria for demonstration of efficacy were defined as a TCRS difference relative to placebo less than or equal to -15 percent, and the upper bound of the 95 percent confidence interval of TCRS difference relative to placebo less than or equal to -10 percent.

16 HOW SUPPLIED/STORAGE AND HANDLING

ODACTRA 12 SQ-HDM tablets are white to off-white, circular freeze-dried sublingual tablets with a debossed pentagon detail on one side.

ODACTRA is supplied as follows:

3 blister packages of 10 tablets (30 tablets total). NDC 52709-1701-3

Store at controlled room temperature, 20ºC-25ºC (68ºF-77ºF). Store in the original package until use to protect from moisture.

17 PATIENT COUNSELING INFORMATION

Advise patients (or their parents/guardians) to read the FDA-approved patient labeling (Medication Guide) and to keep ODACTRA and all medicines out of the reach of children.

Severe Allergic Reactions

- Advise patients (or their parents/guardians) that ODACTRA may cause life-threatening systemic or local allergic reactions, including anaphylaxis. Educate patients (or their parents/guardians) about the signs and symptoms of these allergic reactions *[see Warnings and Precautions (5.1)]*. The signs and symptoms of a severe allergic reaction may include: syncope, dizziness, hypotension, tachycardia, dyspnea,

wheezing, bronchospasm, chest discomfort, cough, abdominal pain, vomiting, diarrhea, rash, pruritus, flushing, and urticaria.
- Ensure that patients (or their parents/guardians) have epinephrine and instruct patients (or their parents/guardians) in its proper use. Instruct patients (or their parents/guardians) who experience a severe allergic reaction to seek immediate medical care, discontinue ODACTRA, and resume treatment only when advised by a healthcare professional to do so *[see Warnings and Precautions (5.1).]*
- Advise patients to read the patient information for epinephrine.
- Inform patients (or their parents/guardians) that the first dose of ODACTRA must be administered in a healthcare setting under the supervision of a healthcare professional and that they will be monitored for at least 30 minutes to watch for signs and symptoms of life-threatening systemic or local allergic reaction *[see Warnings and Precautions (5.1)]*.
- Because of the risk of upper airway compromise, instruct patients (or their parents/guardians) with persistent and escalating adverse reactions in the mouth or throat to discontinue ODACTRA and to contact their healthcare professional *[see Warnings and Precautions (5.2)].*
- Because of the risk of eosinophilic esophagitis, instruct patients (or their parents/guardians) with severe or persistent symptoms of esophagitis to discontinue ODACTRA and to contact their healthcare professional *[see Warnings and Precautions (5.3)].*

Asthma
- Instruct patients (or their parents/guardians) with asthma that if they have difficulty breathing or if their asthma becomes difficult to control, they should stop taking ODACTRA and contact their healthcare professional immediately *[see Warnings and Precautions (5.4)]*.

Administration Instructions
- Instruct patients (or their parents/guardians) to carefully remove the foil from the blister unit with dry hands and then take the sublingual tablet immediately by placing it under the tongue where it will dissolve within 10 seconds. Instruct patients to avoid swallowing for at least 1 minute. Also instruct patients to wash their hands after handling the tablet, and to avoid food or beverages for 5 minutes after taking the tablet *[see Dosage and Administration (2.2)].*
- Advise patients (or their parents/guardians) who miss more than one dose of ODACTRA to contact their healthcare professional before restarting *[see Warning and Precautions (5.1)]*.

Manufactured for: ALK-Abelló A/S

ALK-Abelló A/S, Bøge Allé 6-8, DK-2970 Hørsholm, Denmark

U.S. License No. 1292

Manufactured by:
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MEDICATION GUIDE
ODACTRA™ (OH-dack-trah)
House Dust Mite (*Dermatophagoides farinae* and *Dermatophagoides pteronyssinus*) Allergen Extract
Sublingual Tablets

Carefully read this Medication Guide before you or your child starts taking ODACTRA and each time you get a refill. This Medication Guide does not take the place of talking with your healthcare provider about your or your child's medical condition or treatment. Talk with your healthcare provider if there is something you do not understand or if you want to learn more about ODACTRA.

What is the Most Important Information I Should Know about ODACTRA?

ODACTRA can cause severe allergic reactions that may be life-threatening. Stop taking ODACTRA and get medical treatment right away if you or your child has any of the following symptoms after taking ODACTRA:

- Trouble breathing
- Throat tightness or swelling
- Trouble swallowing or speaking
- Dizziness or fainting
- Rapid or weak heartbeat
- Severe stomach cramps or pain, vomiting, or diarrhea
- Severe flushing or itching of the skin

For home administration of ODACTRA, your doctor will prescribe epinephrine, a medicine you can use if you or your child has a severe allergic reaction after taking ODACTRA. Your doctor will train and instruct you on the proper use of epinephrine.
Talk to your doctor or read the epinephrine patient information if you have any questions about the use of epinephrine.

What is ODACTRA?

ODACTRA is a prescription medicine used for sublingual (under the tongue) immunotherapy to treat house dust mite allergies that can cause sneezing, runny or itchy nose, stuffy or congested nose, or itchy and watery eyes. ODACTRA may be prescribed for persons 5 through 65 years of age who are allergic to house dust mites.
ODACTRA is NOT a medication that gives immediate relief for symptoms of house dust mite allergy.

Who Should Not Take ODACTRA?

You or your child should not take ODACTRA if you or your child:

- has severe, unstable or uncontrolled asthma
- had a severe allergic reaction in the past that included any of these symptoms:
  - Trouble breathing
  - Dizziness or fainting

- Rapid or weak heartbeat

- has ever had difficulty with breathing due to swelling of the throat or upper airway after using any sublingual immunotherapy before.
- has ever been diagnosed with eosinophilic esophagitis.
- is allergic to any of the inactive ingredients contained in ODACTRA. The inactive ingredients contained in ODACTRA are: gelatin, mannitol, and sodium hydroxide.

What Should I Tell My Doctor Before Taking ODACTRA?

Your doctor may decide that ODACTRA is not the best treatment if you or your child:

- has asthma, depending on how severe it is.
- suffers from lung disease such as chronic obstructive pulmonary disease (COPD).
- suffers from heart disease such as coronary artery disease, an irregular heart rhythm, or you or your child has hypertension that is not well controlled.
- is pregnant, plans to become pregnant during the time you will be taking ODACTRA, or is breast-feeding.
- is unable or unwilling to administer epinephrine to treat a severe allergic reaction to ODACTRA.
- is taking certain medicines that enhance the likelihood of a severe reaction, or interfere with the treatment of a severe reaction. These medicines include:
  - beta blockers and alpha-blockers (prescribed for high blood pressure)
  - cardiac glycosides (prescribed for heart failure or problems with heart rhythm)
  - diuretics (prescribed for heart conditions and high blood pressure)
  - ergot alkaloids (prescribed for migraine headache)
  - monoamine oxidase inhibitors or tricyclic antidepressants (prescribed for depression)
  - thyroid hormone (prescribed for low thyroid activity).

- is receiving allergy shots or other immunotherapy under the tongue. Use of more than one of these types of medicines together may increase the likelihood of a severe allergic reaction.

You should tell your doctor if you or your child is taking or has recently taken any other medicines, including medicines obtained without a prescription and herbal supplements. Keep a list of them and show it to your doctor and pharmacist each time you get a new supply of ODACTRA. Ask your doctor or pharmacist for advice before taking ODACTRA.

ODACTRA is not indicated for use in children under 5 years of age or adults over 65 years of age.

Are there any Reasons to Stop Taking ODACTRA?

Stop ODACTRA and contact your doctor if you or your child has any of the following after taking ODACTRA:

- Any type of a serious allergic reaction
- Throat tightness that worsens or swelling of the tongue or throat that causes trouble speaking, breathing, or swallowing

- Asthma or any other breathing condition that gets worse
- Dizziness or fainting
- Rapid or weak heartbeat
- Severe stomach cramps or pain, vomiting, or diarrhea
- Severe flushing or itching of the skin
- Heartburn, difficulty swallowing, pain with swallowing, or chest pain that does not go away or worsens

Also, stop taking ODACTRA following mouth surgery procedures (such as tooth removal), tooth loss or if you or your child develops any mouth infections, ulcers or cuts in the mouth or throat to allow complete healing.

How Should I Take ODACTRA?

Take ODACTRA exactly as your doctor tells you.
ODACTRA is a prescription medicine that is placed under the tongue.

- Take the tablet from the blister package after carefully removing the foil with dry hands.
- Place the tablet immediately under the tongue where it will dissolve within 10 seconds. Do not swallow for at least 1 minute.
- Do not take ODACTRA with food or beverage. Food and beverage should not be taken for the following 5 minutes.
- Wash hands after taking the tablet.

Take the first tablet of ODACTRA in the prescribing doctor’s office. After taking the first tablet, you or your child will be watched for at least 30 minutes for symptoms of a serious allergic reaction.
If you tolerate the first tablet of ODACTRA, you or your child will continue ODACTRA therapy at home by taking one tablet every day. Children should be given each tablet of ODACTRA by an adult who will watch for any symptoms of a serious allergic reaction.
Take ODACTRA every day for as long as your doctor prescribes it, even if you have no allergy symptoms.
If you or your child forgets to take ODACTRA, do not take two tablets. Take the next tablet at your normal scheduled time the next day. If you or your child misses more than one dose of ODACTRA, contact your healthcare provider before restarting.
You or your child may begin to have relief of your house dust mite allergy symptoms within 2 to 3 months of starting ODACTRA.

What are the Possible Side Effects of ODACTRA?

The most commonly reported side effects were throat irritation/tickle, itching in the mouth or ears, swelling of the back of the mouth, lips or tongue, tongue pain, nausea, throat swelling, stomach pain, tongue ulcer/sore on the tongue, and mouth ulcer/sore in the mouth, diarrhea, vomiting, and food tastes different. These side effects, by themselves, were not dangerous or life-threatening. Typically, these common side effects begin within the first week of starting ODACTRA and may reoccur for up to two weeks. These common side effects experienced after taking the first tablet typically last up to one hour.
ODACTRA can cause severe allergic reactions that may be life-threatening. Symptoms of allergic reactions to ODACTRA include:

- Trouble breathing
- Throat tightness or swelling

- Trouble swallowing or speaking
- Dizziness or fainting
- Rapid or weak heartbeat
- Severe stomach cramps or pain, vomiting, or diarrhea
- Severe flushing or itching of the skin

For additional information on the possible side effects of ODACTRA talk with your doctor or pharmacist. You may report side effects to the U.S. Food and Drug Administration (FDA) at 1-800-FDA-1088 or www.fda.gov/medwatch.

How Should I Store ODACTRA?

Keep ODACTRA out of the reach of children.
Throw away any unused ODACTRA after the expiration date which is stated on the carton and blister pack after "EXP."
Store ODACTRA in a dry place at room temperature, 20ºC to 25ºC (68ºF to 77ºF), in the original package.

General Information about ODACTRA

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use ODACTRA for a condition for which it was not prescribed. Do not give ODACTRA to other people, even if they have the same symptoms. It may harm them.
This Medication Guide summarizes the most important information about ODACTRA. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about ODACTRA that was written for healthcare professionals.
For more information, go to: www.ODACTRA.com or call 1-855-782-9323 (toll-free).

Manufactured for: ALK-Abelló A/S

ALK-Abelló A/S, Bøge Allé 6-8, DK-2970 Hørsholm, Denmark
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Swindon, Wiltshire, SN5 8RU UK

This Medication Guide has been approved by the U.S. Food and Drug Administration.
Revised: 2/2025

PRINCIPAL DISPLAY PANEL

NDC 52709-1701-3
House Dust Mite (*Dermatophagoides farinae* and *Dermatophagoides pteronyssinus*) Allergen Extract
ODACTRA

Sublingual Tablets
3 blister packages of 10 tablets (30 tablets total).

ODACTRA

dermatophagoides pteronyssinus and dermatophagoides farinae tablet

Product Information			
Product Type	STANDARDIZED ALLERGENIC	**Item Code (Source)**	NDC:52709-1701
Route of Administration	SUBLINGUAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
DERMATOPHAGOIDES PTERONYSSINUS (UNII: 57L1Z5378K) (DERMATOPHAGOIDES PTERONYSSINUS - UNII:57L1Z5378K)	DERMATOPHAGOIDES PTERONYSSINUS	6 [arb'U]
DERMATOPHAGOIDES FARINAE (UNII: PR9U2YPF3Q) (DERMATOPHAGOIDES FARINAE - UNII:PR9U2YPF3Q)	DERMATOPHAGOIDES FARINAE	6 [arb'U]

Inactive Ingredients	
Ingredient Name	**Strength**

MARINE NON-GELLING GELATIN, HIGH MW (UNII: AHQ60JKI5D)	
MARINE NON-GELLING GELATIN (UNII: JSM64OJO9B)	
MANNITOL (UNII: 3OWL53L36A)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	

Product Characteristics

Color	white (white to off-white)	**Score**	no score
Shape	ROUND	**Size**	12mm
Flavor		**Imprint Code**	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:52709-1701-3	3 in 1 CARTON		
1	NDC:52709-1701-1	10 in 1 BLISTER PACK; Type 0: Not a Combination Product		
2	NDC:52709-1701-5	1 in 1 CARTON		
2		5 in 1 BLISTER PACK; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA125592	01/01/2018	

Labeler - ALK-Abello A S (306020926)

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