WITH MORE ALLERGY IMMUNOTHERAPY OPTIONS, YOU CAN TREAT MORE PATIENTS...

IT'S YOUR MOVE.

ODACTRA is the *first* and *only* FDA-approved sublingual tablet for house dust mite–induced allergic rhinitis, with or without conjunctivitis.

Important Safety Information

WARNING: SEVERE ALLERGIC REACTIONS

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

Indication

ODACTRA is an allergen extract indicated as immunotherapy for house dust mite (HDM)-induced allergic rhinitis, with or without conjunctivitis, confirmed by *in vitro* testing for IgE antibodies to *Dermatophagoides farinae* or *Dermatophagoides pteronyssinus* house dust mites, or skin testing to licensed house dust mite allergen extracts. ODACTRA is approved for use in adults 18 through 65 years of age. ODACTRA is not indicated for the immediate relief of allergic symptoms.

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

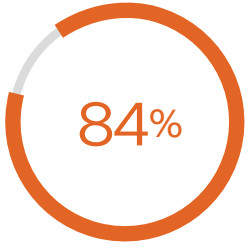
ODACTRA™

House Dust Mite (*Dermatophagoides farinae* and *Dermatophagoides pteronyssinus*) Allergen Extract Tablet for Sublingual Use 12 SQ-HDM

Can your appropriate polysensitized patients benefit from ODACTRA?

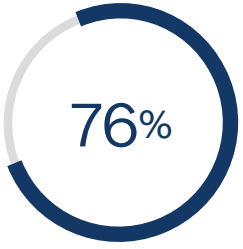
ODACTRA was effective regardless of sensitization status[1,2]

Environmental Exposure Chamber Study (Study 3)



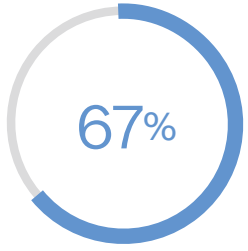
of patients were polysensitized[3]

North American Study (Field Study 1)



of patients were polysensitized[3]

European Study (Field Study 2)



of patients were polysensitized[3]

In the pivotal studies, polysensitized patients were defined as having confirmed diagnosis of HDM-induced AR and additional sensitivities to other allergens, including[3]

Important Safety Information

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 [gelatin, mannitol and sodium hydroxide] contained in this product

Proven efficacy in HDM-induced AR

ODACTRA was studied in the largest clinical trial program in the history of AIT[4]

Involving

>6000

patients with HDM-induced AR

Important Safety Information (continued)

The most common solicited adverse reactions reported in clinical studies for subjects 18 through 65 years of age treated with ODACTRA vs placebo included throat irritation/tickle (67.0% vs 20.8%), itching in the mouth (61.3% vs 14.1%), itching in the ear (51.7% vs 11.7%), and swelling of the uvula/back of the mouth (19.8% vs 2.4%).

AIT=allergy immunotherapy; AR=allergic rhinitis; HDM=house dust mite.

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In the Environmental Exposure Chamber Study...

Proven efficacy that starts to work as early as week 8[5]

ODACTRA significantly reduced nasal symptoms[5]

- The efficacy of ODACTRA in monosensitized and polysensitized patients was demonstrated in a chamber study in which patients underwent 6-hour exposure challenges to determine the average TNSS at week 24[5]
- Statistically significant reductions in the nasal symptoms of AR occurred as early as week 8 and continued to improve toward week 24, the primary end point[3,5]

Reduction in TNSS

WEEK 8 (SECONDARY END POINT)[3,5]

20.4%
REDUCTION IN TNSS*

ODACTRA: 5.34 (n=40)
Placebo: 6.71 (n=39)
95% CI: −33.3%, −6.8%
(*P*<.05)

WEEK 24 (PRIMARY END POINT)[3,5]

48.6%
REDUCTION IN TNSS

ODACTRA: 3.83 (n=36)
Placebo: 7.45 (n=34)
95% CI: −60.2%, −35.3%
(*P*<.05)

- IgG_4 levels increased with ODACTRA vs placebo at week 8 based on the prespecified analyses (*P*<.001)[5]

Important Safety Information (continued)

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. Educate patients to recognize the signs and symptoms of these allergic reactions and instruct them to seek immediate medical care and discontinue therapy should any of these occur. Allergic reactions may require treatment with epinephrine.

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

AR=allergic rhinitis; HDM=house dust mite; IgG_4=immunoglobulin G subclass 4; TNSS=total nasal symptom score; TOSS=total ocular symptom score.

*TNSS is defined as a total score comprising the following: rhinorrhea, nasal congestion, nasal itching, and sneezing.

ODACTRA significantly reduced ocular symptoms[5]

- Significant improvements in ocular symptoms (a secondary end point) relative to placebo were observed at weeks 8 and 24 for ODACTRA vs placebo[5]

Reduction in TOSS

WEEK 24[5]

67.9%
REDUCTION IN TOSS

ODACTRA: 0.61 (n=40)
Placebo: 1.87 (n=40)
95% CI: −87.4%, −41.2%
(*P*<.001)

Study design: A randomized, single-site, placebo-controlled, double-blind, onset-of-action trial was conducted for 24 weeks in adults aged ≥18 years with HDM-induced AR/conjunctivitis, with or without asthma (N=83; ODACTRA=42, placebo=41), using the Vienna Challenge Chamber. Mean age (years/range) was 28 (18-58) for the ODACTRA patients and 27 (19-43) for placebo patients. Mean duration of AR/conjunctivitis was 16 years and 17 years for ODACTRA and placebo patients, respectively. Of ODACTRA patients, 88% were polysensitized. Patients received ODACTRA or placebo and symptoms were scored every 15 minutes during exposure challenges, which occurred at screening and at weeks 8, 16, and 24. The primary efficacy end point was the average TNSS at week 24, which was the sum of the 4 nasal symptoms (runny nose, blocked nose, sneezing, and itchy nose), with a maximum score of 12. A key secondary end point was the average TOSS at weeks 8, 16, and 24. The TOSS was the sum of the 2 ocular symptoms (gritty/red/itchy eyes and watery eyes). There were 10 patients and 9 patients with asthma (ODACTRA and placebo, respectively).[5]

Important Safety Information (continued)

Administer the initial dose of ODACTRA 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 ODACTRA.

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

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In the North American Field Efficacy Study...

Statistically significant effects on HDM-induced AR[1]

ODACTRA reduced TCRS in monosensitized and polysensitized patients[1]

- During the last 8 weeks of the 52-week treatment period, ODACTRA with symptomatic medications produced a significant incremental reduction in AR symptoms vs symptomatic medications alone[3]

Reduction in TCRS

This study was designed to prove clinically significant reduction in symptoms and medication use by 15%, as defined by the FDA[3]

17.2%
REDUCTION IN TCRS[3,*]

ODACTRA: 4.10 (n=566)
Placebo: 4.95 (n=620)
95% CI: −25.0%, −9.7%
(*P*<.001)

- In this study, 31% of subjects had asthma, 48% had conjunctivitis, and 76% were polysensitized to other allergens in addition to HDM[3]
- Do not administer ODACTRA to patients with severe, unstable, or uncontrolled asthma[3]

Important Safety Information (continued)

Patients who have persistent and escalating adverse reactions in the mouth or throat should be considered for discontinuation of ODACTRA.

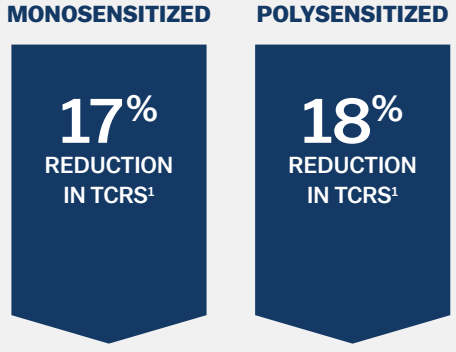
Eosinophilic esophagitis has been reported in association with sublingual tablet immunotherapy. Discontinue ODACTRA and consider a diagnosis of eosinophilic esophagitis in patients who experience severe or persistent gastro-esophageal symptoms including dysphagia or chest pain.

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.

*TCRS is defined as the sum of the rhinitis DSS and the rhinitis DMS.

ODACTRA was effective regardless of sensitization status[1]

Reduction in TCRS in patient subgroups



Study design: A randomized, multicenter, placebo-controlled, double-blind trial was conducted for 52 weeks in patients aged ≥12 years with HDM-induced AR/conjunctivitis, with or without asthma (N=1482; ODACTRA=741, placebo=741). Mean age (years ± SD) was 35 ± 14 for ODACTRA patients and 35 ± 14 for placebo patients. Mean duration of AR was 18 ± 13 years and 19 ± 13 years for ODACTRA and placebo patients, respectively. Of ODACTRA patients, 75% were polysensitized. Patients received ODACTRA or placebo, with the efficacy assessment occurring during the last 8 weeks of treatment, when HDM exposure per physician judgment was expected to be at its peak. The primary efficacy end point was the average TCRS during the last 8 weeks of treatment. The TCRS was the sum of the rhinitis DSS and rhinitis DMS. The rhinitis DSS was the sum of 4 nasal symptoms (runny nose, stuffy nose, sneezing, and itchy nose) scored on a scale of 0 (none) to 3 (severe). The rhinitis DMS was calculated based on daily use of symptom-relieving medications for nasal symptoms.[1,3]

Important Safety Information (continued)

ODACTRA 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.

AR=allergic rhinitis; DMS=daily medication score; DSS=daily symptom score; HDM=house dust mite; TCRS=total combined rhinitis score.

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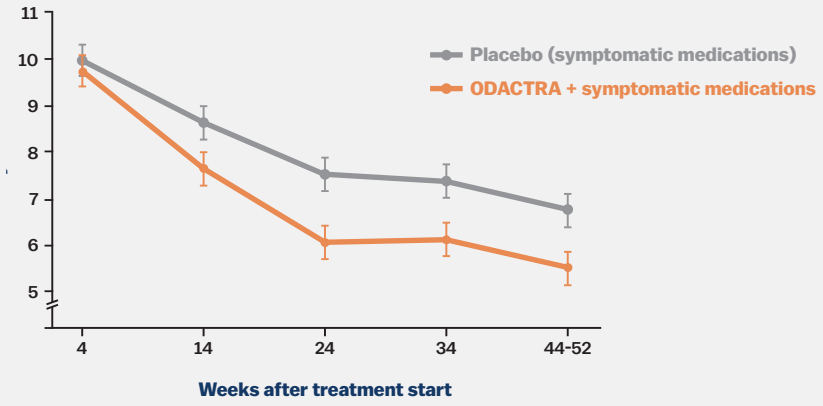
Demonstrated efficacy throughout the year, including polysensitized patients[2]

- The efficacy of ODACTRA in monosensitized and polysensitized patients was demonstrated despite the use of pharmacotherapy, with proven clinical relevance according to a predefined criterion[2,3]
- Statistically significant reduction in combined nasal symptom and medication usage scores occurred as early as week 14 and continued throughout the year[2]

Reduction in TCRS* over 52 weeks



Adapted from Demoly P et al. *J Allergy Clin Immunol*. 2016;137(2):444-451.

- During the last 8 weeks of treatment, ODACTRA with symptomatic medications produced a 16.1% reduction in TCRS compared with symptomatic medications alone (5.71 [n=318] vs 6.81 [n=388]; 95% CI: −25.8, −5.7)[3]

Important Safety Information (continued)

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 or dental extraction.

*TCRS is defined as the sum of the rhinitis DSS and the rhinitis DMS.

Statistically significant reduction in AR symptoms as well as in individual symptoms[2,3]

- 14.1% reduction in rhinitis DSS compared with symptomatic medications alone (95% CI: −23.8%, −3.9%; *P*=.003)[2,3]
- AR symptoms that were measured included[2]
  - Runny nose
  - Blocked nose
  - Sneezing
  - Itchy nose

Statistically significant reduction in AR medications[2,3]

- 18.9% reduction in rhinitis DMS compared with symptomatic medications alone (95% CI: −34.7%, −1.3%; *P*=.024)[3]
- AR medications that were measured included[2]
  - Oral antihistamine (desloratadine tablets, 5 mg)
  - Nasal steroid (budesonide nasal spray, 64 mcg/dose)

Study design: A randomized, multinational, multicenter, placebo-controlled, double-blind trial was conducted for 52 weeks in patients aged 18 to 66 years with HDM-induced AR, with or without asthma, and conjunctivitis (N=656). Mean age (years) was 32.1 ± 10.6 for ODACTRA patients and 32.2 ± 10.9 for placebo patients. There were 152 patients with HDM-induced allergic asthma for both ODACTRA and placebo. Mean duration of AR/conjunctivitis was 9.8 years and 10.0 years for ODACTRA and placebo patients, respectively. Of ODACTRA patients, 66% were polysensitized. Patients received ODACTRA or placebo, with the efficacy assessment occurring during the last 8 weeks of treatment (October 1 through March 15) to avoid overlapping symptoms caused by pollen allergy. The primary efficacy end point was the average TCRS during the last 8 weeks of treatment. The TCRS was the sum of the rhinitis DSS and rhinitis DMS. The rhinitis DSS was the sum of 4 nasal symptoms (runny nose, stuffy nose, sneezing, and itchy nose) scored on a scale of 0 (none) to 3 (severe). The rhinitis DMS was calculated based on daily use of symptom-relieving medications for nasal symptoms.[2,3]

Important Safety Information (continued)

The most common solicited adverse reactions reported in clinical studies for subjects 18 through 65 years of age treated with ODACTRA vs placebo included throat irritation/tickle (67.0% vs 20.8%), itching in the mouth (61.3% vs 14.1%), itching in the ear (51.7% vs 11.7%), and swelling of the uvula/back of the mouth (19.8% vs 2.4%).

AR=allergic rhinitis; DMS=daily medication score; DSS=daily symptom score; HDM=house dust mite; TCRS=total combined rhinitis score.

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Set patient expectations on anticipated adverse events

Maximize treatment success by setting patient expectations of adverse events, which were generally mild to moderate and local in clinical studies[3]

- As with all allergy immunotherapies, auto-injectable epinephrine is used to manage any serious adverse reactions that may occur, such as anaphylaxis, which can include trouble breathing, dizziness, and nausea, vomiting, and diarrhea; however, use of epinephrine was rare and occurred at a rate of only 0.4% (5/1279) for patients receiving ODACTRA vs 0.2% (3/1277) for patients receiving placebo[3,6]
- In Field Study 1,* adverse events tended to be brief (median duration, 30 to 60 minutes), occurred early (within minutes of administration during the first 1 to 7 days), and were limited in recurrence (resolution within <2 weeks)[3]
- Overall discontinuation rates due to adverse events were 8.1% and 3.0% for ODACTRA and placebo, respectively[3]

Percentage of solicited adverse reactions within 28 days after initiation of treatment (Field Study 1,* Safety Analysis Set)[3]

Adverse Reaction	Adverse Reactions of Any Intensity		Adverse Reactions That Were Severe	
	ODACTRA (n=640)	Placebo (n=631)	ODACTRA (n=640)	Placebo (n=631)
Throat irritation/tickle	67.0%	20.8%	0.3%	–
Itching in the mouth	61.3%	14.1%	0.2%	–
Itching in the ear	51.7%	11.7%	0.3%	–
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%	–	–
Throat swelling	13.6%	2.4%	0.2%	–
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%	–	–
Taste alteration/food tastes different	10.0%	3.6%	–	–
Diarrhea	6.9%	3.6%	–	–
Vomiting	2.5%	1.4%	–	–

*North American Field Efficacy Study.

Important Safety Information (continued)

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. Available data on ODACTRA administered to pregnant women are insufficient to inform associated risks in pregnancy.

One tablet, once a day, for unique dosing flexibility

Refer patients to Administration Instructions under "Patient Counseling Information" in the ODACTRA Prescribing Information

Administer first dose in a health care setting under the supervision of a medical professional[3]

Observe the patient for at least 30 minutes to monitor for signs or symptoms of a severe systemic or local allergic reaction[3]

If patient tolerates the first dose, subsequent doses may be taken at home[3,†]

Practice guidelines recommend that patients receiving SCIT for HDM allergens be treated for 3 to 5 years to obtain maximum benefits[7]

Dosing convenience to keep up with a busy lifestyle

Important Safety Information (continued)

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

HDM=house dust mite; SCIT=subcutaneous immunotherapy.

†If a missed dose occurs, it is recommended that the next dose be taken at the normally scheduled time. If more than one dose is missed, patients should contact their physician to discuss re-initiation. In clinical trials, treatment interruptions for up to 7 days were allowed.[3]

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With more AIT options, you can treat more patients...

IT'S YOUR MOVE.

ODACTRA is appropriate for patients with HDM-induced AR, with or without conjunctivitis, who may not be a good fit for SCIT

- Similar results in monosensitized and polysensitized patients in clinical studies[1,2]
- Demonstrated relief of allergic symptoms as early as 8 weeks that continued throughout the year[2,5]
  - ODACTRA is not indicated for the immediate relief of allergic symptoms
- Appropriate for HDM-allergic patients with well-controlled asthma[1]
  - Do not administer ODACTRA to patients with severe, unstable, or uncontrolled asthma[3]
- Use of auto-injectable epinephrine was rare and occurred at a rate of only 0.4% in patients receiving ODACTRA vs 0.2% for placebo[3]
- Adverse events were generally mild to moderate, local, and well tolerated[3]
- ALK is committed to research that furthers your treatment of patients in need of AIT

For more information about ODACTRA, please visit www.ODACTRAHCP.com.

References: 1. Nolte H, Bernstein DI, Nelson HS, et al. Efficacy of house dust mite sublingual immunotherapy tablet in North American adolescents and adults in a randomized, placebo-controlled trial. *J Allergy Clin Immunol*. 2016;138(6):1631-1638. **2.** Demoly P, Emminger W, Rehm D, Backer V, Tommerup L, Kleine-Tebbe J. Effective treatment of house dust mite–induced allergic rhinitis with 2 doses of the SQ HDM SLIT-tablet: results from a randomized, double-blind, placebo-controlled phase III trial. *J Allergy Clin Immunol*. 2016;137(2):444-451. **3.** ODACTRA [prescribing information]. Hørsholm, Denmark: ALK; 2017. **4.** Data on file. Merck Sharp & Dohme Corp. Whitehouse Station, NJ: 2017. **5.** Nolte H, Maloney J, Nelson HS, et al. Onset and dose-related efficacy of house dust mite sublingual immunotherapy tablets in an environmental exposure chamber. *J Allergy Clin Immunol*. 2015;135(6):1494-1501.e6. **6.** Anaphylaxis. American College of Allergy, Asthma, and Immunology website. http://www.acaai.org/allergies/anaphylaxis. Accessed September 14, 2017. **7.** Portnoy J, Miller JD, Williams PB, et al; Joint Taskforce on Practice Parameters; Practice Parameter Workgroup. Environmental assessment and exposure control of dust mites: a practice parameter. *Ann Allergy Asthma Immunol*. 2013;111(6):465-507.

Important Safety Information (continued)

The most common solicited adverse reactions reported in clinical studies for subjects 18 through 65 years of age treated with ODACTRA vs placebo included throat irritation/tickle (67.0% vs 20.8%), itching in the mouth (61.3% vs 14.1%), itching in the ear (51.7% vs 11.7%), and swelling of the uvula/back of the mouth (19.8% vs 2.4%).

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