CENTENE PHARMACY AND THERAPEUTICS
NEW DRUG REVIEW
3Q17 July – August

BRAND NAME
Odactra™

GENERIC NAME
House dust mite (Dermatophagoides farinae and Dermatophagoides pteronyssinus) allergen extract

MANUFACTURER
ALK-Abelló

DATE OF APPROVAL
March 1, 2017

PRODUCT LAUNCH DATE
Undetermined at the time of review; Pending strategy review in U.S. due to end in partnership with Merck & Co.

REVIEW TYPE

☒ Review type 1 (RT1): New Drug Review
Full review of new chemical or biologic agents

☐ Review type 2 (RT2): New Indication Review
Abbreviated review of new dosage forms of existing agents that are approved for a new indication or use

☐ Review type 3 (RT3): Expedited CMS Protected Class Drug Review
Expedited abbreviated review of Centers for Medicare & Medicaid Services protected class drugs (anticonvulsants, antidepressants, antineoplastic, antipsychotics, antiretrovirals, and immunosuppressants)

☐ Review type 5 (RT5): Abbreviated Reviews for Intravenous Chemotherapy Agents
Abbreviated review for intravenous chemotherapy agents which are usually covered under the medical benefit

FDA APPROVED INDICATION(S)
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 in adults 18 years through 65 years of age.

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OFF-LABEL USES
Not applicable

CLINICAL EFFICACY[1,2,3,4]
The efficacy of Odactra for the treatment of house dust mite (HDM)-induced allergic rhinitis was investigated in two double-blind, placebo-controlled, randomized clinical field efficacy studies (Studies 1 and 2) and one environmental exposure chamber (EEC) study.

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. Subjects 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. Subjects were required to be symptomatic and were not taking symptom-relieving allergy medications at enrollment. Subjects 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 subjects 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 subject population was 76% White, 11% African American, 7% Asian, and 59% female. The mean age of subjects 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 subjects daily on a scale of 0 (none) to 3 (severe) and then summed. Subjects 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.

Secondary endpoints included the average rhinitis DSS, rhinitis DMS, total combined score (TCS; sum of rhinoconjunctivitis DSS and rhinoconjunctivitis DMS), and AR/C symptoms assessed by using a visual analog scale (VAS; scale 5 0-100) during the last 8 weeks of treatment

Subjects 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 primary efficacy results showed that during the efficacy assessment period, a statistically significantly lower average TCRS was observed with 12 SQ-HDM compared to placebo ($P < 0.001$) with a treatment difference based on medians corresponding to an improvement of 17% (95% CI, 10% to 25%). From baseline TCRS of 7.94 in both arms, average TCRS during the last 8 week of treatment decreased to 4.10 (95% CI, 2.00 to 6.40) in the treatment arm versus 4.95 in the placebo arm (95% CI, 2.70 to 7.55), with a treatment difference of -0.80 (95% CI, -1.20 to -0.40; $p < 0.001$). One patient discontinued treatment in the active arm due to lack of efficacy.

Study 2 (European Field Efficacy Study)
This double-blind, placebo-controlled, randomized field efficacy study evaluated adult subjects 18 through 66 years of age comparing Odactra (12 SQ-HDM) (N=318), 6 SQ-HDM (N=336), and placebo (N=338) administered as a sublingual tablet daily for a duration of approximately 12 months in 12 European countries. Subjects 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, subjects were required to be symptomatic despite taking symptom-relieving allergy medications during the baseline period.

In this study, 46% of subjects 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 subjects were female. The mean age of subjects 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.

Key secondary end points were AR symptom, AR medication, Rhinoconjunctivitis quality of life questionnaire with standardized activities (RQLQ), and total rhinoconjunctivitis scores averaged over the last 8 weeks of treatment.

The primary efficacy results showed that the absolute reduction in the TCRS compared with the placebo group was 1.18 ($P < 0.002$) for the 6 SQ-HDM group and 1.22 ($P < 0.001$) for the 12

SQ-HDM group. The primary analysis showed a statistically significant difference from placebo for both active groups, being greater than the prespecified clinical relevance criterion of an absolute difference of 1 compared with placebo. Relative differences from the placebo group in TCRS by using adjusted means and medians ranged from 18% to 22%. The difference from placebo was numerically higher for the 12 SQ-HDM group than for the 6 SQ-HDM group,

Two patients discontinued treatment from the 6 SQ-HDM arm as well as from the placebo arm due to lack of efficacy.

Study 3 (Environmental Exposure Chamber Study)
This double-blind, placebo-controlled, randomized environmental exposure (EEC) study evaluated adult subjects 18 through 58 years of age comparing Odactra (N=42) and placebo (N=41) administered as a sublingual tablet daily for approximately 24 weeks. Subjects 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 subjects 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 subject population was 90% White, <1% African American, 8% Asian, and 43% female. The mean age of subjects was 27 years.

The primary endpoint was the difference relative to placebo in the average Total Nasal Symptom Score (TNSS) at Week 24. The 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 primary efficacy results showed that at week 24 (primary efficacy evaluation time point), the improvement in TNSSs relative to placebo was 48.6% (95% CI, 35.3% to 60.2%) with the 12 SQ-HDM dose and 26.6% (95% CI, 11.2% to 39.6%) with the 6 SQ-HDM dose. The mean differences in TNSSs versus placebo at week 24 were significant for both the 12 SQ-HDM and 6 SQ-HDM doses, with a treatment difference of -3.62 in TNSS vs placebo in the 12 SQ-HDM arm.

CONTRAINDICATIONS
Odactra is contraindicated in:
- Severe, unstable or uncontrolled asthma
- History of any severe systemic allergic reaction or any severe local reaction to sublingual allergen immunotherapy
- A history of eosinophilic esophagitis
- Hypersensitivity to any of the inactive ingredients contained in this product

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BLACK BOX WARNINGS

- 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.

DRUG INTERACTIONS

Not applicable

ADVERSE REACTIONS

The most common solicited adverse reactions reported in ≥10% of subjects 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
- nausea
- tongue pain
- throat swelling
- tongue ulcer/sore on the tongue
- stomach pain
- mouth ulcer/sore in the mouth
- taste alteration/food tastes different

DOSAGE AND ADMINISTRATION

One tablet daily; Place the tablet immediately under the tongue where it will dissolve within 10 seconds. Do not swallow for at least 1 minute. Administer the first dose of Odactra under the supervision of a physician with experience in the diagnosis and treatment of allergic diseases. Observe patients in the office for at least 30 minutes following the initial dose.

PRODUCT AVAILABILITY

Tablet: 12 SQ-HDM

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THERAPEUTIC ALTERNATIVES

DRUG NAME	USAGE REGIMEN (route of admin/frequency of use)	COMMENTS
Subcutaneous Immunotherapy (SCIT)	Various	
OTC loratadine (Claritin)	10 mg PO QD	
OTC loratadine-D (Claritin-D 12 and 24 hour)	1 tablet PO BID (12 hr) QD (24 hr)	
OTC cetirizine (Zyrtec)	10 mg PO QD	
OTC fexofenadine (Allegra Allergy)	60 mg PO BID or 180 mg PO QD	
Fluticasone priopionate (Flonase)	1-2 sprays each nostril QD	
Triamcinolone acetonide (Nasacort AQ)	2 sprays each nostril QD	
Mometasone furoate monohydrate (Nasonex)	2 sprays each nostril QD	
Azelastine (Astelin)	2 sprays each nostril BID	
Montelukast (Singulair)	10 mg PO QD	

Boldface indicates generic availability

Utilization Management Recommendation

- There is significant potential for inappropriate use and utilization management should be considered for the following reason(s):

  i) To prevent inappropriate use of medications that have a higher potential to cause patient harm and lead to increased medical utilization compared to therapeutic alternatives.
  (1) Opportunity exists to obtain clinically significant medical or laboratory information necessary to determine appropriate use of the medication.
  (a) To ensure confirmation by positive skin test or in vitro testing for pollen-specific IgE antibodies for House Dust Mites (*Dermatophagoides farinae or Dermatophagoides pteronyssinus*)
  (2) Evidence-based national treatment guidelines recommend that patients try pharmacotherapy first

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ii) Recommended utilization management tool(s): (check all that apply)
(1) ☒ Prior authorization
(2) ☐ Quantity limits
(3) ☐ Provider newsletter
(4) ☐ Hard block (plan exclusion)
(5) ☐ Messaging
(6) ☐ Electronic step therapy
(7) ☐ Clinical Program

Product Comparison [5,6,7]

- CPAC score: 57 vs. Subcutaneous immunotherapy (SCIT) (allergen extract of Standardized Mite *Dermatophagoides farinae* and *Dermatophagoides* pteronyssinus) – Equal therapeutic outcomes anticipated.
- Equal therapeutic outcomes are anticipated for Odactra and SCIT, therefore it would be appropriate to provide equal access to both or to require a trial of one before the other.
- It would be clinically appropriate to require a trial of symptomatic pharmacotherapy (i.e. antihistamines, nasal steroids) prior to initiation of Odactra.

REFERENCES

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