HEALTH PLANS
UNIVERSITY OF UTAH

Medical Policy

Sublingual Immunotherapy (SLIT)

Policy MP-064

Origination Date: 01/27/2021

Reviewed/Revised Date: 02/15/2023

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Disclaimer:

1. Policies are subject to change in accordance with State and Federal notice requirements.
2. Policies outline coverage determinations for U of U Health Plans Commercial and Healthy U (Medicaid) plans. Refer to the "Policy" section for more information.
3. Services requiring prior-authorization may not be covered, if prior-authorization is not obtained.
4. This Medical Policy does not guarantee coverage or payment of the service. The service must be a benefit in the member's plan and the member must be eligible for coverage at the time of service. Additional payment guidelines may be applied that are not included in this policy.

Description:

Allergic rhinitis, or allergic rhinosinusitis, is characterized by paroxysms of sneezing, rhinorrhea, and nasal obstruction, often accompanied by itching of the eyes, nose, and palate. Postnasal drip, cough, irritability, and fatigue are other common symptoms.

Ten to 30 percent of adults and up to 40 percent of children suffer from allergic rhinitis in the United States. Most patient's symptoms can be managed adequately with environmental modifications, use of saline wash, antihistamines, topical nasal steroids or other agents.

For patient with resistant disease, who have severe symptoms, or who have been identified through allergy testing to have specific allergies immunotherapy may be employed to reduce disease severity and morbidity. Subcutaneous injection of allergen-specific immunotherapy (SCIT) is the standard approach for treating allergies. Patients are administered a series of progressively more potent individualized preparations over a series of years which allows the body to develop tolerance to the offending agent.

Due to the inconvenience of multiple injections, particularly in children, alternative delivery routes have been investigated; of these, sublingual immunotherapy (SLIT) is the most prominent. SLIT involves the administration of a diluted dose of an allergen in the form of a liquid or a tablet under the tongue, which allows the allergen to contact the oral mucosa. Generally, patients are instructed to hold the drops or tablet under the tongue for approximately 30 seconds and to repeat this treatment up to 3 times daily. This practice is thought to desensitize the patient to the allergen, as would conventional immunotherapy by injection. SLIT has been studied as a treatment for patients with allergic rhinitis (AR) and

asthma associated with sensitivity to seasonal allergens such as grass and pollen, and to other allergens such as dust mites, mold, pet dander, or nuts.

Policy Statement and Criteria

1. Commercial Plans

U of U Health Plans does NOT cover Sublingual Immunotherapy (SLIT) for the treatment of any condition or disease (including but not limited to allergic rhinitis and allergic rhinoconjunctivitis), as it is considered unproven/investigational due to insufficient evidence of efficacy and safety.

2. Medicaid Plans

Coverage is determined by the State of Utah Medicaid program; if Utah State Medicaid has no published coverage position and InterQual criteria are not available, the U of U Health Plans Commercial criteria will apply. For the most up-to-date Medicaid policies and coverage, please visit their website at: https://medicaid.utah.gov/utah-medicaid-official-publications/ or the Utah Medicaid code Look-Up tool

CPT/HCPCS codes covered by Utah State Medicaid may still require further evaluation to determine medical necessity for coverage.

Clinical Rationale

Off-label use of sublingual drops prepared from commercial allergen extracts is widely practiced in the United States (U.S.). Commercial aqueous extract products are not FDA approved for sublingual administration, and these have not been rigorously studied in double-blind placebo-controlled studies. Thus, effective and safe dose ranges have not been characterized for commercial aqueous allergen extracts (marketed for subcutaneous immunotherapy [SCIT]) used in the preparation of nonapproved SLIT drops. Because of insufficient clinical data, use of aqueous SLIT formulations have not been endorsed by the American Academy of Allergy, Asthma & Immunology/American College of Allergy, Asthma & Immunology Joint Task Force (Mahler et al., 2019).

Scadding and colleagues (2018) conducted a randomized double-blind, placebo-controlled, 3-parallel-group study known as the GRASS trial to assess whether 2 years of treatment with grass pollen SLIT, compared with placebo, provides improved nasal response to allergen challenge at 3-year follow-up. Adults (N=106) with moderate to severe seasonal allergic rhinitis (AR) (interfering with usual daily activities or sleep) were included with study groups divided as follows: 36 participants received 2 years of SLIT (daily tablets containing 15 µg of major allergen Phleum p 5 and monthly placebo injections), 36 received subcutaneous immunotherapy (monthly injections containing 20 µg of Phleum p 5 and daily placebo tablets) and 34 received matched double placebo. Nasal allergen challenge was performed before treatment, at 1 and 2 years of treatment, and at 3 years (1 year after treatment discontinuation). Primary outcome was total nasal symptom scores (TNSS) comparing SLIT vs placebo at year 3. Subcutaneous immunotherapy was included as a positive control. The study was not powered to compare SLIT with subcutaneous immunotherapy. At 3 years, 92 individuals completed the study. Researchers concluded that among patients with moderate to severe seasonal AR, 2 years of sublingual

grass pollen immunotherapy was not significantly different from placebo in improving the nasal response to allergen challenge at 3-year follow-up.

A systematic review of immunotherapy for asthma identified 18 randomized controlled trials on the efficacy of sublingual immunotherapy (SLIT) and concluded that SLIT is associated with improved asthma symptoms, disease-specific quality of life, medication use, and pulmonary function. The authors noted several limitations to the available data (e.g., uncertainty about whether changes in asthma symptom scores were clinically meaningful, lack of statistically significant differences in pulmonary function or quality of life between treatment and placebo arms). In conclusion, the authors found that there was insufficient evidence about the efficacy of SLIT in children (Lin, et al. 2018).

In 2021, Hayes conducted a health technology assessment on liquid sublingual immunotherapy for the treatment of allergic rhinitis. Limitations of the studies include: small sample size and lack of power analyses for relevant outcomes, limited or unclear length of follow-up, inadequate reporting rates for treatment adherence and absence of between-treatment group statistical comparisons for adverse events. The available studies have provided mixed evidence that SLIT may improve symptoms and reduce medication use in patients with allergic rhinitis or rhinoconjunctivitis compared with placebo treatment. However, benefits over placebo treatment were not found in all studies, thus questions remain regarding the longevity of benefits due to limited follow-up. The authors concluded that due to the lack of a U.S. FDA approved liquid for SLIT and because of the body of evidence being low in quality and small in size, standardization of the extracts, dosing, and patient selection have not yet been determined. Furthermore, additional large, well-destined clinical studies with long term follow-up are needed to optimize patient selection criteria and treatment parameters.

As of July 2020, Medicare does not cover antigens if they are to be administered sublingually, i.e., by placing drops under the patient's tongue. This kind of allergy therapy has not been proven to be safe and effective. Antigens are covered only if they are administered by injection. See the National Coverage Determination (NCD) for Antigens Prepared for Sublingual Administration (110.9).

In 2020, the American Academy of Allergy, Asthma and Immunology (AAAAI) found no FDA-approved SLIT liquid (drops) formulations. The effectiveness of SLIT with U.S. allergen extract drops is still under investigation and the effectiveness of mixtures of allergens is not known. There is a wide range of effective and ineffective doses of SLIT liquid formulations across the published literature and expert opinion has been that each formulation needs to prove its safe and effective dosing regimen. The FDA-approved product information of the four SLIT tablets includes a warning about the possibility of severe allergic reactions from SLIT and a recommendation that an epinephrine autoinjector be prescribed to patients receiving allergy tablets in the event a severe allergic reaction should occur.

In 2020, Dykewicz et. al. concluded that sublingual drops are still not FDA-approved at this time. The following text is a quotation from the Joint Task Force on Practice Parameters (JTFPP) on SLIT: ‘‘although alternative regimens and preparations for SLIT have been proposed and may be used off-label in the United States (e.g., use of liquid SCIT extract for sublingual delivery or use of specific sublingual drops or other sublingual tablets), these products and formulations do not have FDA approval at present and have not been systematically studied in a rigorous manner in US populations. Use of such products or formulations as prescribed SLIT therapy is currently off-label, at a practitioner’s discretion, and is without recommendation for any current particular indication in the US populations. Therefore, off-label use of aqueous SLIT extracts or any other non-FDA approved SLIT formulation is not endorsed’’

Applicable Coding

CPT Codes

95165 Professional services for the supervision of preparation and provision of antigens for allergen immunotherapy; single or multiple antigens (specify number of doses)

95199 Unlisted allergy/clinical immunologic service or procedure

HCPCS Codes

No applicable codes

References:

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3. Centers for Medicare and Medicaid Services (CMS). (1996). "National Coverage Determination (NCD) for Antigens Prepared for Sublingual Administration (110.9)" Accessed: November 16, 2020. Available at: https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=155&ncdver=1&DocID=110.9&LCDId=33777&ver=79&bc=gAAAABAAAAAA&
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5. Hayes, Inc. (2021). Health Technology assessment. "Liquid Sublingual Immunotherapy". Accessed: February 18, 2021. Available at: https://evidence.hayesinc.com/report/dir.liquidslit5040
6. Lin SY, Azar A, Suarez-Cuero C, et al. The role of immunotherapy in the treatment of asthma. Comparative Effectiveness Review #19 AHRQ Publication No. 17(18)-EHC02-EF Agency for Healthcare Research and Quality (AHRQ). March 2018.
7. Mahler V, Esch RE, Kleine-Tebbe J, et al. Understanding differences in allergen immunotherapy products and practices in North America and Europe. J Allergy Clin Immunol. 2019 Mar;143(3):813-828.
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