

Sublingual Immunotherapy (SLIT)

Policy MP-064

Origination Date: 1/27/2021

Reviewed/Revised Date: 02/10/2021

Next Review Date: 02/10/2022

Current Effective Date: 04/10/2021

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.

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:

<http://health.utah.gov/medicaid/manuals/directory.php> or the [Utah Medicaid code Look-Up tool](#)

3. Medicare Plans

Coverage is determined by the Centers for Medicare and Medicaid Services (CMS); if a coverage determination has not been adopted by CMS and InterQual criteria are not available, the U of U Health Plans Commercial criteria will apply. For the most up-to-date Medicare policies and coverage, please visit their search website at:

<http://www.cms.gov/medicare-coverage-database/overview-and-quick-search.aspx?from2=search1.asp&> or [the manual website](#)

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-designed 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.

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:

1. American Academy of Allergy, Asthma and Immunology (AAAAI) Reviewed September 28, 2020. Accessed November 16, 2020. Available at: <https://www.aaaai.org/conditions-and-treatments/library/allergy-library/sublingual-immunotherapy-for-allergic-rhinitis>
2. 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=gAAAABAAAA&>
3. Hayes, Inc. (2021). Health Technology assessment. "Liquid Sublingual Immunotherapy". Accessed: February 18, 2021. Available at: <https://evidence.hayesinc.com/report/dir.liquidslit5040>
4. 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.
5. 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.
6. Scadding GW, Calderon MA, Shamji MH, et al. Effect of 2 Years of Treatment With Sublingual Grass Pollen Immunotherapy on Nasal Response to Allergen Challenge at 3 Years Among Patients With Moderate to Severe Seasonal Allergic Rhinitis: The GRASS Randomized Clinical Trial. JAMA. 2017 Feb 14;317(6):615-625.

Disclaimer:

This document is for informational purposes only and should not be relied on in the diagnosis and care of individual patients. Medical and Coding/Reimbursement policies do not constitute medical advice, plan preauthorization, certification, an explanation of benefits, or a contract. Members should consult with appropriate health care providers to obtain needed medical advice, care, and treatment. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the member's individual benefit plan that is in effect at the time services are rendered.

The codes for treatments and procedures applicable to this policy are included for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

U of U Health Plans makes no representations and accepts no liability with respect to the content of any external information cited or relied upon in this policy. U of U Health Plans updates its Coverage Policies regularly, and reserves the right to amend these policies and give notice in accordance with State and Federal requirements.

No part of this publication may be reproduced, stored in a retrieval system or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from U of U Health Plans.

"University of Utah Health Plans" and its accompanying logo, and its accompanying marks are protected and registered trademarks of the provider of this Service and or University of Utah Health. Also, the content of this Service is proprietary and is protected by copyright. You may access the copyrighted content of this Service only for purposes set forth in these Conditions of Use.

© CPT Only – American Medical Association