ARIA-EAACI care pathways for allergen immunotherapy in respiratory allergy

Bousquet, Jean; Pfaar, Oliver; Agache, Ioana; Bedbrook, Anna; Akdis, Cezmi A; et al; Schmid-Grendelmeier, Peter

Abstract: Allergen immunotherapy (AIT), the gradually increasing repeated administration of high doses of allergens to allergic patients, offers the potential for immune tolerance against reactions to the natural exposures to specific allergens. AIT may lead to the long-lasting remission of allergic symptoms and is the only disease-modifying intervention in IgE-mediated allergic respiratory diseases.

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ARIA-EAACI care pathways for allergen immunotherapy in respiratory allergy

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BOUSQUET ET AL.

18. Allergist, La Rochelle, France

19. Paediatric Allergy, Department of Asthma, Allergy and Respiratory Science, Guys' Hospital, King's College London, London, UK

20. Department of Medical Sciences, Allergy and Clinical Immunology Unit, University of Torino & Mauriziano Hospital, Torino, Italy

21. Imperial College and National Heart and Lung Institute, London, UK

22. Institute for Immunological Research, University of Cartagena, Cartagena, Colombia

23. Allergy Section, Department of Internal Medicine, Hospital Vall d'Hebron & ARADyAL Research Network, Barcelona, Spain

24. Servicio de Imunologia y Alergia, Hospital Dona Estefânia, Centro Hospitalar de Lisboa Central, Lisbon, Portugal

25. Division of Allergy/immunology, University of South Florida, Tampa, Fla, USA

26. SOS Allergology and Clinical Immunology, USL Toscana Centro, Prato, Italy

27. Allergy and Immunology Laboratory, Metropolitan University, Simon Bolivar University, Barranquilla, Colombia

28. David Tatishvili Medical Center, David Tatishvili Medical University-AETI Medical School, Tbilisi, Georgia

29. Departments of Medicine and Health Research Methods, McMaster University, Hamilton, ON, Canada

30. Latvian Association of Allergists, University Children's Hospital, Riga, Latvia

31. Fundação ProAR, Federal University of Bahia and GARD/WHO Planning Group, Salvador, Brazil

32. Medical Consulting Czarlewski, Levallois, France

33. Department of Medical Sciences and Public Health and Unit of Allergy and Clinical Immunology, University Hospital "Duilio Casula", University of Cagliari, Cagliari, Italy

34. Department of Pulmonology, Division of Allergy, Hôpital Arnaud de Villeneuve, University Hospital of Montpellier, France

35. Unité de Recherche en Pharmacologie Respiratoire, Pôle des Maladies des Voies Respiratoires, Hôpital Foch, Université Paris Saclay, Suresnes, France

36. Medical Faculty, University Clinic of Pulmology and Allergy, Skopje, Republic of Macedonia

37. National Heart and Lung Institute, Imperial College London, UK

38. Clinical Research Center for Allergy and Rheumatology, NHO Sagamihara National Hospital, Sagamihara, Japan

39. Pediatric Allergy and Immunology Unit, Children’s Hospital, Ain Shams University, Cairo, Egypt

40. Faculty of Medicine, Clinic of Children's Diseases, Vilnius University, Vilnius, Lithuania

41. National Center for Disease Control and Public Health of Georgia, Tbilisi, Georgia

42. CHU Clermont-Ferrand, Unité d’Allergologie de l’Enfant, Pole pédiatrique, Hospital Estaing, Clermont-Ferrand, France

43. Division of Allergy, The Bambino Gesù Children's Hospital IRCCS, Rome, Italy

44. Department of Otorhinolaryngology, Academic Medical Centers, Amsterdam, The Netherlands

45. Faculdade de Medicina, CINVESTIS, Center for Health Technology and Services Research, Universidade do Porto, Porto, Portugal

46. Allergist, Reims, France

47. Department of Internal Medicine, Allergology and Clinical Immunology, Silesian University of Medicine, Katowice, Poland

48. Division of Allergy and Immunology, Divşkapı Yıldırım Beyazıt Training and Research Hospital, Ankara, Turkey

49. Department of Pulmonary Diseases, Cerrahpasa Faculty of Medicine, Istanbul University-Cerrahpasa, Istanbul, Turkey

50. Allergy and Immunology Division, Clinica Ricardo Palma, Lima, Peru

51. Department of Internal Medicine, Section of Allergy, Erasmus MC, Rotterdam, the Netherlands

52. Fundación Ayre, Instituto Medico Alas, Salta, Argentina

53. Center of Allergy and Immunology, Georgian Association of Allergology and Clinical Immunology, Tbilisi, Georgia

54. Latvian Association of Allergists, Center of Tuberculosis and Lung Diseases, Riga, Latvia

55. Immunology and Allergy Division, Clinical Hospital, University of Chile, Santiago, Chile

56. Skin and Allergy Hospital, Helsinki University Hospital, Helsinki, Finland

57. Hans Christian Andersen Children's Hospital, Odense University Hospital, Odense, Denmark

58. Department of Pathophysiology and Allergy Research, Medical University of Vienna, Vienna, Austria

59. Pediatric Allergy and Immunology Unit, Children's Hospital, Ain Shams University, Cairo, Egypt

60. Department of Clinical Immunology and Allergy, Oncology Institute of St Elisabeth, Bratislava, Slovakia

61. Department of Internal Medicine and Infectious Diseases, St Joseph University, Hotel Dieu de France Hospital, Beirut, Lebanon

62. Servicio de Alergia e Immunología, Clínica Santa Isabel, Buenos Aires, Argentina

63. Department of Allergology and Clinical Immunology of the Kazakh National Medical University, Kazakhstan Association of Allergology and Clinical Immunology, Kazakhstan

64. Allergy Center of Children’s Clinic of Tartu University Hospital, Tartu, Estonia

65. Ukrainina Medical Stomatological Academy, Poltava, Ukraine

66. Pediatric Allergy and Asthma Unit, Hacettepe University School of Medicine, Ankara, Turkey

67. National Research Center, Institute of Immunology, Federal Medicobiological Agency, Laboratory of Molecular Immunology, Russia

68. Department of Otolaryngology, Head and Neck Surgery, Universitätsmedizin Mainz, Mainz, Germany

69. Departments of Immunology and Dermatology/Allergology, University Medical Center Utrecht, The Netherlands

70. Department of Immunology and Allergy, Healthy Ageing Research Center, Medical University of Lodz, Poland

71. Department of Otorhinolaryngology, Head and Neck Surgery, Semmelweis University, Budapest, Hungary

72. Department of Clinical Science and Education, Södersjukhuset, Karolinska Institutet, Stockholm, Sweden

73. Division of Internal Medicine, Asthma and Allergy, Barlicki University Hospital, Medical University of Lodz, Poland

74. Department of Pathology, Faculty of Medicine, Institute of Biomedical Sciences, Vilnius University Vilnius, Lithuania

75. Quality Use of Respiratory Medicines Group, Woolcock Institute of Medical Research, University of Sydney, Sydney, NSW, Australia

76. Department of Dermatology and Allergology, University of Helsinki and Helsinki University, Helsinki, Finland

77. Department of Pediatric Pneumology and Immunology, Charité Universitätsmedizin, Berlin, Germany

78. KYoMed INNOV, Montpellier, France

79. Division of Paediatric Allergy, University of Cape Town, Cape Town, South Africa

80. Center of Excellence in Asthma and Allergy, Médica Sur Clinical Foundation and Hospital, Mexico City, Mexico

81. Department of Paediatrics, Oslo University Hospital, Oslo, Norway

82. Departmental Unit of Allergology & Respiratory Diseases, Fondazione Poliambulanza, Brescia, Italy
1Department of Allergy, Allergy and Asthma Medical Group and Research Center, San Diego, California, USA
2The University of Mississippi Medical Center, Division of Clinical Immunology and Allergy, Laboratory of Behavioral Immunology Research, Jackson, Mississippi, USA
3Allergy, Asthma and Immunology, Faculty of Medicine, University of Malta, University of Medicine, La Valette, Malta
4Faculty of Medicine, Clinic for Pulmonary Diseases, Clinical Center of Serbia, University of Belgrade, Belgrade, Serbia
5Croatian Pulmonary Society, Zagreb, Croatia
6Danish Allergy Centre, University of Copenhagen, Copenhagen, Denmark
7Department of Medicine (RCSI), Bon Secours Hospital, Dublin, Ireland
8Faculty of Medicine and Surgery, Mater Dei Hospital Malta, University of Medicine, La Valette, Malta
9Faculty of Medicine and Surgery, University of Copenhagen, Copenhagen, Denmark
10Allergy Center, CUF Descobertas Hospital, Lisbon, Portugal
11FRI-Clinical Research International-Ltd, Hamburg, Germany
12ENT Department, Rhinology Unit & Smell Clinic, Hospital Clinic, Barcelona, Spain
13Scientific Centre of Children's Health, Russian National Research Medical University, Moscow, Russia
14Center of Allergy, Immunology and Respiratory Diseases, Santa Fe, Argentina
15Hospital of the Hospitalar Brothers in Buda, Budapest, Hungary
16Department of Allergy, Medical University of Gdańsk, Gdańsk, Poland
17European Federation of Allergy and Airways Diseases Patients’ Associations, Brussels, Belgium
18Department of Allergy, Immunology and Respiratory Medicine, Central Clinical School, Monash University, Victoria, Australia
19Department of Infection and Immunity, Luxembourg Institute of Health, Esch-sur-Alzette, Luxembourg
20Department of Medicine and Microbiology, APC Microbiome Ireland, University College Cork, Cork, Ireland
21National Hospital Organization, Tokyo National Hospital, Tokyo, Japan
22Department of Otorhinolaryngology, Chiba University Hospital, Chiba, Japan
23Department of Otolaryngology, Nippon Medical School, Tokyo, Japan
24Department of Pediatrics, Allergy Unit, University of Messina, Messina, Italy
25Department of Biochemistry and Molecular Biology, School of Chemistry, Complutense University of Madrid, Madrid, Spain
26Department of Immunology and Allergy, Faculty of Medicine and Faculty Hospital in Pilsen, Charles University in Prague, Pilsen, Czech Republic
27Division of Infection, Immunity & Respiratory Medicine, Royal Manchester Children's Hospital, University of Manchester, Manchester, UK
28Department of Allergy and Clinical Immunology, Ajou University School of Medicine, Suwon, South Korea
29Allergy and Respiratory Diseases, Ospedale Policlinico San Martino -University of Genoa, Italy
30Department of Medicine, Division of Allergy and Clinical Immunology, Agency of Health ASL Salerno, “Santa Maria della Speranza” Hospital, Battipaglia, Salerno, Italy
31Department of Pediatrics, Nippon Medical School, Tokyo, Japan
32Ecole Polytechnique Palaiseau, IRBA (Institut de Recherche bio-Médicale des Armées), Bretegny, France
33School of Medicine, Children's Hospital Srebrnjak, Zagreb, University J.J. Strossmayer, Osijek, Croatia
34University Hospital ‘Sv Ivan Rilski’, Sofia, Bulgaria
35Allergy and Clinical Immunology Unit, Centro Hospitalar e Universitário de Coimbra, Coimbra, Coimbra, Portugal
36Pediatric Allergy and Clinical Immunology Department, Hospital Sant Joan de Déu, Barcelona, Spain
37Salford Royal NHS Foundation Trust NHS England North, Salford, UK
38Pediatric Allergy and Clinical Immunology, Hospital Angeles Pedregal, Mexico City, Mexico
39Hospital de Clínicas, University of Parana, Brazil
40Division of Allergy Asthma and Clinical Immunology, Emek Medical Center, Afula, Israel
41Department of Otolaryngology-Head and Neck Surgery, Eye and Ear University Hospital, Beirut, Lebanon
42Tisch Institute, Medical School, University of Edinburgh, Edinburgh, UK
43Department of Prevention of Environmental Hazards, Allergy and Immunology, Medical University of Warsaw, Warsaw, Poland
44Allergy and Clinical Immunology Department, Centro Medico-Docente La Trinidad, Caracas, Venezuela
45Asthma Reference Center - Escola Superior de Ciências, Santa Casa de Misericórdia of Vitória-Espírito Santo, Vitória, Brazil
46Faculty of Medicine, Fundación Jimenez Diaz, CIBERES, Autonoma University of Madrid, Spain
47The Royal National ENT Hospital, University College London, UK
48Immunomodulation and Tolerance Group, Imperial College London, London, UK
49Department of Dermatology, Allergy Unit, University Hospital of Zurich, Zürich, Switzerland
50The Usher Institute of Population Health Sciences and Informatics, The University of Edinburgh, Edinburgh, UK
51PROMISE Department, University of Palermo, Palermo, Italy
52Sociedad Paraguaya de Alergia Asma e Immunología, Clínica Sisul, Allergy & Asthma, Asuncion, Paraguay
53Finnish Meteorological Institute (FMI), Helsinki, Finland
54Department of Pediatrics, Division of Allergy, Clinical Immunology and Rheumatology, Federal University of São Paulo, São Paulo, Brazil
55Kurzgaz National Centre of Cardiology and Internal Medicine, Euro-Asian Respiratory Society, Bishkek, Kyrgyzstan
56Department of Pediatrics, Division of Respiratory Medicine, Hospital Nacional de Niños, Universidad de Costa Rica, San Jose, Costa Rica
57Department of Pediatrics, Hospital Nacional de Niños, San José, Costa Rica
58Department of Respiratory Medicine, University Hospital Olomouc, Czech Republic
59Centre for Inflammation Research, Child Life and Health, The University of Edinburgh, Edinburgh, UK
60Royal Brompton and Harefield NHS Foundation Trust, London, UK
61Department of Respiratory Medicine, Copenhagen University Hospital Hvidovre, Copenhagen, Denmark
62Department of Immunology, Faculty of Health Sciences, Cova da Beira, Covilhã, Portugal
63Imunologia, Centro Hospitalar Universitario de Coimbra, Coimbra, Portugal
64Allergy Unit, Málaga Regional University Hospital-IBIMA, Málaga, Spain
65Allergist, Montevideo, Uruguay
66Department of General ORL, H&NS, ENT-University Hospital Graz, Medical University of Graz, Graz, Austria
67Pneumology and Allergy Department, CIBERES, Clinical & Experimental Respiratory Immunology, IDIBAPS, University of Barcelona, Barcelona, Spain
68Department of Social Medicine, Health Planning Unit, Faculty of Medicine, University of Crete, Crete, Greece
Allergen immunotherapy (AIT), the gradually increasing repeated administration of high doses of allergens to allergic patients, offers the potential for immune tolerance against reactions to the natural exposures to specific allergens. AIT may lead to the long-lasting remission of allergic symptoms and is the only disease-modifying intervention in IgE-mediated allergic respiratory diseases.
This Pocket Guide was developed by an ARIA and EAACI joint study group from a background paper of the ARIA-MASK study group and from the EAACI guidelines on allergen immunotherapy.

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AIT is a proven therapeutic option for the treatment of allergic rhinitis, conjunctivitis, and/or asthma using sublingual (SLIT) or subcutaneous (SCIT) routes.

However, AIT is more expensive than symptomatic treatments for allergic diseases (excluding biologicals). It is justified (i) in patients with rhinitis otherwise uncontrolled by symptomatic treatment or (ii) as an add-on to regular asthma treatment in controlled or partially-controlled asthmatic patients sensitised to house dust mites aiming to decrease asthma exacerbations, rescue and controller medication, and to improve quality of life.

Care pathways are structured multi-disciplinary care plans detailing the key steps of patient care. They promote the translation of guideline recommendations to their application in clinical practice.

Although many international and national AIT guidelines have been produced, this is the first care pathway for AIT.

This pocket guide applies to sublingual (SLIT) and subcutaneous (SCIT) immunotherapy for allergic rhinitis. It has been revised by members from 65 countries (Figure 1).

2 | ALLERGENS TO BE ADMINISTERED

The decision to prescribe AIT should be based on relevant symptoms during allergen exposure, demonstration of sensitisation to the relevant allergens, and availability of good-quality extracts with proven efficacy and safety.

Some allergen extracts are approved for marketing in the EU (list in annex) with some others also approved by national health agencies.

For certain products, efficacy and safety have been demonstrated in appropriate clinical studies on adults and children. The extrapolation to untested products, allergens or a different population from the one evaluated in the trial is not appropriate and not in line with current guidelines as there is no class-effect in AIT.

Both monosensitised and polysensitised patients can be treated. However, in the latter case, the most clinically relevant allergen(s) should be used when symptoms are clearly present with allergen source exposure and when allergy tests confirm clinical findings.

3 | STRATIFICATION OF ALLERGIC PATIENTS

Precision medicine aims at the customisation of healthcare, tailored to the characteristics of each individual patient. The stratification of patients into subpopulations is the basis of clinical decision making (Figure 2).

In allergic diseases, patient stratification is required to:

• Propose the appropriate pharmacotherapy.
• Identify the most suitable candidates for AIT.
• Reduce the amount of time and resources needed to match the right patient to an optimal care management programme.
• Optimise costs as expensive therapeutic interventions are not necessary or suitable for all patients.

Patient stratification may also help to improve the patient’s engagement.

3.1 | Precision medicine in the indication of AIT

1. Precise diagnosis with history, skin prick tests and/or specific IgE and, if applicable, component-resolved in vitro testing. In some cases, where the above-mentioned diagnostic tools do not allow for precise diagnosis, allergen provocation testing (nasal, ocular and, in some cases, bronchial) may be needed.

2. Proven indications: Allergic rhinitis, conjunctivitis and/or asthma.

3. Symptoms predominantly induced by the relevant allergen exposure.

4. Patient stratification:
   ○ Poor control of nasal or ocular symptoms despite optimal medications according to guidelines with documented adherence to treatment.
   ○ Exceptions to requiring optimum symptomatic treatment prior to considering AIT include unacceptable side effects of the medications.
   ○ Allergic asthma fully controlled under background asthma medication (see EAACI HDM-AIT GL)
   ○ However, for partially controlled asthma, HDM-AIT may facilitate achieving asthma control (see EAACI HDM-AIT GL)

5. Good clinical documentation of efficacy and safety for the AIT product with relevant trials.

6. The patient’s (and caregiver’s) views represent an essential component.

3.2 | Biomarkers

There are currently no in vivo or in vitro biomarkers validated for monitoring the efficacy of AIT although several potential candidates are currently being investigated.
FIGURE 1  Countries with Pocket Guide members

FIGURE 2  Proposed Flow of Precision Medicine approach in allergic diseases. *examples of exceptions: Thunderstorm-induced asthma, patient with moderate rhinitis and severe asthma during pollen season
4 | mHEALTH

Apps can be used:

- To acquire real-world evidence to confirm the efficacy of AIT in situations where randomised controlled trials are difficult to perform.
- To assess air quality index including pollen exposure and air pollution.
- By physicians and patients for stratification of patients and follow-up.

5 | RHINITIS (WITH OR WITHOUT CONJUNCTIVITIS) IN ADOLESCENTS AND ADULTS

The selection of pharmacotherapy and AIT for patients with AR and/or allergic conjunctivitis may be better supported by evidence algorithms to aid patients and healthcare professionals jointly determine the treatment and its step-up or step-down strategy depending on rhinitis control (shared decision-making).

A simple algorithm is proposed as an aid for physicians to determine the treatment of their patients (Figure 3).

5.1 | Treatment algorithm using visual analogue scale (VAS)

In the case of remaining ocular symptoms, add intra-ocular treatment.

6 | RHINITIS (WITH OR WITHOUT CONJUNCTIVITIS) IN CHILDREN

AIT is effective, has long-term beneficial effects after cessation, and may delay or prevent the onset of asthma. AIT can be initiated in children with moderate/severe rhinitis that is not controlled by appropriate medications according to guidelines.

7 | ASTHMA

An algorithm for HDM-driven allergic asthma diagnosis and management is proposed by the EAACI guidelines.

For patients with concomitant allergic rhinitis and sensitised to house dust mite—with persisting asthma symptoms despite low-moderate dose of inhaled corticosteroids—SLIT can be considered, provided FEV1 is >70% predicted.

House dust mite SLIT should initially be considered as an add-on therapy to controller treatment, and reduction in asthma controllers should be performed gradually under the supervision of a physician.

Immunotherapy is not indicated for the treatment of acute exacerbations, and patients must be informed of the need to seek medical attention immediately if their asthma deteriorates suddenly (Figure 4).

8 | MULTIMORBIDITY

One strength of AIT is that it has the potential to control all allergic diseases related to a specific allergen, including rhinitis, conjunctivitis and asthma.
9 | SAFETY

9.1 | Subcutaneous immunotherapy (SCIT)

Local reactions: A typical reaction is redness and swelling at the injection site immediately or several hours after the injection. Sometimes, sneezing, nasal congestion or hives can occur.

Systemic reactions: Serious reactions to injections are very rare and require immediate medical attention. Symptoms of an anaphylactic reaction can include swelling in the throat, wheezing or tightness in the chest, nausea and dizziness. The most serious reactions develop within 30 min after the injection, and patients are advised to wait in their doctor’s surgery for at least 30 min after an injection. Severe bronchospasm can also occur, especially in patients where asthma is not controlled.

9.2 | Sublingual immunotherapy (SLIT)

Allergen drops or tablets have a more favourable safety profile than injections. The initial dose should be performed in the doctor’s surgery, and patients are advised to remain in the surgery for at least 30 min...
after administration. Thereafter, SLIT can be administered at home once the first dose has been given under the supervision of a physician.

Allergic reactions: The majority of patients will experience mild local reactions of the oropharyngeal passage. This is usually controlled by predosing with an antihistamine 30 min before the administration of SLIT. Sometimes, sneezing, nasal congestion or hives can occur. Anaphylaxis is rarely described.

In some countries, SLIT tablets include a warning about possible severe allergic reactions, and adrenaline auto-injectors are routinely recommended. This is not the case in Europe.

**CONFLICT OF INTEREST**

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PK reports personal fees from Adamed, Berlin Chemie Menarini, Boehringer Ingelheim, AstraZeneca, Lekam, Novartis, Polpharma, GSK, Polpharma, Sanofi, teva.

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FS reports speaker and advisory fees from AstraZeneca, Novartis, Sanofi, GSK, Teva and Lusomedicamenta.

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BS reports personal fees from Allergopharma, during the conduct of the study; grants from National Health Programm, grant, personal fees from Polpharma, ASTRA, personal fees from Mylan, Adamed, patient ombudsman, national Centre for Research and Development, Polish Allergology Society.

JS reports grants and personal fees from Sanofi, personal fees from GSK, Novartis, Astra Zeneca, Mundipharma, Faes Farma.

GS reports personal fees from ALK, and leads on the BSACI Rhinitis Guidelines and lead for EUFOREA on Allergic Rhinitis.
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TZ reports and Organizational affiliations: Committee member: WHO-Initiative “Allergic Rhinitis and Its Impact on Asthma” (ARIA). Member of the Board: German Society for Allergy and Clinical Immunology (DGAKI). Head: European Centre for Allergy Research Foundation (ECARF). Secretary General: Global Allergy and Asthma European Network (GA²LEN). Member: Committee on Allergy Diagnosis and Molecular Allergology, World Allergy Organization (WAO).

ORCID
Jean Bousquet https://orcid.org/0000-0002-4061-4766
Victoria Cardona https://orcid.org/0000-0003-2197-9767
Ralph Mösges https://orcid.org/0000-0002-1928-810X
Dermot Ryan https://orcid.org/0000-0002-4115-7376
Manuel Soto-Quiros https://orcid.org/0000-0003-3425-3463
Isabel Skypala https://orcid.org/0000-0003-3629-4293
Mihaela Zidarn https://orcid.org/0000-0003-0515-5207

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