

Review

# Adrenaline nasal spray in emergency management: An initial expert opinion

Regina Treudler<sup>1</sup>, Knut Brockow<sup>2</sup>, Kirsten Beyer<sup>3,4</sup>, Ludger Klimek<sup>5</sup>, Lars Lange<sup>6</sup>, Sabine Schnadt<sup>7</sup>, Johannes Ring<sup>2</sup>, and Margitta Worm<sup>8</sup>

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<sup>1</sup>Institute of Allergology, Charité – Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, <sup>2</sup>Department of Dermatology and Allergology am Biederstein, Faculty of Medicine and Health, Technical University of Munich, Munich, <sup>3</sup>Department of Pediatric Respiratory Medicine, Immunology and Critical Care Medicine, Charité Universitätsmedizin Berlin, <sup>4</sup>German Center for Child and Adolescent Health (DZKJ), Berlin, <sup>5</sup>Center for Rhinology and Allergology, Wiesbaden, <sup>6</sup>Department of Pediatrics and Adolescent Medicine, St. Marien-Hospital, Bonn, <sup>7</sup>German Allergy and Asthma Association (DAAB). (DAAB), Mönchengladbach, and <sup>8</sup>Department of Dermatology, Venerology and Allergology, Charité – Universitätsmedizin Berlin, Berlin, Germany

## Key words

adrenaline – anaphylaxis  
– allergy – epinephrine –  
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**Abstract.** Adrenaline is the drug of choice for the treatment of anaphylaxis. Up to now, intramuscular administration using an autoinjector has been recommended in national and international guidelines as the first-line treatment for anaphylaxis. Various adrenaline autoinjectors are available on the German market as emergency medication for immediate treatment by medical laypersons and specialists. Recently, a nasally administered adrenaline preparation was introduced for the first time and is available on the market. There are mainly data on healthy control subjects, which show a good adrenaline level and an expected effect on blood pressure and heart rate. To date, there is little clinical experience in the world literature for patients with anaphylaxis in children/adolescents and none in adults or from Germany. Therefore, we would like to discuss theoretically the use of adrenaline via the nasal route of administration in the care of anaphylaxis patients and compare it with the intramuscular administration of adrenaline autoinjectors.

## Introduction

Anaphylaxis is an acute, potentially life-threatening reaction that can affect the entire body and requires rapid and effective treatment [3, 10, 14]. The most common triggers of anaphylaxis are insect venoms, foods, and medications [14, 20], but many other, sometimes rare triggers have also been described [18, 19]. Intramuscular administration into the lateral thigh is established worldwide and is the first-line treatment for a systemic allergic reaction as soon as two or more organ systems are affected simultaneously or consecutively, but at the latest when manifestations extend beyond the skin and gastrointestinal tract and occur in the lower respiratory tract or cardiovascular system [14, 21]. However, there are various barriers to the quick and easy use of adrenaline via autoinjectors (AAI), such as administration by laypeople (including caregivers), in children, or in situations where

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Correspondence to: Prof. Dr. med. Regina Treudler, Institute of Allergology, Charité – Universitätsmedizin Berlin, Hindenburgdamm 30, 12203 Berlin, Germany, [Regina.treudler@charite.de](mailto:Regina.treudler@charite.de)

Table 1. Possible barriers that may lead to the non-use or non-carrying of an adrenaline autoinjector (AAI).

Barriers to use
Lack of knowledge among medical/pharmaceutical staff about guideline-compliant AAI use [7, 22]
Lack of knowledge among patients regarding use with regard to <ul style="list-style-type: none"> <li>– possible dangers of anaphylaxis without adrenaline administration</li> <li>– timing and</li> <li>– practical procedure for AAI use [16, 23]</li> </ul>
Refusal or delay in use due to administration via a needle or the recommendation to go to a clinic for monitoring after use
Fear of side effects
Barriers to carrying the AAI
Size/weight of the AAI
Possible stigmatization
Temperature-dependent storage of the AAI

there is uncertainty about the necessity of administration [16, 23]. In addition, AAI are not available during an emergency situation if they are not regularly carried by those affected [23]. According to data from the literature, pharmaceutical and medical personnel are also uncertain about when and how adrenaline should be administered intramuscularly in cases of anaphylaxis [7, 22]. Several products are available in Germany for the intramuscular administration of adrenaline: Fastjekt (Viatris, Troisdorf, Germany), Jext (ALK-Abello, Reinbek, Germany), Anapen (Bioprojet, Berlin, Germany). In recent years, nasal administration of adrenaline has been successfully developed as an alternative emergency treatment for anaphylaxis [2, 5, 12]. An intranasal adrenaline preparation (EURNeFFy, ALK-Abello, Wedel, Germany [1]) was recently approved in Europe and has been available on the German market since June 26, 2025. In the following, we would like to discuss the importance of a nasal form of adrenaline administration for the treatment of anaphylaxis patients.

## Adrenaline nasal spray

Adrenaline nasal spray was developed for the emergency treatment of anaphylaxis. It is a spray that delivers a dose of 2 mg of adrenaline to the nasal mucosa. It is suitable for people weighing 30 kg or more. The product has already been approved in the USA, where also a dose variant containing 1 mg of adrenaline to be used for people aged 4 years and older and weighing between 15 kg and 30 kg is already available [2,

9]. Approval of the product containing 1 mg of adrenaline is also being sought in Europe. EURNeFFy contains sodium metabisulfite and benzalkonium chloride as additives. Nasal administration of drugs is well established and has been introduced for the administration of a variety of other drugs [5], including diazepam and sumatriptan. The addition of a carrier substance (dodecyl maltoside, Intravail) facilitates the absorption of adrenaline by increasing the permeability of the mucosal cells [13]. This improves the absorption of adrenaline into the systemic circulation.

## Handling

The nasal adrenaline preparation is used topically as a nasal spray and does not require an injection. It is important not to test the spray with a test dose prior to use, as only one single dose can be administered. If there is no improvement in symptoms within the first 10 minutes, a second dose is recommended. The preparation is only available as a double pack. The shelf life is specified as 30 months from the date of manufacture. No special storage conditions are required, as the medication is designed to remain stable even at high temperatures. Training devices are available from the company for patient training. The currently available training devices are for single use only and are intended to raise awareness during training that no control spray should be administered. A reusable training device would be desirable so that the patient's environment can also become more familiar with its use.

Table 2. Comparison: nasal vs. intramuscular administration with a single dose [1].

Administration	Intramuscular (auto-injector)	Intramuscular (syringe)	Nasal
Application	Previous standard	Alternative standard for medical personnel	New
Suitable for laypeople	Yes	No	Yes
Injection	Yes	Yes	No
Time (minutes) to maximum serum level (median/range)	10 (2 – 45)	45 (3.9 – 360)	20 – 30 (2 – 240)
Max. serum level in pg/mL* (mean)	581	277	448 – 485

\*The Food and Drug Administration (USA) considered 175 pg/mL to be the lower limit for efficacy (communications from ALK-Abelló, Wedel, Germany, and ARS Pharmaceuticals, San Diego, CA, USA).

Table 3. Criteria to aid decision-making with regard to intramuscular or nasal administration of adrenaline by laypersons.

Questions		Preference	
		Intra-muscular	Nasal
1.	Has successful anaphylaxis patient training already been carried out with an AAI?	++	+
2.	Has training been provided to caregivers using AAI?	++	+
3.	Has an AAI been used correctly by the patient before?	++	(+)
4.	Is the body weight less than 30 kg?	+++	–
5.	Are there any difficulties with the application technique of the AAI (e.g., visual impairment)?	–	+++
6.	Was the AAI not carried in the past due to size, storage, or portability issues?	+	++
7.	Has the AAI not been used in the past despite an acute reaction, e.g., due to reservations about an injection at the daycare center?	(+)	+++
8.	Is there such a thing as needle phobia?	–	+++
9.	Is there a reluctance to use new preparations?	++	(+)
10.	Are high or low storage temperatures to be expected (e.g., outdoor sports, travel to countries with high temperatures)?	(+)	+++
11.	Are there any pre-existing conditions of the nose that may preclude nasal administration of adrenaline (e.g., previous surgery, empty nose syndrome)?	+++	–
12.	Is there a contact allergy to benzalkonium chloride?	+++	(+)
13.	Is there a preference for a particular application?	+++	+++
14.	Is adrenaline mainly needed seasonally, making a longer shelf life advantageous?	+	++

Degree of preference: +++ very strong, ++ strong, + less strong, (+) possible, – not suitable; AAI = adrenaline auto-injector.

## Effect and efficacy

Studies in healthy subjects have shown that the nasal adrenaline preparation reaches serum levels comparable to those achieved by manual intramuscular administration of adrenaline using a syringe within a few minutes of application, and serum levels comparable to those achieved with Fastjekt after 15 minutes (Table 2). Comparable desired adrenergic effects are also achieved [2, 5, 8, 12]. The desired adrenergic effects were also demonstrated in cases of swelling of the nasal mucosa due to allergic rhinitis (shown in subjects after nasal provocation testing) and in patients with upper respiratory tract infections [11]. A few data on

clinical use in children with immediate-type reactions after oral food provocation are available from a registration study in Japan and a case series in the USA [4]. In addition, data from an animal model (dogs) show that even in cases of hypotension, there is no effect on the absorption of nasal adrenaline in anesthetized dogs [17].

## Safety

The most common side effect of nasal adrenaline administration is local irritation of the nasal mucosa. In addition, particularly after administration of a second dose, some subjects also experienced headaches, nervousness, and tremors [1, 2, 5, 12].

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## Indication

The indication for prescribing an adrenaline preparation is based on the recommendations of the guideline for acute treatment and management of anaphylaxis [8]. The choice of adrenaline preparation and form of administration (intramuscular vs. intranasal) should be based on shared decision making with the patient. Possible criteria to aid decision-making are listed in Table 3.

## Expert opinion

Based on pharmacokinetic and pharmacodynamic data in human subjects, intranasal administration of adrenaline using a nasal spray for the treatment or prevention of anaphylaxis has been approved as an emergency medication for the treatment of anaphylaxis in many countries. The possibility of nasal administration of adrenaline represents an enrichment of the therapeutic spectrum in the treatment of anaphylaxis. Which patients are suitable for intramuscular and which for nasal administration should currently be considered on an individual basis [6]. Data will be needed in the future to identify patient groups that particularly benefit from this route of administration. Health economic considerations should not be ignored [15]. Here, it can be taken into account whether adrenaline has already been used repeatedly (e.g., for food allergies) or whether it is a seasonal emergency medication (e.g., for insect venom allergies) that is unlikely to be needed for months at a time. In addition, it would be desirable to be able to prescribe a single adrenaline nasal spray. Although up to 10% of anaphylaxis patients require a second dose of adrenaline, the medication is often not used for years for various reasons and is discarded unused [7].

The experts were unable to reach a consensus on the question of prescribing an adrenaline auto-injector and an adrenaline nasal spray at the same time. The majority opinion was that, not least for economic reasons, a medical decision should be made regarding one or the other method of administration. On the other hand, few experts argued that the possibility of simultaneous prescription should be considered in selected cases.

Overall, we hope that the barriers to adrenaline use – as they exist today for patients and other users – can be reduced with the introduction of the new preparation and that anaphylaxis will be treated more frequently than before with adrenaline as early as possible in accordance with guidelines.

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## References

- [1] ALK-Abello. Fachinformation EURNeffy. 2025.
- [2] Casale TB, Ellis AK, Nowak-Węgrzyn A, Kaliner M, Lowenthal R, Tanimoto S. Pharmacokinetics/pharmacodynamics of epinephrine after single and repeat administration of neffy, EpiPen, and manual intramuscular injection. *J Allergy Clin Immunol.* 2023; 152: 1587-1596. [CrossRef PubMed](#)
- [3] Dribin TE, Muraro A, Camargo CA Jr, Turner PJ, Wang J, Roberts G, Anagnostou A, Halken S, Liebermann J, Worm M, Zuberbier T, Sampson HA, Alvaro-Lozano M, Arasi S, Ben-Shoshan M, Beyer K, Campbell DE, Campbell RL, Cardona V, Chinthrajah RS, et al; GA(2)LEN Anaphylaxis Study Team. Anaphylaxis definition, overview, and clinical support tool: 2024 consensus report-a GA2LEN project. *J Allergy Clin Immunol.* 2025; S0091-6749(25)00072-7. Epub ahead of print. [CrossRef PubMed](#)
- [4] Ebisawa M, Takahashi K, Takahashi K, Yanagida N, Sato S, Lieberman J, Pistiner M, Spergel JM, Lowenthal R, Tanimoto S. Epinephrine Nasal Spray Improves Allergic Symptoms in Patients Undergoing Oral Food Challenge, Phase 3 Trial. *J Allergy Clin Immunol Pract.* 2025; S2213-2198(25)00630-0. Epub ahead of print. [CrossRef PubMed](#)
- [5] Ellis AK, Casale TB, Kaliner M, Oppenheimer J, Spergel JM, Fleischer DM, Bernstein D, Camargo CA Jr, Lowenthal R, Tanimoto S. Development of neffy, an Epinephrine Nasal Spray, for Severe Allergic Reactions. *Pharmaceutics.* 2024; 16: 811. [CrossRef PubMed](#)
- [6] Golden DBK, Greenhawt M, Shaker MS. Prescribing nasal epinephrine spray: Confidence limits with novel treatments. *J Allergy Clin Immunol.* 2025; S0091-6749(25)00650-5. Epub ahead of print. [CrossRef PubMed](#)
- [7] Grabenhenrich LB, Dölle S, Rüeff F, Renaudin J-M, Scherer K, Pföhler C, Treudler R, Koehli A, Mahler V, Spindler T, Lange L, Bilò MB, Papadopoulos NG, Hourihane JOB, Lang R, Fernández-Rivas M, Christoff G, Cichocka-Jarosz E, Worm M. Epinephrine in Severe Allergic Reactions: The European Anaphylaxis Register. *J Allergy Clin Immunol Pract.* 2018; 6: 1898-1906.e1. [CrossRef PubMed](#)
- [8] Greenhawt M, Lieberman J, Blaiss M, Bernstein DI, Oppenheimer J, DuBuske L, Fleischer D, Dworaczek DA. Pharmacokinetic and Pharmacodynamic Profile of Epinephrine Nasal Spray Versus Intramuscular Epinephrine Autoinjector in Healthy Adults. *J Allergy Clin Immunol Pract.* 2024; 12: 3274-3282.e2. [CrossRef PubMed](#)
- [9] In brief: Epinephrine 1 mg nasal spray (neffy). *Med Lett Drugs Ther.* 2025; 67: 71. [CrossRef PubMed](#)
- [10] Muraro A, Worm M, Alviani C, Cardona V, DunnGalvin A, Garvey LH, Riggioni C, de Silva D, Angier E, Arasi S, Bellou A, Beyer K, Bijlhout D, Bilò MB, Bindslev-Jensen C, Brockow K, Fernandez-Rivas M, Halken S, Jensen B, Khaleva E, et al; European Academy of Allergy and Clinical Immunology, Food Allergy, Anaphylaxis Guidelines Group. EAACI guidelines: Anaphylaxis (2021 update). *Allergy.* 2022; 77: 357-377. [CrossRef PubMed](#)
- [11] Oppenheimer J, Casale TB, Camargo CA Jr, Fleischer DM, Bernstein D, Lowenthal R, Tanimoto S. Upper respiratory tract infections have minimal impact on neffy's pharmacokinetics or pharmacodynamics. *J Allergy Clin Immunol Pract.* 2024; 12: 1640-1643.e2. [CrossRef PubMed](#)
- [12] Pouessel G, Neukirch C. Alternatives to Injectable Adrenaline for Treating Anaphylaxis. *Clin Exp Allergy.* 2025; 55: 36-51. [CrossRef PubMed](#)
- [13] Rabinowicz AL, Carrazana E, Maggio ET. Improvement of Intranasal Drug Delivery with Intravail® Alkylsaccharide Excipient as a Mucosal Absorption Enhancer Aiding in the Treatment of Conditions of the Central Nervous System. *Drugs R D.* 2021; 21: 361-369. [CrossRef PubMed](#)
- [14] Ring J, Beyer K, Biedermann T, Bircher A, Fischer M, Fuchs T, Heller A, Hoffmann F, Huttegger I, Jakob T, Klimek L, Kopp MV, Kugler C, Lange L, Pfaar O, Rietschel E, Rueff F, Schnadt S, Seifert R, Stöcker B, et al. Guideline (S2k) on acute therapy and management of anaphylaxis: 2021 update: S2k-Guideline of the German Society for Allergology and Clinical Immunology (DGAKI), the Medical Association of German Allergologists (AeDA), the Society of Pediatric Allergology and Environmental Medicine (GPA), the German Academy of Allergology and Environmental Medicine (DAAU), the German Professional Association of Pediatricians (BVKJ), the Society for Neonatology and Pediatric Intensive Care (GNPI), the German Society



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- [15] Shaker MS, Oppenheimer J, Rider NL, Golden DBK, Anagnostou A, Greenhawt M. A health economic analysis of noninjectable epinephrine compared with intramuscular epinephrine. *Ann Allergy Asthma Immunol.* 2025; 134: 587-593.e1. [CrossRef PubMed](#)
- [16] Song TT, Worm M, Lieberman P. Anaphylaxis treatment: current barriers to adrenaline auto-injector use. *Allergy.* 2014; 69: 983-991. [CrossRef PubMed](#)
- [17] Sparapani S, Authier S, Lowenthal R, Tanimoto S. The impact of anaphylaxis on the absorption of intranasal epinephrine in anaesthetized non-native beagle dogs. *J Allergy Clin Immunol Glob.* 2023; 2: 100165. [CrossRef PubMed](#)
- [18] Treudler R. Emerging and Novel Elicitors of Anaphylaxis: Collegium Internationale Allergologicum Update 2024. *Int Arch Allergy Immunol.* 2024; 185: 794-802. [CrossRef PubMed](#)
- [19] Treudler R, Worm M, Bauer A, Dickel H, Heine G, Jappe U, Klimek L, Raulf M, Wedi B, Wiczorek D, Francuzik W, Jakob T, Pfaar O, Ring J, Rueff F, Schnadt S, Werfel T, Wurpts G, Zarnowski J, Zuberbier T, et al. Occupational anaphylaxis: A Position Paper of the German Society of Allergology and Clinical Immunology (DGAKI). *Allergol Select.* 2024; 8: 407-424. [CrossRef PubMed](#)
- [20] Worm M, Eckermann O, Dölle S, Aberer W, Beyer K, Hawranek T, Hompes S, Koehli A, Mahler V, Nemat K, Niggemann B, Pfohler C, Rabe U, Reissig A, Rietschel E, Scherer K, Treudler R, Ruëff F. Triggers and treatment of anaphylaxis: an analysis of 4,000 cases from Germany, Austria and Switzerland. *Dtsch Arztebl Int.* 2014; 111: 367-375. [PubMed](#)
- [21] Worm M, Fox AT, Wickman M, Ring J, Ebisawa M, Pouessel G, Smith P. Adrenaline auto injectors pharmacokinetic/pharmacodynamic studies and potential consequences for clinical practice. *Clin Transl Allergy.* 2023; 13: e12323. [CrossRef PubMed](#)
- [22] Worm M, Molaie N, Dölle S. Level of knowledge among pharmacists regarding anaphylaxis and the use of epinephrine autoinjectors. *J Dtsch Dermatol Ges.* 2018; 16: 1315-1321. [PubMed](#)
- [23] Zarnowski J, Wilkens L, Treudler R. Significant handling errors and education gaps regarding the use of the emergency kit among adult patients with Hymenoptera venom allergy. *Allergol Select.* 2025; 9: 1-7. [CrossRef PubMed](#)