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Take CME Exams

An Epinephrine Nasal Spray (*neffy*) for Anaphylaxis

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The FDA has approved an epinephrine nasal spray (*neffy* – ARS Pharma) for emergency treatment of type 1 hypersensitivity reactions including anaphylaxis in patients who weigh ≥30 kg. It is the first noninjectable epinephrine product to be approved for this indication.

Pronunciation Key

neffy: neh' fee

INJECTABLE EPINEPHRINE — Multiple epinephrine auto-injector formulations are available for emergency treatment of anaphylaxis (see Table 1). *EpiPen* and its generics have been used effectively for years. A generic version of *Adrenaclick* (brand no longer manufactured) is similar to *EpiPen* in size and functionality. *AUVI-Q* provides visual signals and audio instructions, has an automatic needle retraction system, and appears to be more convenient to carry and easier to use than *EpiPen*.[1] Because of differences in device design and instructions for use, these auto-injectors are not interchangeable and pharmacists cannot substitute one for another.

An epinephrine prefilled syringe *(Symjepi)* is also FDA-approved for emergency treatment of anaphylaxis. It requires the user to manually inject the needle and push down the plunger, which may be difficult for some patients, particularly children.[2]

Some injectable epinephrine products have not been consistently available in recent years; at press time, *EpiPen*, the generic version of *Adrenaclick,* and *Symjepi* were on back order with no estimated return date.[3]

THE NEW FORMULATION – Each *neffy* nasal spray device contains a single 2-mg dose of epinephrine and is about the size of a teabag; the product is supplied in packages containing two devices. The drug delivery system is the same as that used in several other FDA-approved nasal sprays, including naloxone *(Narcan)*. An absorption-enhancing agent *(Intravail)*, which is also used in nasal spray formulations of drugs such as sumatriptan *(Tosymra)* and diazepam *(Valtoco)*, increases epinephrine bioavailability.[4]

Key Points: *neffy*

- **Description:** The first epinephrine nasal spray.
- **Indication:** Emergency treatment of type 1 hypersensitivity reactions including anaphylaxis in patients who weigh ≥30 kg.
- **Clinical Studies:** In studies in healthy subjects, the nasal spray appeared to be pharmacologically comparable to injectable epinephrine.
- **Adverse Effects:** Throat irritation, headache, nasal discomfort, a jittery sensation, tremor, and rhinorrhea can occur.
- **Dosage:** One 2-mg spray intranasally; the dose can be repeated 5 minutes later if symptoms do not improve.
- **Cost:** The wholesale acquisition cost of a package containing two single-use devices is $710; according to the manufacturer, the cost for most patients with commercial insurance will not exceed $25.
- **Conclusion:** The *neffy* nasal spray could be more convenient to use than injectable epinephrine for some individuals. It has not been studied in persons with underlying structural nasal conditions.

CLINICAL STUDIES — As with injectable epinephrine products for treatment of anaphylaxis, no efficacy trials were required for FDA approval of *neffy*. Approval was based on the results of five pharmacologic studies (summarized in the package insert) in a total of 175 healthy adults and 42 healthy children 8-17 years old who weighed ≥30 kg. Exposure to epinephrine and changes in blood pressure and pulse rate following a 2-mg dose of the nasal spray were comparable to those following a 0.3-mg IM dose, including in subjects with seasonal allergic rhinitis who underwent a nasal allergen challenge. The nasal spray has not been studied in persons with underlying structural nasal conditions, such as polyps or a history of nasal injury or surgery.

ADVERSE EFFECTS — The most common adverse effects of two doses of *neffy* in adults (incidence 7-19%) were throat irritation, headache, nasal discomfort, a jittery sensation, tremor, and rhinorrhea. Similar adverse effects were observed in children. The nasal spray solution contains sodium metabisulfite, which could cause a hypersensitivity reaction in patients with a sulfite allergy, but a history of sulfite sensitivity should not deter emergency use of the product.

Table 1. Some Epinephrine Products for Anaphylaxis[1]

Product	Usual Adult Dosage[2]	Cost[3]
Auto-Injectors		
EpiPen (Mylan) generic (Mylan,[4] Teva)	0.3 mg IM or SC	$608.60[5] 300.00[5]
generic (Amneal)[6]	0.3 mg IM or SC	300.00[7]
AUVI-Q (Kaléo)	0.3 mg IM or SC	621.90[8]
Syringe		
Symjepi (US Worldmeds)	0.3 mg IM or SC	250.00[9]
Nasal Spray		
neffy (ARS Pharma)	2 mg intranasally	710.00[10]

1. In patients who weigh ≥30 kg.
2. A second dose can be administered using a new device if needed.
3. Approximate WAC for two doses. WAC = wholesaler acquisition cost or manufacturer's published price to wholesalers; WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource® Monthly. September 5, 2024. Reprinted with permission by First Databank, Inc. All rights reserved. ©2024. www.fdbhealth.com/policies/drug-pricing-policy.
4. The Mylan product is an authorized generic drug.
5. Mylan provides free epinephrine auto-injectors to eligible uninsured or underinsured patients who are from families earning up to 400% of the federal poverty level (https://aspe.hhs.gov/poverty-guidelines). Manufacturer-issued coupons for *EpiPen* and its authorized generic are available for patients with commercial insurance.
6. Authorized generic of *Adrenaclick*, which has been discontinued.
7. Available at discounted prices at some pharmacies (at CVS pharmacies, the cash price is $110.00 for a package containing two auto-injectors).
8. Kaléo provides free *AUVI-Q* auto-injectors to eligible uninsured patients who are from families earning up to 250% of the federal poverty level (https://aspe.hhs.gov/poverty-guidelines). According to the manufacturer, the out-of-pocket cost should not exceed $35 for most patients with standard commercial insurance or $150 for patients with high-deductible commercial insurance.
9. A manufacturer-issued coupon card reduces the copay to $0 for commercially insured patients and reduces the cost by $100 for uninsured patients.
10. Wholesale acquisition cost according to the manufacturer. According to the manufacturer, the out-of-pocket cost should not exceed $25 for most patients with commercial insurance or $199 for those using coupons from discount sites such as GoodRx.

DOSAGE, ADMINISTRATION, AND COST — The recommended dosage of *neffy* is one 2-mg spray administered into one nostril. If symptoms do not improve after 5 minutes, a second spray may be administered into the same nostril using a new device. The devices should be stored at room temperature, but excursions up to 50° C (122° F) are permitted; injectable epinephrine formulations only permit excursions to 30° C (86° F). At temperatures below -15° C (5° F), the nasal spray solution freezes and the device does not deliver epinephrine. Like other epinephrine products, *neffy* should be replaced before its expiration date. The shelf life of *neffy* is 30 months, which is longer than injectable epinephrine products (generally 12-18 months).

According to the manufacturer, the out-of-pocket cost for two *neffy* nasal spray devices should not exceed $25 for most patients with commercial insurance or $199 for those using coupons from discount sites such as GoodRx.[5]

CONCLUSION — The *neffy* nasal spray offers a new, potentially more convenient route of epinephrine delivery for emergency treatment of anaphylaxis in adults and children who weigh ≥30 kg. Whether its effectiveness differs from that of injectable epinephrine remains to be determined. Until data on the efficacy of *neffy* become available, some expert clinicians are advising patients to also carry an injectable epinephrine product. *Neffy* has not been studied in patients with underlying structural nasal conditions, such as polyps or a history of injury or surgery. ■

1. Auvi-Q epinephrine auto-injector returns. Med Lett Drugs Ther 2017; 59:33.
2. An epinephrine prefilled syringe (Symjepi) for anaphylaxis. Med Lett Drugs Ther 2019; 61:25.
3. American Society of Health-System Pharmacists. Current drug shortages. Available at: https://bit.ly/3Qs7ETT. Accessed September 26, 2024.
4. AK Ellis et al. Development of neffy, an epinephrine nasal spray, for severe allergic reactions. Pharmaceutics 2024; 16:811.
5. ARS Pharma Press Release. ARS Pharmaceuticals receives FDA approval of neffy (epinephrine nasal spray), the first and only needle-free treatment for type I allergic reactions, including anaphylaxis. August 9, 2024. Available at: https://bit.ly/4cyySk4. Accessed September 26, 2024.