

# The Medical Letter<sup>®</sup>

## on Drugs and Therapeutics

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# The Medical Letter®

## on Drugs and Therapeutics

Volume 66 (Issue 1713)

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### ▶ An Epinephrine Nasal Spray (*neffy*) for Anaphylaxis

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  $\geq 30$  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*.<sup>1</sup> 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.<sup>2</sup>

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.<sup>3</sup>

**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

#### Key Points: *neffy*

- ▶ **Description:** The first epinephrine nasal spray.
- ▶ **Indication:** Emergency treatment of type 1 hypersensitivity reactions including anaphylaxis in patients who weigh  $\geq 30$  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.

as sumatriptan (*Tosymra*) and diazepam (*Valtoco*), increases epinephrine bioavailability.<sup>4</sup>

**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  $\geq 30$  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<sup>1</sup>**

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

- In patients who weigh  $\geq 30$  kg.
- A second dose can be administered using a new device if needed.
- 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.
- The Mylan product is an authorized generic drug.
- 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.
- Authorized generic of *Adrenaclick*, which has been discontinued.
- Available at discounted prices at some pharmacies (at CVS pharmacies, the cash price is \$110.00 for a package containing two auto-injectors).
- 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.
- A manufacturer-issued coupon card reduces the copay to \$0 for commercially insured patients and reduces the cost by \$100 for uninsured patients.
- 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.<sup>5</sup>

**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  $\geq 30$  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. ■

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