Self-Administration of Intranasal Epinephrine (*neffy*) Using the Aptar Unit Dose System Compared to EpiPen and Symjepi

Richard Lowenthal, MS, MBA[1]; Brian T. Dorsey, MSc[1]; Robert Hasson, BA[2]; Anthony D. Andre, PhD, CPE[3]; Sarina Tanimoto, MD, PhD[1]
[1]ARS Pharmaceuticals, Inc., San Diego, CA, USA; [2]Pacific Link Consulting, Inc., San Diego, CA, USA; [3]Interface Analysis Associates, Saratoga, CA, USA

RATIONALE

- Systemic hypersensitivity reactions that lead to anaphylaxis can be life-threatening. These reactions typically occur outside of a hospital setting and are almost always unexpected
- Delays in treating hypersensitivity reactions can result in progression to anaphylaxis and may result in death due to airway obstruction or vascular collapse
- Epinephrine auto-injectors are the current standard of care outside of the hospital setting; however, a lack of injection compliance is a potentially significant cause of treatment failure and indicates the need for alternate modes of administration
  - Intranasal (IN) administration of epinephrine represents the most viable alternative to injection
- We present the findings of 2 studies (Human Factors Validation and In-Use Clinical studies) that investigated the IN administration of *neffy* or saline using the Aptar Unit Dose System (UDS)
  - EpiPen, Symjepi, and *neffy* were the 3 devices tested in the In-Use Clinical study (**Figure 1**); only *neffy* was tested in the Human Factors Validation study

METHODS

Human Factors Validation Study

- Ninety participants were included in the Human Factors Validation study, including 15 each in the following user groups:
  - Adult patients with EpiPen experience
  - Adolescent patients with EpiPen experience
  - Adult patients without EpiPen experience
  - Adolescent patients without EpiPen experience
  - Passers-by without EpiPen experience
  - Healthcare providers with EpiPen experience
- All participants were placed into a simulated emergency scenario, where they had to respond to a severe allergic reaction, either their own allergic reaction or someone else experiencing a severe allergic reaction. All participants were observed as they attempted to administer a dose with the product in its secondary packaging (as one would carry it) and performed follow-up tasks
- Participants were then given a second scenario, where time had elapsed and their (or the patient's) symptoms got worse. All participants were observed again to evaluate if and how they administered a second dose. All participants were then presented with the full product (carton, devices, and instructions for use [IFU]) and asked knowledge task questions regarding critical information presented on the carton and in the IFU

In-Use Clinical Study

- The In-Use Clinical study was a randomized crossover study in which 36 participants were asked to self-administer *neffy*, Symjepi, and EpiPen. *neffy* was dosed to 1 nostril using the Aptar UDS, which is identical to the planned commercial product. EpiPen and Symjepi were dosed per product label instructions by intramuscular injection to the left anterolateral thigh
- All participants were provided with scripted training on each device at least 4 weeks before study enrollment. No additional assistance from study personnel was provided during the self-administration period

RESULTS

Human Factors Validation Study Dosing

- First dose: When placed in an emergency situation, where the participant had to self-administer a first dose or administer a first dose to someone else during a severe allergic reaction, all participants (90/90; 100%) successfully removed the nasal spray from the packaging, inserted the nasal spray into the nostril, and pushed up on the plunger to administer the dose
- Second dose: When presented with a scenario where time had elapsed and the patient's symptoms got worse, all participants (90/90; 100%) successfully delivered a second dose, both to themselves and to others. Most subjects (80/90; 89%) correctly delivered the second dose to the other nostril

In-Use Clinical Study Dosing

- *neffy:* All participants (36/36; 100%) successfully completed all administration tasks
- EpiPen: All participants (36/36; 100%) successfully completed all administration tasks. Ten participants (27.8%) did not hold the pen down for 3 seconds, and 22 participants (61.1%) did not massage the injection site following the injection
- Symjepi: One participant (1/36; 2.8%) did not push the plunger down and failed to complete the administration task. Of the remaining 35 participants, 5 participants (14.3%) did not hold pen down for 2 seconds, 1 subject (2.9%) pulled the needle out too soon as they pressed the plunger (resulting in a wet injection or partial dose), and 26 subject (74.3%) did not massage the injection site
- The average dosing time was shortest for *neffy* (29.22 seconds), followed by EpiPen (37.64 seconds) and Symjepi (46.46 seconds) (**Table 1 and Figure 2**)

Figure 1. EpiPen, Symjepi, and *neffy* Devices

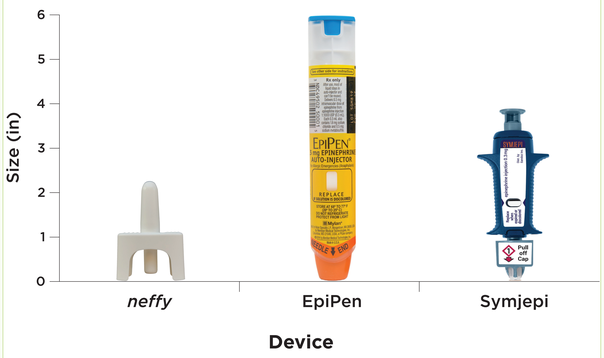
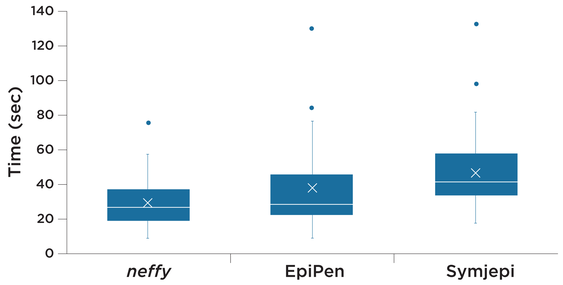


Table 1. Time to Administration, by Product

Product	Time to Administration (seconds)		
	Mean	Median	Range
neffy	29.22	26.37	9.36-75.74
EpiPen	37.64	28.53	8.84-130.26
Symjepi	46.46	41.57	17.55-133.17

Figure 2. Time (seconds) to Administration, by Product



DISCUSSION

- *neffy* was correctly administered by all participants in both the Human Factors Validation and In-Use Clinical studies
- EpiPen was also correctly administered by all participants in the In-Use Clinical study; however, 27.8% of participants failed to hold the pen down for the required time (3 seconds), and a majority of participants (61.1%) did not massage the injection site, as instructed in the label
- Symjepi was correctly administered by 97.2% of participants; 1 participant failed to push the plunger down and did not complete the administration, and a majority of participants (74.3%) did not massage the injection site after injection, as instructed in the label

CONCLUSIONS

- In the Human Factors Validation study, participants that were naïve and untrained in the use of the Aptar UDS were able to safely and successfully administer *neffy* during a simulated emergency scenario, either to themselves or another participant
- No dosing errors were observed following *neffy* administration, even when significant time (4 weeks) elapsed between training and administration
- In the In-Use Clinical study, dosing errors were observed with both EpiPen and Symjepi

Presented at the Annual Meeting of the American Academy of Allergy, Asthma and Immunology; February 25-28, 2022; Phoenix, AZ

Copyright © 2022. All rights reserved.