Epinephrine Nasal Powder - a sustainable and reliable option for the treatment of anaphylaxis

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Purpose:

Orexo is developing OX640, a preservative-free nasal epinephrine powder formulation for treatment of anaphylaxis, designed to be stable across a wide temperature range and to have a prolonged shelf-life compared to liquid formulations. This work investigated stability of the powder formulation in comparison to a commercial autoinjector. From a sustainability perspective, OX640 offers potential advantages in terms of material use, expiration date, and waste reduction thanks to its novel powder formulation and needle-free design.

Methods:

The OX640 formulation included 1 mg of epinephrine, along with trehalose, maltodextrin and sucrose laurate and was produced by an optimized spray-drying process. The powder was filled into a unidose nasal powder delivery system (Aptar Pharma, France) with a fill weight of 25 mg and placed in protective storage tubes with desiccant. Stability (epinephrine content, enantiomeric proportion and epinephrine degradation) of OX640 and the autoinjector was evaluated using HPLC-UV methods under accelerated storage conditions (40°C/75% RH) and under extreme conditions (50°C at ambient RH) for 6 months (OX640 only).

Results:

The spray drying process yielded a free-flowing, rapidly dissolving powder with a narrow particle size distribution, optimal for nasal deposition (10-100 µm). OX640 exhibited minimal degradation and racemization of epinephrine for up to 12 months, whereas the autoinjector showed a decrease in assay from 105% to 73% and an enantiomeric purity of only 76%, resulting in a nominal dose of approximately 55% after 12 months, **Figure 1 and 2**. Even at 50°C, OX640 remained remarkably stable with less than 1% total degradation, still delivering the full dose without the need for antioxidants or preservatives, **Table 1**. SEM images can be seen in **Figure 3**.

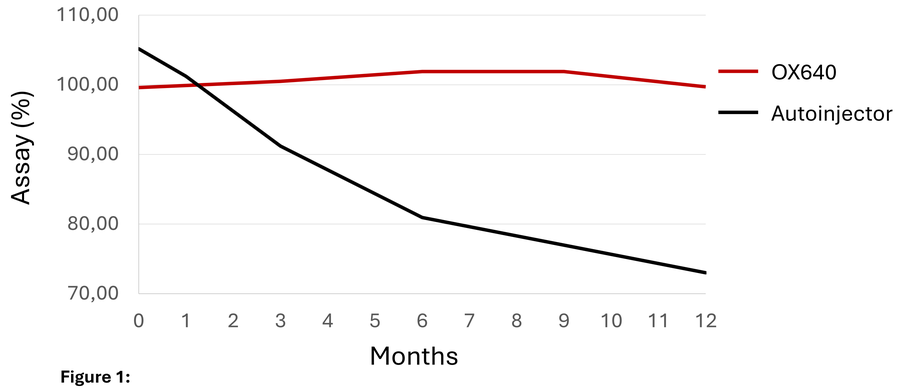

Figure 1:

Degradation of epinephrine expressed as epinephrine content in relation to target dose (%) after storage at **40°C** and 75% relative humidity

Table 1:

Stability of OX640 stored at **50°C** for 6 months

	Initial	1 M	3 M	6 M
Epinephrine content (%)	99.6	100.3	100.7	99.9
Epinephrine degradation (%)	≤0.10	≤0.10	0.27	0.57

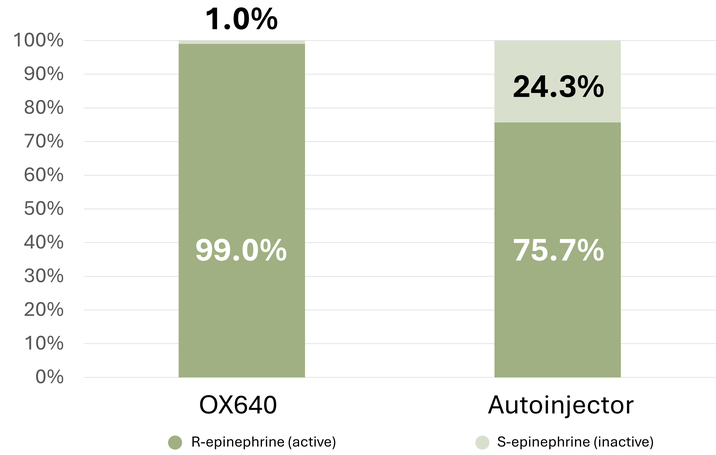

Figure 2:

Enantiomeric purity/content in percentage after storage at **40°C** and 75% relative humidity after 12 months. R-epinephrine is the native and active form of epinephrine, while S-epinephrine is inactive (~10% rel. activity)

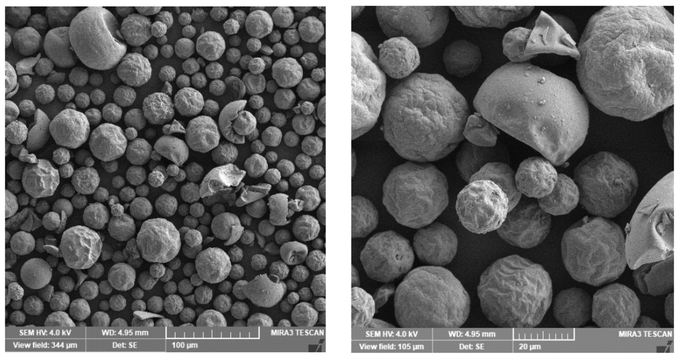

Figure 3:

Scanning Electron Microscope (SEM) images of one typical batch of OX640 at two different magnifications

Conclusions:

The OX640 epinephrine nasal powder provided superior stability compared to the autoinjector, providing for longer shelf-life and less strict storage conditions. This may benefit patients with risk of anaphylaxis by reducing the need for refills and ensuring access to effective, non-degraded medication when needed.

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