

Nemera

ADVANCIA®: A TRUE PLATFORM & INNOVATIVE SYSTEM OFFERING EFFICIENT NASAL DOSE DELIVERY

Millions of people suffering from allergic rhinitis use nasal sprays manufactured by Nemera every day. In this article, company Global Category Manager, ENT Products, Pascale Farjas, provides an overview of the company's nasal delivery platform, Advancia®.

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The intranasal route is widely used both for prescription and over-the-counter (OTC) drugs. It is an attractive option for locally acting / topical drugs (e.g. nasal decongestants or nasal steroids), as well as for systemic acting drugs (anti-migraine medication, hormones, etc), boasts a rapid onset of action and it is very convenient.

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Moreover, treatments via the nasal route are self-administered and therefore nasal delivery systems have a positive impact on compliance. Patients should be able to rely on their nasal spray anytime during the treatment, especially during allergy-related symptoms. That's why the device must be user-friendly and convenient to carry around.

Nemera offers standard delivery devices for nasal, buccal and auricular routes for both OTC and prescription drugs. They

are recognised and valued by patients and pharmaceutical companies alike. The company guarantees precision and dose consistency, to ensure an optimal treatment.

The development of the multidose nasal spray, Advancia®, illustrates perfectly Nemera's patient-oriented innovation process. The new technology pump provides outstanding performance responding to increasing regulatory requirements for nasal sprays.

Advancia® (see Figure 1), is the high performing metering pump platform that patients can count on. With accurate dosing, patients can be confident that each dose is fully delivered. Advancia® offers an alternative to improve treatment compliance in an increasingly demanding nasal spray market. Designed to be a step ahead of today's pumps, Advancia® is based on a new system combining user-independence and preservative-free features in one single system.

A TRUE PLATFORM

Advancia® is offered in various different configurations (two pump engines, two fittings, three doses), making it a true nasal drug delivery platform suitable for:

- Lifecycle management of off-patent allergic rhinitis products and OTC decongestants
- New combination treatments that target nasal allergies (e.g. steroids + antihistamines)
- Pipeline allergy molecules
- New drugs in development through the nasal route.

Advancia® Crimp-on is covered in a US DMF Type III.



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PATENTED ANTI-CLOGGING ACTUATOR

The Advancia® platform's closing tip prevents clogging, which can be a particular problem with formulations prone to crystallisation. The patented closing tip mechanism (shown in Figure 2):

1. Ensures that no contamination can enter through the actuator orifice
2. Provides protection from crystallisation and clogging issues
3. Avoids evaporation to guarantee excellent prime retention.

This benefit improves patient compliance and can drastically reduce the number of complaints due to non-functioning pumps.

Other key product features of Advancia® include:

- User-independence
- Excellent dose consistency
- Long prime retention
- Mechanical closing tip to prevent clogging issues
- No metal part in contact with the formulation
- Plastic components made of polyolefins only (PE and PP) which comply with EP-USP-FDA regulations
- DMF available
- One-step snap-on process to boost productivity on filling lines.

Example specifications for different configurations of Advancia® are summarised in Table 1.

USER STUDIES

The patients' voice is the key driver of all Nemera product development. Patient insights and human factors studies are at the heart of the innovation process. We conduct user studies to make sure our products respond to patient needs, and to benchmark Nemera delivery systems *versus* competition. Two user studies were performed with Advancia® in 2011 and 2013 with 30 patients, including children, adults and seniors, with a double objective:

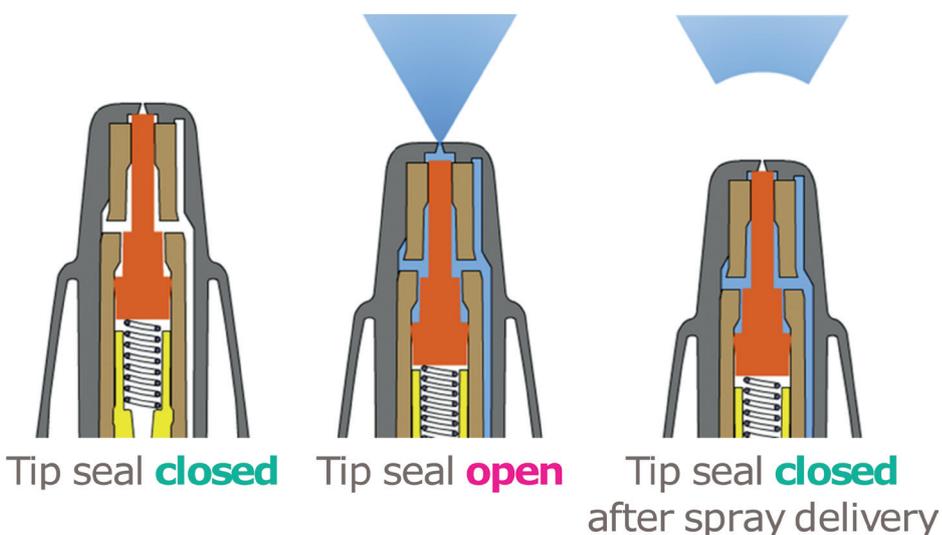
- Demonstrate the user-independence feature of Advancia®
- Benchmark Advancia® against competition on dose consistency.



Snap-on

Crimp-on

Figure 1: Advancia® is a nasal drug delivery platform based on a new system combining user-independence and preservative-free features in one single system.



Tip seal closed

Tip seal open

Tip seal closed after spray delivery

Figure 2: The patented closing tip mechanism that prevents clogging.

	Advancia® Std	Advancia® PF*
Fitment	Crimp-on 20 mm Snap-on 20 mm*	Snap-on 20 mm
Doses (µl)	50, 100, 140*	50, 100, 140*
Raw materials in contact with the formulation	PE, PP, gasket raw materials, silicone	PE, PP, silicone
Nasal actuators	 Crimp-on: AD5701	 Snap-on: AD5705

* in development

Table 1: Specifications of different Advancia configurations.

Comparison with Competitor Pumps

Regardless of the design, the reproducibility of the dose is one of the most crucial attributes as this parameter may affect the delivery of the drug substance to the intended biological target. As shown in Figure 3, Advancia® is the best performing pump, both on dose adjusting *versus* nominal value and reproducibility, independently of the user. As a reminder, pump spray weight delivery acceptance criteria should control the weight of the individual sprays to within 15% of the target weight and their mean weight to within 10% of the target weight.

Because of user-independence feature, the activation speed is higher for Advancia® than for other pumps (illustrated by white diamonds on the graph in Figure 3). This is a specific and patented design. This feature is achieved with a commitment point, designed to accumulate energy at the beginning of the stroke. As a consequence, the user cannot stop the pump actuation before the end of the stroke and will have a full dose delivered.

Designed with Users' Real Lives in Mind

Patient feedback from the user studies was also collected on Advancia® Snap-

**Comparison of Dose accuracy and Speed actuation
Advancia® vs. Competitive devices**

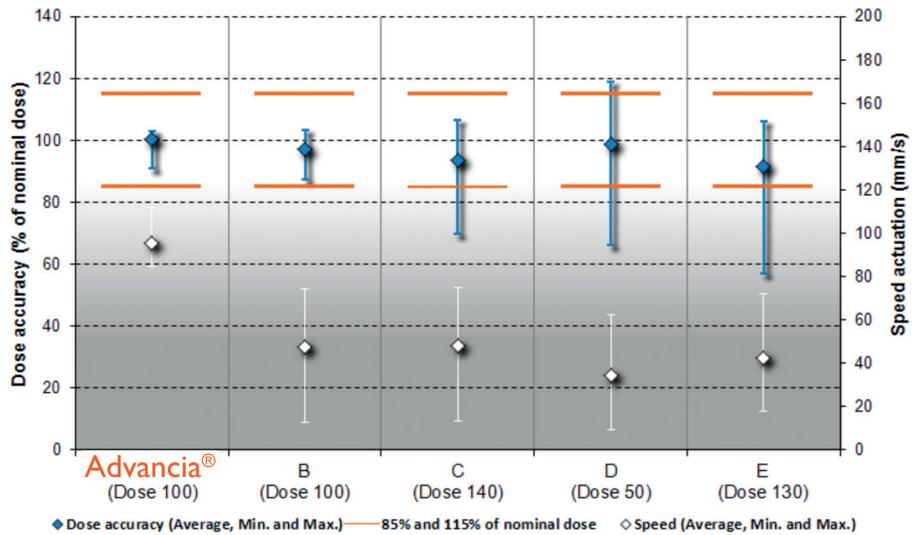


Figure 3: Comparison of dose accuracy and speed of actuation from Advancia® with competitor devices.

on and four competitor devices. While the competitor devices look alike, Advancia® Snap-on was perceived to have outstanding style and usage features. Users highlighted its “all-inclusive design”, perfectly adapted to real life situations where users carry their drug with them. The sleek, all integrated design of Advancia® makes it less prone to

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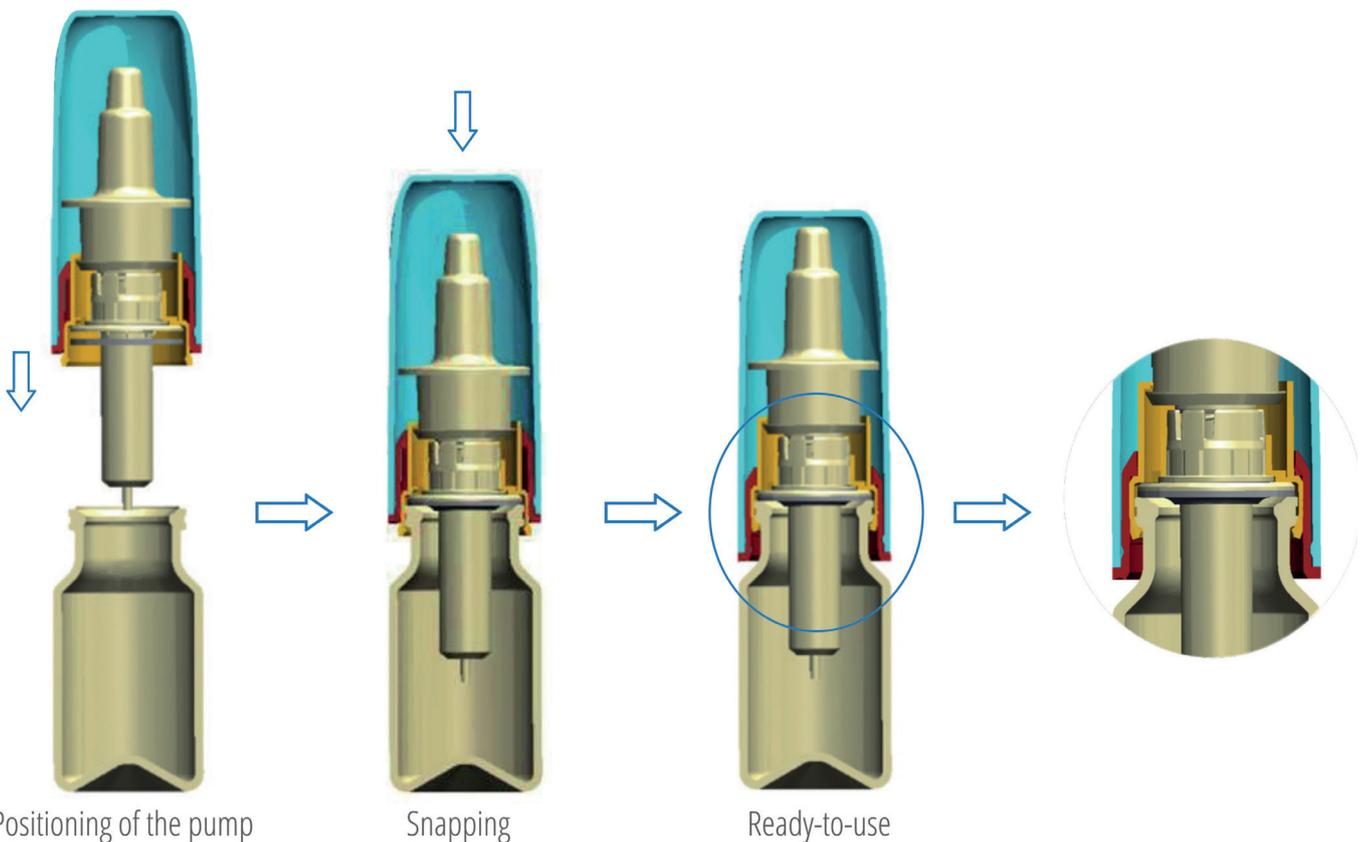


Figure 4: Advancia’s design means it is an easy-to-fill system with one-step assembly.

accumulating dirt in a bag or a pocket, whereas the overcap makes it easier to manipulate and less prone to getting lost than the classic small caps present on other devices. Moreover, the actuator is designed to be ergonomically sound for all users including children.

In summary, Advancia® was shown to be the best performing pump, both on dose accuracy and reproducibility, independently of the user. Users also highlighted Advancia®'s integrated Snap-on design, well-suited to today's on-the-go lifestyle.

EASY TO FILL, ONE-STEP ASSEMBLY

The design of Advancia® allows for a simple, efficient process during product filling and assembly (Figure 4). In terms of production, the main advantages of the Advancia® Snap-on system compared with competitors' devices are:

- No radial stress on bottle neck avoiding risk of glass bottles breakage or plastic bottles deformation or damage

- Sealing at the beginning of assembly process avoiding presence of foreign particles in the bottle due to friction between parts
- "Tamper Evident": very difficult to remove the system & not easy to re-place the actuator correctly onto the bottle
- Similar assembly force profile whatever the bottle is (material, neck design, etc).

Indeed, the assembly force required to snap the Advancia® system onto the bottle is very similar from one bottle to another, as opposed to standard snap-on systems where the bottle neck design can have a high impact on the assembly force profile.

ADVANCIA® CRIMP-ON: AVAILABLE NOW!

Nemera invested more than €10 million in Advancia®. A new European ISO8 clean room building with new injection moulding and assembly machines was constructed, with a focus on safety and quality with 100% tolerance controls and visual inspection on critical areas. As such,

the next-generation nasal spray pump, Advancia®, is now in production with annual capacity of 45 million units after full ramp-up...

... and in early 2017, a preservative-free version of Advancia® Snap-On version will be available for customer sampling.

ABOUT THE COMPANY

Nemera is a world leader in the design, development and manufacturing of drug delivery solutions. It has more than 50 engineers working in development, over 30000 m² of clean-room manufacturing, sales in 47 countries, 750 million+ devices produced yearly and over 1300 employees. Nemera has four plants in Europe and the US at Neuenburg, Germany; La Verpillière, France (Figure 5); Le Tréport, France; and Buffalo Grove, IL, US.

Nemera's portfolio includes devices across the board of drug delivery routes including parenteral; pulmonary; transdermal; buccal / auricular; and ophthalmic. This is in addition to the nasal offering described here.



Figure 5: Nemera's Innovation Centre at La Verpillière, near Lyon, France.

Nemera



nasal/
buccal/
auricular



pulmonary



dermal/
transdermal



parenteral



ophthalmic

SP270+

Advancia®

**SP270 PUMP PLATFORM
FOR ENT SOLUTIONS AND SUSPENSIONS
AND ADVANCIA NEW USER INDEPENDENT
NASAL SPRAY PLATFORM**

Nemera provides solutions for the pharmaceutical industry, including standard innovative products, development of custom devices and contract manufacturing.

we put
**patients
First**