# A single centre, double blind, randomised, parallel group study to explore the efficacy and tolerability of intranasal fluticasone propionate compared with placebo delivered by the OptiNose device in adult subjects with chronic rhinosinusitis.

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| **Ethical review** | Approved WMO |
| **Status** | Pending |
| **Health condition type** | Upper respiratory tract disorders (excl infections) |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON30750

**Source**
ToetsingOnline

**Brief title**
OptiNose Intranasal Fluticasone Propionate and Chronic Rhinosinusitis

### Condition

- Upper respiratory tract disorders (excl infections)

**Synonym**
chronic rhinosinusitis

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** OptiNose UK Ltd
**Source(s) of monetary or material Support:** OptiNose UK Ltd;South Marston Park;Wiltshire SN3 4TG;Verenigd Koninkrijk

## Intervention

**Keyword:** Chronic rhinosinusitis, fluticasone propionate, OptiNose device, Phase IIa

## Outcome measures

### Primary outcome

Efficacy Parameters:

·Change from baseline to last visit (Visit 5) in Visual Analogue Scale (VAS) overall symptom score for chronic rhinosinusitis. Change from baseline to other timepoints will be a secondary endpoint.

·Change from baseline to each visit in the Clinician assessment of nasal blockage on nasendoscopy using the Lund and Mackay scoring system.

·Monthly change from baseline (mean daily score over the last 7 days of run-in) in morning and evening combined averaged symptom score for each month from patient Diary.

·Change from baseline to each visit in the Rhinosinusitis Outcome Measure 31 (RSOM-31).

·The change from baseline in the inflammatory mucosa measured using magnetic resonance imaging (MRI) at 12 weeks.

·Change from baseline to each visit in nasal volume and cross-sectional area

measured using acoustic rhinometry.

·Change from baseline to each visit in peak nasal inspiratory flow (PNIF)

·Use of rescue medication.

**Secondary outcome**

Safety Parameters:

·Adverse events

·Vital signs

·Clinical laboratory tests (hematology, clinical chemistry, urinalysis)

·Morning plasma cortisol concentration

·physical examination.

# Study description

**Background summary**

A phase IIa, single centre, randomised, prospective, double-blind, parallel group study. Patients will be divided into two treatment groups; one group that will receive fluticasone propionate, the other group the placebo. The OptiNose device is primed and positioned in one nostril and the subject blows into the mouthpiece of the device. This exhalation against the resistance of the device closes the soft palate due to positive pressure, so separating the nasal and oral cavities and avoiding lung deposition which enables smaller particles to be delivered. In addition, it establishes bi-directional airflow through the nose. Blowing through the device triggers the breath-actuation mechanism and releases the dose from the nasal spray. After this 12 week-study, results of the two treatments will be compared and analysed to judge if the fluticasone propionate and the way of admission really is a benefit for the patient.

**Study objective**

The aim of this study is to investigate if bidirectional delivery, by

delivering more drug to the region of the sinus ostia, improves upon the efficacy of current nasal steroids in chronic rhinosinusitis.

to get information about the efficacy, safety and tolerability of fluticasone propionate using the OptiNose device in subjects with chronic rhinosinusitis.

**Study design**

A phase IIa, single centre, randomised, prospective, double-blind, parallel group, placebo-controlled study.

**Intervention**

Half of the group (20 subjects) will receive 400 micrograms twice dialy (total daily dose of 800 micrograms) of the investigated productl (Fluticasone Propionate) and the other half will receive placebo twice dialy .

**Study burden and risks**

Three risks with consequent precautions need to be highlighted:
In very rare cases (<1/10,000), hypersensitivity reactions, with respiratory symptoms (bronchospasm) and anaphylactic reactions have been reported. These manifestations might become very serious and even life-threatening. As a precaution, the protocol dictates that special mention will be made to the subject that there have been very rare reports of a severe allergic reaction to fluticasone propionate. If any subject suddenly develops a rash, swelling (usually of the face, lips or tongue) or difficulty with breathing, the subject should stop using the study medication and contact the Principal Investigator immediately. All subjects should be asked specifically if they have experienced prior reactions to fluticasone propionate. AEs associated with nasal administration of fluticasone propionate are presented in Table 6.
The bioavailability of and hence systemic exposure to fluticasone is expected to be far below any levels that can give systemic side-effects and adverse events. However, it is important that the subjects do not take any potent P450/CYP 3A inhibitors (which can increase the fluticasone propionate plasma concentrations several hundred fold, resulting in marked suppression of serum cortisol concentrations). As a precaution, subjects that are receiving any P450/CYP 3A inhibitor are to be excluded.
Although the clinical data indicate otherwise, there is a theoretical possibility that fluticasone propionate can lead to developmental and birth-defects. Therefore, pregnant subjects, or subjects that might become pregnant, must be excluded.

See Table 6 Expected Adverse Events

As with other nasal sprays, unpleasant taste and smell and headache have been

reported.
As with other nasal sprays, dryness and irritation of the nose and throat, and epistaxis have been reported.
Nasal septal perforation has also been reported following the use of intranasal corticosteroids.
Systemic effects of some nasal corticosteroids may occur, particularly when prescribed at high doses for prolonged periods.
Undesirable effects resulting from Flixonase Aqueous Nasal Spray (SPC).
Frequencies are defined as: very common (>1/10), common (>1/100 and <1/10), uncommon (>1/1000 and <1/100), rare (>1/10,000 and <1/1000) and very rare (<1/10,000) including isolated reports. Very common, common and uncommon events were generally determined from clinical trial data. Rare and very rare events were generally determined from spontaneous data. In assigning adverse event frequencies, the background rates in placebo groups were not taken into account.

# Contacts

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# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

### Age

Adults (18-64 years)
Elderly (65 years and older)

## Inclusion criteria

- Male and female subjects aged between 18 and 65 years of age.
- Subjects must have chronic rhinosinusitis which is defined as at least 12 weeks history of two or more of:
* Blockage/congestion
* Discharge: anterior/post nasal drip
* Facial pain/pressured
* Reduction or loss of smell
And either:
* Mucopurulent discharge from the middle meatus or
* Edema/mucosal obstruction primarily in the middle meatus.
- Subjects must have no clinically significant abnormal serum biochemistry, haematology and urine examination values on screening.
- Subjects must have verified airflow through both nostrils and an ability to close their soft palate.
- The subject must have the ability to create bi-directional flow using a placebo OptiNose device with a nasal outflow of >20 L/min.
- The subject must have the ability to trigger the Breath Actuation Mechanism of an OptiNose device in accordance with the Instructions For Use.

## Exclusion criteria

- Subjects who have visible pedunculated polyps on nasal endoscopy.
- Subjects who have undergone surgical treatment for nasal polyps during the previous 3 months.
- Subjects with a diagnosis of cystic fibrosis.
- Subjects with other disease likely to interfere with the study parameters, evidence of any serious or unstable concurrent disease or psychological disorder.
- A hypersensitivity or contraindication to steroids or any excipients.
- Subjects who have received depot or oral steroids during the previous 3 months.
- Subjects with a requirement for more than 1000 µg beclomethasone (or equivalent) per day for the treatment of asthma.
- Subjects taking inhaled steroids who have not been on a stable dose for 3 months or more.
- Subjects who are unable to cease treatment with intranasal steroids, or intranasal sodium cromoglycate, decongestants or antihistamines at the Screening Visit.
- Subjects currently receiving leukotriene receptor antagonists, nasal atropine or ipratropium bromide, beta blockers or neuroleptics.
- Subjects who are unable to cease treatment with saline rinsing at the Screening Visit.
- Subjects using devices that dilate the nostrils to improve nasal breathing.
- Subjects being treated with ritonavir or other potent CYP3A inhibitors as listed in Appendix 2 of the protocol due to the potential for greatly increased fluticasone plasma concentrations.

- Subjects with a history of operations where metal objects were used and retained in the body or those with a pacemaker or other implants e.g. cochlear implants and artificial heart valves.
- Subjects with a history of a penetrating injury to the eye with a metal object or those who have worked with metal at high speed.
- A history of drug or alcohol abuse.
- Subjects with an inability to communicate well with the investigator (i.e. language problem,poor mental development or impaired cerebral function)
- Subjects with a cleft palate.
- Subjects who have participated in a New Chemical Entity study within the previous 16 weeks or a marketed drug study within the previous 12 weeks.

# Study design

## Design

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| Study phase: | 2 |
| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Double blinded (masking used) |
| Control: | Placebo |
| Primary purpose: | Treatment |

## Recruitment

NL

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| Recruitment status: | Pending |
| Start date (anticipated): | 01-03-2007 |
| Enrollment: | 40 |
| Type: | Anticipated |

# Ethics review

Approved WMO

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| Date: | 02-04-2007 |
| Application type: | First submission |

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| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 18-10-2007 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 09-01-2008 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |

# Study registrations

## Followed up by the following (possibly more current) registration

No registrations found.

## Other (possibly less up-to-date) registrations in this register

No registrations found.

## In other registers

| Register | ID |
|---|---|
| EudraCT | EUCTR2006-006341-13-NL |
| CCMO | NL15630.018.07 |