# A randomised, single dose, crossover, open label, placebo controlled confirmatory study with interim analysis in healthy volunteers to characterise the acid neutralisation activity of Gaviscon Double Action Tablets in the fasted state, using an intragastric and oesophageal pH catheter

Published: 17-05-2016
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The primary objective of this confirmatory study is to investigate the acid neutralisation action of Gaviscon Double Action Tablets versus placebo tablets, within the stomach.The secondary objective of this study is to assess the safety of the test...

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| **Ethical review** | Not approved |
| **Status** | Will not start |
| **Health condition type** | Other condition |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON42922

**Source**
ToetsingOnline

**Brief title**
RB2-NL-1519 (CS0253)
Acid neutralisation confirmatory pH monitoring study

### Condition

- Other condition

- Gastrointestinal disorders

**Synonym**
gastric acid reflux, Healthy volunteers, heartburn

**Health condition**

GORD

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Reckitt Benckiser Healthcare (Ltd) UK
**Source(s) of monetary or material Support:** Reckitt Beckiser Healthcare (UK) LtD

## Intervention

**Keyword:** Acid neutralisation, Healthy volunteers, Placebo - controlled, Randomised

## Outcome measures

### Primary outcome

The primary endpoint will be the mean percentage of time that pH * 4 over 0-30 minutes post-dose across electrodes 5 to 10. The primary analysis will be the comparison of this endpoint between Gaviscon Double Action Tablets and placebo tablets.

### Secondary outcome

Secondary endpoints are:

* The mean percentage of time that pH * 4 over the interval 30-60 minutes post-dose across electrodes 5 to 10.

* The mean percentage of time that pH * 3 over the intervals 0-30 minutes and 30-60 minutes post-dose across electrodes 5 to 10.

* The mean percentage of time that pH * 3 and pH * 4 over the 10 minute

intervals post-dose across electrodes 5 to 10.

* The percentage of time that pH * 3 and pH * 4 over the 10 minute and 30

minute intervals at each electrode.

These endpoints will be compared between Gaviscon Double Action Tablets and

placebo.

For both treatments, the following will be displayed non-comparatively:

* The pH value measured every 4 seconds during each monitoring period at each

electrode.

# Study description

**Background summary**

Reckitt Benckiser (RB) is interested in understanding the antacid effect of sodium alginate formulations. This confirmatory mode of action study is being conducted to characterise the acid neutralisation activity of the Investigational Medicinal Product (IMP), Gaviscon Double Action Tablets, by comparing antacid action with a tablet placebo. Data from this study will be used commercially to support acid neutralisation claims for Gaviscon Double Action formulations.

An exploratory study (RB reference GA1406) has been completed on Gaviscon Double Action Liquid and has confirmed suitable methodology for the detection of changes in intragastric pH. This utilised a custom designed (European Conformity [CE] marked) 10 electrode pH catheter that measured pH simultaneously in various positions through the stomach in fasted conditions. The same custom designed (CE marked) catheter will be used in this study (schematic provided in Appendix 1).

Following the GA1406 exploratory study, a confirmatory study is being conducted (RB2-NL-1518) to characterise the acid neutralisation activity of Gaviscon Double Action Liquid. Data is also required for the tablet formulation. This study is being run as a confirmatory study to demonstrate the mode of action of the Gaviscon Double Action Tablets. The effect of the change of format on drug release and subsequent antacid effect needs to be confirmed as the liquid is an easily swallowed suspension, containing dissolved and undissolved antacid active pharmaceutical ingredients (APIs), while the chewable tablets require

mastication prior to swallowing to enable release of the antacid APIs.

This study is also required to support the roll out of Gaviscon Double Action in both product formats, due to potential regulatory non-acceptance of data bridging between product formats.

An additional study (GA1402) is being conducted to assess symptomatic relief from heartburn and indigestion in patients following Gaviscon Double Action Tablet administration.

**Study objective**

The primary objective of this confirmatory study is to investigate the acid neutralisation action of Gaviscon Double Action Tablets versus placebo tablets, within the stomach.

The secondary objective of this study is to assess the safety of the test formulation.

**Study design**

The study will be a single centre, randomised, single dose, crossover, open-label, placebo controlled confirmatory mode of action study, with interim analysis to characterise the acid neutralisation activity of Gaviscon Double Action Tablets (4 tablets) in fasted healthy volunteers, using an intragastric and oesophageal pH catheter.

The study is not blinded.

**Intervention**

Subjects will attend the Clinical Unit on 4 occasions over approximately 7 weeks (one pre-study screening visit [within 21 days prior to the first treatment visit], two treatment visits [each including an overnight stay] and one post-study follow-up visit [3-7 days after end of the second treatment visit]). During each treatment period, subjects will stay in the Clinical Unit from the evening prior to dosing until approximately 2 h after dosing. Doses during treatment periods are separated by a minimum washout period of 5 days and a maximum of 14 days. Potential suitable subjects will be identified according to QPS standard procedures. Written informed consent will be obtained prior to any pre-study procedures.

Screening: The pre-study procedures will consist of baseline characteristics, medical history, physical examination, concomitant medication, vital signs, ECG, haematology, clinical biochemistry, viral serology, urine pregnancy test for female subjects, urinalysis, urinary drugs of abuse and alcohol breath test

assessments.

Treatment Periods (1 and 2): Subjects who fulfil all the screening eligibility criteria will return to the Clinical Unit for the first treatment period, where eligibility for entry onto the study will be confirmed. Eligibility will be checked against the inclusion/exclusion criteria. For treatment period 2, eligibility will be checked against the withdrawal criteria. Upon entry into the Clinical Unit on Day -1 of each treatment period, concomitant medications will be recorded, an alcohol breath test, urinary drugs of abuse test, urine pregnancy test (female subjects), vital signs, ECG and physical examination will be conducted. The subject will remain in the Clinical Unit overnight.
On Day 1, eligible subjects will be randomised to one of the two treatment sequence groups and transferred to the Martini Hospital endoscopy suite.
Fasted subjects will undergo nasal endoscopy, in order to locate the Squamocolumnar Junction (SCJ) and will have the pH catheter inserted according to the measurements obtained during the nasal endoscopy.
Following catheter insertion, the subjects will rest for at least 60 minutes.
Baseline pH readings will be taken every 4 seconds for 30 (up to 45) minutes to enable the pH readings to stabilise. Any subject whose pH recordings do not stabilise or who meet any of the withdrawal criteria will be withdrawn from the study.
Each subject will be dosed with either Gaviscon Double Action Tablets or placebo tablets and pH will be recorded for a further 65 minutes (± 5 minutes) after which the pH catheter will be removed via simple traction.
Within 30 minutes of catheter removal, the subject will be given a drink and light snack before being transferred back to the Clinical Unit. At the Clinical Unit, the subject will receive a meal and the scheduling of Treatment Period 2 will be confirmed, the subject will be provided with a *Volunteer Participation Card* and the subjects may leave the Clinical Unit. Adverse events (AEs) will be solicited by non-leading questions throughout the study.
During the stay in the Clinical Unit subjects will receive meals, and general/dietary restrictions will apply.
Post Study Follow-up Visit: The post-study follow-up visit will be conducted 3 to 7 days after the end of Treatment Period 2. Concomitant medication, AEs, physical examination, vital signs, ECG, haematology, clinical biochemistry, urine pregnancy test (for female subjects) and urinalysis will be recorded.

The total volume of blood drawn from each subject during the study will be approximately 16 ml.

**Study burden and risks**

The potential risks to subjects taking part in the present study are considered to be low. The adverse reactions that occur very rarely (<1/10,000) as a result of taking sodium alginate products are allergic manifestations such as urticaria or bronchospasm, anaphylactic or anaphylactoid reactions as a result of a subject being sensitive to any of the active substances (sodium alginate,

sodium bicarbonate and calcium carbonate) or any of the excipients (e.g. hydroxybenzoates [parabens]). Other adverse reactions include increased plasma sodium levels especially for those with renal and cardiovascular conditions on a highly restricted salt diet and high doses of calcium may cause alkalosis, hypercalcaemia, acid rebound, milk alkali syndrome or constipation. However as the subjects in this study are healthy volunteers and the subjects are receiving only a single dose, the risk of these adverse reactions are considered very low.
The nasal endoscopy, guide wire and catheter insertion/positioning involves risks to the subjects including bleeding, perforation of the oesophagus, stomach or duodenum and reactions to any drugs administered as part of the procedure, such as local anaesthetics. In the GA1406 study, there were 5 subjects who experienced nasal mucus blood tinged/nose bleeding/nasal pain, out of the 20 subjects enrolled, which were related to the nasal endoscopy procedure, all of which were resolved. The risk to the subject for this adverse event (AE) is considered low.
Healthy volunteers are not expected to derive any benefit from participation in the study, however through their participation in this trial they will provide further clinical data to help characterise the antacid action of Gaviscon Double Action Tablets. This will provide support for indications such as hyperacidity and excess stomach acid and will better inform consumers about the action and potential benefits of sodium alginate formulations. For this reason, the risk benefit balance for the current study is considered to be acceptable.

## 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

Only subjects to whom all of the following conditions apply will be included:
1. Male or female subjects who have given written informed consent.
2. Age: * 18 years * 50 years.
3. Body Mass Index (BMI): * 18.5 and * 24.9 kg/m2.
4. Height * 1.90 metres
5. Healthy as determined by past medical history, physical examination, vital signs, ECG, and laboratory tests at screening.

## Exclusion criteria

Subjects to whom any of the following conditions apply must be excluded:
1. A history of gastro-oesophageal reflux or active gastrointestinal disease (gastroduodenal ulcer, gastrointestinal haemorrhage, mechanical obstruction or perforation) within the last year.
2. Clinically significant diseases of any body system.
3. A medical history that is associated with an increased risk in study procedures (e.g. basal skull fracture or those who have undergone trans-sphenoidal surgery).
4. Hospitalisation within the previous 3 months for major surgery or medical illness.
5. A clinically significant illness within the 4 weeks prior to screening.
6. Ingestion of any prescription medication or non-prescription medication within the 7 days, prior to the screening visit, which the Principal Investigator considers may interfere with the study.
7. Ingestion of antacids, H2 antagonists, motility stimulants (e.g. prokinetics, macrolide antibiotics such as erythromycin and azithromycin, and 5HT agonists such as sumatriptan) or other medicines for relief of symptoms of acid reflux disease 2 weeks prior to the screening visit and during the study and/or have taken proton pump inhibitors in the 4 weeks prior to the screening visit and during the study.
8. Those who are currently taking any of the following medications: antihistamines, tetracyclines, digoxin, quinolones including fluoroquinolone, iron salts, neuroleptics, thyroxine and levothyroxine, penicillamine, beta-blockers (e.g. atenolol, metoprolol, propranolol), glucocorticoid, chloroquine, biphosphonates, ketoconazole, eltrombopag and thiazide

diuretics.
9. A history of drug hypersensitivity, which in the opinion of the Principal Investigator might interfere with the study.
10. A history of allergy or intolerance to the Investigational Medicinal Products (IMP) or the following formulation constituents: e.g. macrogol 20,000, mannitol (E421], copovidone, acesulfame K, aspartame (E951), mint flavour, carmoisine lake (E122), magnesium stearate, xylitol DC (contains carmellose sodium).
11. A current or recent history (within 1 year of the screening visit) of alcohol abuse or significant abuse/misuse of any legal or illegal drugs, substances and solvents.
12. Those with a positive screen/test for drugs of abuse and/or alcohol.
13. Those who regularly (weekly) consume excessive amounts of alcohol (> 8 units for men and > 6 units for women in one consumption, excessive amounts as defined by the UK National Office of Statistics).
14. Those who have consumed more than 2 units of alcohol per day in the 7 days prior to the screening visit and from the screening visit up to 48 hours before admission to the Clinical Unit for Treatment Period 1.
15. Those who have consumed alcohol within the 48 hours before admission to the Clinical Unit for Treatment Period 1 and there is insufficient time for the visit to be rescheduled.
16. Those who regularly consume excessive quantities of caffeine (> 6 cups of tea, coffee or cola per day), according to the Investigator*s judgement.
17. Those who have consumed caffeine-containing food and drinks within the 48 hours before admission to the Clinical Unit for Treatment Period 1 and there is insufficient time for the visit to be rescheduled.
18. Those who are either unable to refrain from using tobacco/nicotine during the study treatment periods or unable to smoke less than 6 cigarettes (or equivalent) per day.
19. Those with any clinically significant abnormal laboratory result, in the opinion of the Principal Investigator.
20. Known human immunodeficiency virus (HIV) positive status, or a positive viral serology screen.
21. Female subjects of child bearing potential who are unwilling to use an effective method of contraception unless they are abstaining from sexual intercourse in line with the preferred and usual lifestyle of the subject, for the entire study duration (see section 4.4).
22. Male subjects who are not willing to use an effective method of contraception for the entire study duration, unless anatomically sterile or where abstaining from sexual intercourse in line with the preferred and usual lifestyle of the subject (see section 4.4).
23. Female subjects who are pregnant or lactating.
24. Those who are unable to communicate well with the Investigator (i.e. language or neurodevelopmental disorders) in the opinion of the Investigator.
25. Those previously randomised into this study.
26. Those who are an employee at the study site.
27. Those who are a partner or first-degree relative of the Investigator.
28. Those who have participated in a clinical study in the 3 months prior to the screening visit.
29. Those who have participated in 4 (or more) clinical studies in the 10 months prior to the screening visit.
30. Those who have donated more than 1.5 litres of blood in the 10 months prior to the screening visit.

31. Those who are unable, in the opinion of the Investigator, to comply fully with the study requirements.

# Study design

## Design

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| Study phase: | 3 |
| Study type: | Interventional |
| Intervention model: | Crossover |
| Allocation: | Randomized controlled trial |
| Masking: | Open (masking not used) |
| Control: | Placebo |
| Primary purpose: | Treatment |

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Will not start |
| Enrollment: | 12 |
| Type: | Anticipated |

## Medical products/devices used

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|---|---|
| Generic name: | pH catheter |
| Registration: | Yes - CE intended use |
| Product type: | Medicine |
| Brand name: | Gaviscon Dual 250 Mg / 106,5 Mg / 187,5 Mg Kautabletten |
| Registration: | Yes - NL intended use |

# Ethics review

Approved WMO

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|---|---|
| Date: | 17-05-2016 |
| Application type: | First submission |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek |

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| | (Assen) |
| Not approved | |
| Date: | 20-07-2016 |
| Application type: | First submission |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |

# 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 | EUCTR2016-000538-22-NL |
| CCMO | NL57733.056.16 |