Clinical trial results:
A randomised, assessor blind, placebo controlled exploratory study in healthy volunteers, to characterise the acid neutralisation activity of sodium alginate oral suspension in the fasted state, using a custom-designed intragastric and oesophageal pH catheter.

Summary

EudraCT number	2014-003158-15
Trial protocol	NL
Global end of trial date	13 July 2015

Results information

Result version number	v1 (current)
This version publication date	28 September 2017
First version publication date	28 September 2017

Trial information

Trial identification

Sponsor protocol code	GA1406

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Reckitt Benckiser Healthcare (UK) Ltd
Sponsor organisation address	Dansom Lane, Hull, United Kingdom, HU8 7DS
Public contact	Clinical Research Director, Clinical Research, Reckitt Benckiser Healthcare (UK) Limited, clinicalrequests@rb.com
Scientific contact	Clinical Research Director, Clinical Research, Reckitt Benckiser Healthcare (UK) Limited, clinicalrequests@rb.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	23 January 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 July 2015
Global end of trial reached?	Yes
Global end of trial date	13 July 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the intragastric acid neutralisation action of sodium alginate oral suspension versus placebo liquid.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice (GCP) and the ethical principles contained within the Declaration of Helsinki, as referenced in EU Directive 2001 / 20 / EC.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 April 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 20
Worldwide total number of subjects	20
EEA total number of subjects	20

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	20
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was a single-centre study conducted in Netherlands.

Pre-assignment

Screening details:

Subjects enrolled were 20. Group 1 subjects were 6 and Group 2 subjects were 14.

Period 1

Period 1 title	Treatment 1
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Liquid Cohort (Group II): Treatment P

Arm description:

Placebo Liquid 2 x 10 ml sachets single dose by mouth under fasted condition.

Total 14 subjects received Placebo in Period 1 (8 subjects) and Period 2 (6 subjects) with 5 to 14 days washout period between dosing. Two subjects withdrew from the study during washout period.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral liquid
Routes of administration	Oral use

Dosage and administration details:

Placebo Liquid 20 ml sachets single dose by mouth under fasted condition.

Arm title	Tablet Cohort (Group I): Treatment B

Arm description:

2 x Chewable tablets (calcium carbonate 680 mg and magnesium carbonate 80 mg per tablet) single dose by mouth under fasted condition.

This was a separate group to assess the suitability of the custom-designed pH catheter and pH monitoring methodology.

Arm type	non-comparative
Investigational medicinal product name	Chewable tablets (calcium carbonate 680 mg and magnesium carbonate 80 mg)
Investigational medicinal product code	
Other name	Rennie Kauwtabletten
Pharmaceutical forms	Chewable tablet
Routes of administration	Oral use

Dosage and administration details:

2 x Chewable tablets (Calcium Carbonate 680mg and Magnesium Carbonate 80mg per tablet) by mouth.

Number of subjects in period 1	Liquid Cohort (Group II): Treatment P	Tablet Cohort (Group I): Treatment B
Started	14	6
Completed	12	6
Not completed	2	0
Consent withdrawn by subject	2	-

Period 2

Period 2 title	Treatment 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Liquid Cohort (Group II) - Treatment A

Arm description:

Sodium Alginate 20 ml single dose by mouth under fasted condition

Total 12 subjects completed period 1 and 2 in group II (Liquid Cohort).

Arm type	Experimental
Investigational medicinal product name	Sodium Alginate Oral Suspension
Investigational medicinal product code	
Other name	Gaviscon Double Action Liquid
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Sodium Alginate 20 ml (sodium alginate 500 mg , sodium bicarbonate 213 mg, and calcium carbonate 325 mg per sachet) sachet by mouth.

Number of subjects in period 2[1]	Liquid Cohort (Group II) - Treatment A
Started	12
Completed	12

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Six subjects were in Group I (Tablet cohort). This was a separate group to assess the suitability of the custom-designed pH catheter and pH monitoring methodology.

Baseline characteristics

Reporting groups	
Reporting group title	Treatment 1
Reporting group description:	
All subjects (AS) population: All subjects recruited to the study.	

Reporting group values	Treatment 1	Total	
Number of subjects	20	20	
Age categorical Units: Subjects			
Adults (18-64 years)	20	20	
Age continuous Units: years			
arithmetic mean	25.4		
standard deviation	± 5.6	-	
Gender categorical Units: Subjects			
Female	8	8	
Male	12	12	
Ethnicity Units: Subjects			
Not Hispanic or Latino	20	20	
Race Units: Subjects			
Caucasian	19	19	
Asian	1	1	
Height Units: cm			
arithmetic mean	178.01		
standard deviation	± 9.36	-	
Weight Units: kg			
arithmetic mean	69.87		
standard deviation	± 9.79	-	
BMI			
BMI - Body Mass Index			
Units: kg/m2			
arithmetic mean	21.9		
standard deviation	± 1.4	-	

End points

End points reporting groups

Reporting group title	Liquid Cohort (Group II): Treatment P

Reporting group description:

Placebo Liquid 2 x 10 ml sachets single dose by mouth under fasted condition.

Total 14 subjects received Placebo in Period 1 (8 subjects) and Period 2 (6 subjects) with 5 to 14 days washout period between dosing. Two subjects withdrew from the study during washout period.

Reporting group title	Tablet Cohort (Group I): Treatment B

Reporting group description:

2 x Chewable tablets (calcium carbonate 680 mg and magnesium carbonate 80 mg per tablet) single dose by mouth under fasted condition.

This was a separate group to assess the suitability of the custom-designed pH catheter and pH monitoring methodology.

Reporting group title	Liquid Cohort (Group II) - Treatment A

Reporting group description:

Sodium Alginate 20 ml single dose by mouth under fasted condition

Total 12 subjects completed period 1 and 2 in group II (Liquid Cohort).

Primary: Mean Percentage of Time that pH ≥4 Over 0-30 Minutes Post-Dose Across Electrodes 5 to 10 in Liquid Cohort (Group II)

End point title	Mean Percentage of Time that pH ≥4 Over 0-30 Minutes Post-Dose Across Electrodes 5 to 10 in Liquid Cohort (Group II)[1]

End point description:

Intention-to-treat (ITT) population: All subjects who were recruited to the study and had some pH data for at least one treatment visit.

End point type	Primary

End point timeframe:

From 0 to 30 minutes post-dose in visit 2 (Period 1) and visit 3 (Period 2)

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Tablet cohort (Group I) was used only to assess the methodology and was not included in the analysis of the primary endpoint.

End point values	Liquid Cohort (Group II): Treatment P	Liquid Cohort (Group II) - Treatment A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	12		
Units: Percentage of time (%)				
arithmetic mean (standard deviation)	4.7 (± 8.7)	46.8 (± 29.2)		

Statistical analyses

Statistical analysis title	Treatment A versus P at pH ≥4 over >0 - ≤30 min
Comparison groups	Liquid Cohort (Group II): Treatment P v Liquid Cohort (Group II) - Treatment A
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0004
Method	ANCOVA

Secondary: Mean Percentage of Time that pH ≥4 Over 30-60 Minutes Post-Dose Across Electrodes 5 to 10

End point title	Mean Percentage of Time that pH ≥4 Over 30-60 Minutes Post-Dose Across Electrodes 5 to 10

End point description:

ITT population.

This endpoint was compared between sodium alginate oral suspension and placebo. For calcium carbonate / magnesium carbonate chewable tablets, this endpoint was assessed non-comparatively.

End point type	Secondary

End point timeframe:

From 30 to 60 minutes post-dose in visit 2 (Period 1) and visit 3 (Period 2)

End point values	Liquid Cohort (Group II): Treatment P	Tablet Cohort (Group I): Treatment B	Liquid Cohort (Group II) - Treatment A	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	6	12	
Units: Percentage of time (%)				
arithmetic mean (standard deviation)	3.9 (± 9.8)	12.1 (± 16.2)	15.7 (± 31.8)	

Statistical analyses

Statistical analysis title	Treatment A versus P at pH ≥4 over >30 - ≤60 min
Comparison groups	Liquid Cohort (Group II): Treatment P v Liquid Cohort (Group II) - Treatment A
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1379
Method	ANCOVA

Secondary: Mean Percentage of Time that pH ≥3 Over 0-30 and 30-60 Minutes Post-Dose Across Electrodes 5 to 10

End point title	Mean Percentage of Time that pH ≥3 Over 0-30 and 30-60

	Minutes Post-Dose Across Electrodes 5 to 10

End point description:

ITT population.

This endpoint was compared between sodium alginate oral suspension and placebo. For calcium carbonate / magnesium carbonate chewable tablets, this endpoint was assessed non-comparatively.

End point type	Secondary

End point timeframe:

Up to 60 minutes post-dose in visit 2 (Period 1) and visit 3 (Period 2)

End point values	Liquid Cohort (Group II): Treatment P	Tablet Cohort (Group I): Treatment B	Liquid Cohort (Group II) - Treatment A	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	6	12	
Units: Percentage of time (%)				
arithmetic mean (standard deviation)				
Interval >0 - ≤30 min	6.6 (± 9.2)	57.2 (± 20.5)	49 (± 30.2)	
Interval >30 - ≤60 min	6.6 (± 17.4)	16.5 (± 18)	16.8 (± 33.2)	

Statistical analyses

Statistical analysis title	Treatment A versus P at pH ≥3 over > 0 - ≤ 30 min
Comparison groups	Liquid Cohort (Group II): Treatment P v Liquid Cohort (Group II) - Treatment A
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0024
Method	ANCOVA

Statistical analysis title	Treatment A versus P at pH ≥3 over >30 - ≤60 min
Comparison groups	Liquid Cohort (Group II): Treatment P v Liquid Cohort (Group II) - Treatment A
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3601
Method	ANCOVA

Secondary: Mean Percentage of Time that pH ≥3 and pH ≥4 over 10 Minute Intervals post-dose across electrodes 5 to 10

End point title	Mean Percentage of Time that pH ≥3 and pH ≥4 over 10 Minute Intervals post-dose across electrodes 5 to 10

End point description:

ITT population.

This endpoint was compared between sodium alginate oral suspension and placebo. For calcium carbonate / magnesium carbonate chewable tablets, this endpoint was assessed non-comparatively.

End point type	Secondary

End point timeframe:

Up to 60 minutes post-dose in visit 2 (Period 1) and visit 3 (Period 2)

End point values	Liquid Cohort (Group II): Treatment P	Tablet Cohort (Group I): Treatment B	Liquid Cohort (Group II) - Treatment A	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	6	12	
Units: Percentage of time (%)				
arithmetic mean (standard deviation)				
pH ≥3 over >0 - ≤10 min	11.4 (± 13.4)	60 (± 17)	69.7 (± 20.5)	
pH ≥3 over >10 - ≤20 min	4.5 (± 8.7)	67.7 (± 31.5)	49.8 (± 40.6)	
pH ≥3 over >20 - ≤30 min	3.9 (± 9.1)	43.4 (± 29.3)	26.9 (± 43.2)	
pH ≥3 over >30 - ≤40 min	6.2 (± 16.4)	14.1 (± 12.2)	20.2 (± 36.5)	
pH ≥3 over >40 - ≤50 min	6.4 (± 16.8)	14.3 (± 16.7)	15.8 (± 33.7)	
pH ≥3 over >50 - ≤60 min	7.2 (± 19)	21.1 (± 39.1)	14.2 (± 30.5)	
pH ≥4 over >0 - ≤10 min	8.6 (± 11.2)	54.9 (± 16.9)	66.1 (± 20)	
pH ≥4 over >10 - ≤20 min	3.3 (± 8.5)	60.7 (± 30.5)	48 (± 40.8)	
pH ≥4 over >20 - ≤30 min	2.3 (± 8.3)	32.5 (± 22.9)	25.8 (± 41.9)	
pH ≥4 over >30 - ≤40 min	3.3 (± 8.8)	8.3 (± 7.8)	18.2 (± 34.3)	
pH ≥4 over >40 - ≤50 min	2.7 (± 7.8)	8.9 (± 11.1)	15.2 (± 32.5)	
pH ≥4 over >50 - ≤60 min	5.6 (± 14.3)	18.9 (± 39.3)	13.4 (± 29.1)	

Statistical analyses

Statistical analysis title	Treatment A versus P at pH ≥3 over >0 - ≤10 min
Comparison groups	Liquid Cohort (Group II): Treatment P v Liquid Cohort (Group II) - Treatment A
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA

Statistical analysis title	Treatment A versus P at pH ≥3 over >10 - ≤20 min
Comparison groups	Liquid Cohort (Group II): Treatment P v Liquid Cohort (Group II) - Treatment A

Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004
Method	ANCOVA

Statistical analysis title	Treatment A versus P at pH ≥3 over >20 - ≤30 min
Comparison groups	Liquid Cohort (Group II): Treatment P v Liquid Cohort (Group II) - Treatment A
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1314
Method	ANCOVA

Statistical analysis title	Treatment A versus P at pH ≥3 over >30 - ≤40 min
Comparison groups	Liquid Cohort (Group II): Treatment P v Liquid Cohort (Group II) - Treatment A
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1972
Method	ANCOVA

Statistical analysis title	Treatment A versus P at pH ≥3 over >40 - ≤50 min
Comparison groups	Liquid Cohort (Group II): Treatment P v Liquid Cohort (Group II) - Treatment A
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3306
Method	ANCOVA

Statistical analysis title	Treatment A versus P at pH ≥3 over >50 - ≤60 min
Comparison groups	Liquid Cohort (Group II): Treatment P v Liquid Cohort (Group II) - Treatment A

Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3875
Method	ANCOVA

Statistical analysis title	Treatment A versus P at pH ≥4 over >0 - ≤10 min
Comparison groups	Liquid Cohort (Group II): Treatment P v Liquid Cohort (Group II) - Treatment A
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA

Statistical analysis title	Treatment A versus P at pH ≥4 over >10 - ≤20 min
Comparison groups	Liquid Cohort (Group II): Treatment P v Liquid Cohort (Group II) - Treatment A
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0033
Method	ANCOVA

Statistical analysis title	Treatment A versus P at pH ≥4 over >20 - ≤30 min
Comparison groups	Liquid Cohort (Group II): Treatment P v Liquid Cohort (Group II) - Treatment A
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1317
Method	ANCOVA

Statistical analysis title	Treatment A versus P at pH ≥4 over >30 - ≤40 min
Comparison groups	Liquid Cohort (Group II): Treatment P v Liquid Cohort (Group II) - Treatment A

Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2167
Method	ANCOVA

Statistical analysis title	Treatment A versus P at pH ≥4 over >40 - ≤50 min
Comparison groups	Liquid Cohort (Group II): Treatment P v Liquid Cohort (Group II) - Treatment A
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2819
Method	ANCOVA

Statistical analysis title	Treatment A versus P at pH ≥4 over >50 - ≤60 min
Comparison groups	Liquid Cohort (Group II): Treatment P v Liquid Cohort (Group II) - Treatment A
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3953
Method	ANCOVA

Secondary: Mean Percentage of Time that pH ≥3 and pH ≥4 Over the 10 minute intervals at each electrode

End point title	Mean Percentage of Time that pH ≥3 and pH ≥4 Over the 10 minute intervals at each electrode

End point description:

ITT population.

This endpoint was compared between sodium alginate oral suspension and placebo. For calcium carbonate/magnesium carbonate chewable tablets, this endpoint was assessed non-comparatively.

End point type	Secondary

End point timeframe:

Up to 60 minutes post-dose in visit 2 (Period 1) and visit 3 (Period 2)

End point values	Liquid Cohort (Group II): Treatment P	Tablet Cohort (Group I): Treatment B	Liquid Cohort (Group II) - Treatment A	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	6	12	
Units: Percentage of time (%)				
arithmetic mean (standard deviation)				
Electrode 1 pH ≥3 over >0 - ≤10 min	99 (± 1.1)	99.5 (± 0)	99.4 (± 0.4)	
Electrode 2 pH ≥3 over >0 - ≤10 min	95.4 (± 8.1)	99.5 (± 0)	98.8 (± 0.9)	
Electrode 3 pH ≥3 over >0 - ≤10 min	49 (± 42.4)	94 (± 4.9)	89.3 (± 9.4)	
Electrode 4 pH ≥3 over >0 - ≤10 min	27.2 (± 34.7)	88.2 (± 5.3)	76.4 (± 19.9)	
Electrode 5 pH ≥3 over >0 - ≤10 min	35.4 (± 40)	82.8 (± 6)	77.5 (± 16.7)	
Electrode 6 pH ≥3 over >0 - ≤10 min	22.9 (± 32.9)	79.3 (± 9.7)	81.6 (± 14.5)	
Electrode 7 pH ≥3 over >0 - ≤10 min	3.3 (± 7)	70.9 (± 17)	74.7 (± 18.5)	
Electrode 8 pH ≥3 over >0 - ≤10 min	4.4 (± 9.1)	40 (± 27.3)	59 (± 32.3)	
Electrode 9 pH ≥3 over >0 - ≤10 min	1.4 (± 2.4)	37.1 (± 26)	61.8 (± 33)	
Electrode 10 pH ≥3 over >0 - ≤10 min	1 (± 1.9)	49.7 (± 36.9)	63.4 (± 26.5)	
Electrode 1 pH ≥3 over >10 - ≤20 min	99.4 (± 0.4)	99.5 (± 0)	99.5 (± 0)	
Electrode 2 pH ≥3 over >10 - ≤20 min	94.2 (± 18.7)	98.5 (± 1.1)	99.4 (± 0.2)	
Electrode 3 pH ≥3 over >10 - ≤20 min	48.7 (± 41.4)	66 (± 35.1)	59.6 (± 40.2)	
Electrode 4 pH ≥3 over >10 - ≤20 min	14.9 (± 33)	65.8 (± 28.8)	37.5 (± 38.8)	
Electrode 5 pH ≥3 over >10 - ≤20 min	13.5 (± 27.7)	70.4 (± 35.1)	38.3 (± 40.7)	
Electrode 6 pH ≥3 over >10 - ≤20 min	9.7 (± 24.2)	78.8 (± 33.2)	47.7 (± 44.7)	
Electrode 7 pH ≥3 over >10 - ≤20 min	0.6 (± 2)	81.7 (± 36.5)	49.7 (± 43)	
Electrode 8 pH ≥3 over >10 - ≤20 min	2 (± 5.4)	48.9 (± 46.3)	50.6 (± 42.6)	
Electrode 9 pH ≥3 over >10 - ≤20 min	1 (± 2.8)	63.3 (± 44.4)	55.2 (± 42.7)	
Electrode 10 pH ≥3 over >10 - ≤20 min	0.6 (± 2.1)	63.1 (± 39.6)	57.6 (± 39)	
Electrode 1 pH ≥3 over >20 - ≤30 min	99.1 (± 0.6)	99.5 (± 0)	99.3 (± 0.4)	
Electrode 2 pH ≥3 over >20 - ≤30 min	92.4 (± 19.7)	98.8 (± 0.6)	98.2 (± 2)	
Electrode 3 pH ≥3 over >20 - ≤30 min	37.8 (± 38.2)	50.1 (± 35.9)	50.3 (± 45.9)	
Electrode 4 pH ≥3 over >20 - ≤30 min	10.1 (± 26.1)	20.8 (± 23.9)	25.5 (± 38.2)	
Electrode 5 pH ≥3 over >20 - ≤30 min	7.3 (± 25.6)	42.5 (± 33.9)	23.8 (± 41.8)	
Electrode 6 pH ≥3 over >20 - ≤30 min	10.3 (± 25.8)	52 (± 33.6)	32.9 (± 48.4)	
Electrode 7 pH ≥3 over >20 - ≤30 min	0.7 (± 2.3)	41.7 (± 33.4)	24.9 (± 45)	
Electrode 8 pH ≥3 over >20 - ≤30 min	4.9 (± 18.2)	32.3 (± 37.7)	24.9 (± 45)	
Electrode 9 pH ≥3 over >20 - ≤30 min	0.3 (± 0.9)	42.6 (± 40.3)	26.8 (± 44.3)	
Electrode 10 pH ≥3 over >20 - ≤30 min	0.1 (± 0.4)	49.3 (± 39.3)	28.2 (± 43.6)	
Electrode 1 pH ≥3 over >30 - ≤40 min	98.9 (± 1.2)	99.4 (± 0.3)	99.3 (± 0.6)	
Electrode 2 pH ≥3 over >30 - ≤40 min	94.2 (± 13.6)	98.5 (± 0.8)	97.1 (± 5.7)	
Electrode 3 pH ≥3 over >30 - ≤40 min	46.5 (± 42.8)	46.6 (± 40)	49 (± 45.8)	
Electrode 4 pH ≥3 over >30 - ≤40 min	9.5 (± 26.2)	3.1 (± 3.8)	23.6 (± 37)	
Electrode 5 pH ≥3 over >30 - ≤40 min	7.2 (± 26.4)	5 (± 5.7)	15.3 (± 35.1)	
Electrode 6 pH ≥3 over >30 - ≤40 min	12.3 (± 31.3)	6.9 (± 7.7)	25.3 (± 43.3)	
Electrode 7 pH ≥3 over >30 - ≤40 min	0.1 (± 0.5)	11.5 (± 18.6)	17.4 (± 35.6)	
Electrode 8 pH ≥3 over >30 - ≤40 min	7.2 (± 26.6)	14.3 (± 16.8)	20.6 (± 38.8)	
Electrode 9 pH ≥3 over >30 - ≤40 min	6.3 (± 23.3)	21.6 (± 26.6)	22.3 (± 40.9)	
Electrode 10 pH ≥3 over >30 - ≤40 min	4.2 (± 15.1)	25.4 (± 30.2)	20.4 (± 38.6)	
Electrode 1 pH ≥3 over >40 - ≤50 min	99.3 (± 0.6)	98.4 (± 1.9)	98.9 (± 0.9)	
Electrode 2 pH ≥3 over >40 - ≤50 min	97.5 (± 3.4)	96.6 (± 5.9)	93.5 (± 15.4)	
Electrode 3 pH ≥3 over >40 - ≤50 min	44.5 (± 40)	34 (± 30.2)	48.5 (± 45.5)	
Electrode 4 pH ≥3 over >40 - ≤50 min	9.8 (± 26.1)	1.4 (± 1.8)	20.6 (± 36.3)	
Electrode 5 pH ≥3 over >40 - ≤50 min	7 (± 24.6)	6.3 (± 9.3)	17 (± 38.6)	

Electrode 6 pH ≥3 over >40 - ≤50 min	12.9 (± 33.1)	13.6 (± 21.4)	24.9 (± 45)	
Electrode 7 pH ≥3 over >40 - ≤50 min	0.5 (± 1.6)	12.7 (± 19.8)	9.6 (± 28.7)	
Electrode 8 pH ≥3 over >40 - ≤50 min	7.3 (± 26.6)	16.5 (± 25.6)	11.1 (± 29.5)	
Electrode 9 pH ≥3 over >40 - ≤50 min	7.1 (± 26.6)	19 (± 19.2)	16.3 (± 38.1)	
Electrode 10 pH ≥3 over >40 - ≤50 min	3.4 (± 12.7)	17.6 (± 22.5)	15.9 (± 37.2)	
Electrode 1 pH ≥3 over >50 - ≤60 min	98.9 (± 1.2)	99.4 (± 0.3)	99.3 (± 0.5)	
Electrode 2 pH ≥3 over >50 - ≤60 min	97 (± 4.8)	98.6 (± 1.2)	98.2 (± 1.5)	
Electrode 3 pH ≥3 over >50 - ≤60 min	53.8 (± 42.5)	30.3 (± 30.8)	43.9 (± 40.3)	
Electrode 4 pH ≥3 over >50 - ≤60 min	13.3 (± 31.2)	23.1 (± 39.7)	17.9 (± 35.7)	
Electrode 5 pH ≥3 over >50 - ≤60 min	7.3 (± 26.5)	19.9 (± 39.6)	17.3 (± 38.5)	
Electrode 6 pH ≥3 over >50 - ≤60 min	14.1 (± 33.2)	19.7 (± 39.6)	25.4 (± 44.7)	
Electrode 7 pH ≥3 over >50 - ≤60 min	0.2 (± 0.9)	25.3 (± 41.9)	8.3 (± 28.7)	
Electrode 8 pH ≥3 over >50 - ≤60 min	7.3 (± 26.6)	23.3 (± 40.7)	8.4 (± 28.7)	
Electrode 9 pH ≥3 over >50 - ≤60 min	7.1 (± 26.6)	17.6 (± 40.1)	16 (± 37.5)	
Electrode 10 pH ≥3 over >50 - ≤60 min	7.3 (± 26.6)	20.8 (± 39.2)	9.8 (± 26)	
Electrode 1 pH ≥4 over >0 - ≤10 min	98.7 (± 2)	99.5 (± 0)	99.4 (± 0.4)	
Electrode 2 pH ≥4 over >0 - ≤10 min	94.4 (± 11)	99.5 (± 0)	98.7 (± 0.9)	
Electrode 3 pH ≥4 over >0 - ≤10 min	46.4 (± 43.2)	89.1 (± 11.1)	87.5 (± 10.9)	
Electrode 4 pH ≥4 over >0 - ≤10 min	24.6 (± 33.6)	86.3 (± 6.8)	73.5 (± 21.8)	
Electrode 5 pH ≥4 over >0 - ≤10 min	28.6 (± 36.7)	79.9 (± 7.9)	75.8 (± 18.7)	
Electrode 6 pH ≥4 over >0 - ≤10 min	18 (± 28.6)	75.7 (± 9.2)	80.6 (± 15.6)	
Electrode 7 pH ≥4 over >0 - ≤10 min	1.5 (± 2.9)	68.1 (± 16.4)	73.6 (± 19.3)	
Electrode 8 pH ≥4 over >0 - ≤10 min	1.7 (± 4.8)	32.1 (± 30.4)	57.7 (± 32.7)	
Electrode 9 pH ≥4 over >0 - ≤10 min	0.9 (± 1.8)	28.7 (± 27)	53.8 (± 31.7)	
Electrode 10 pH ≥4 over >0 - ≤10 min	0.7 (± 1.7)	45.1 (± 34.7)	55.2 (± 30.7)	
Electrode 1 pH ≥4 over >10 - ≤20 min	99.4 (± 0.4)	99.5 (± 0)	99.5 (± 0)	
Electrode 2 pH ≥4 over >10 - ≤20 min	93.1 (± 22.4)	98.3 (± 1.4)	99.4 (± 0.2)	
Electrode 3 pH ≥4 over >10 - ≤20 min	42.6 (± 39)	59.1 (± 38.7)	56.2 (± 41.1)	
Electrode 4 pH ≥4 over >10 - ≤20 min	14 (± 32.9)	55.3 (± 27)	35.4 (± 38.3)	
Electrode 5 pH ≥4 over >10 - ≤20 min	10.7 (± 26.2)	65.4 (± 35.7)	36.8 (± 41.6)	
Electrode 6 pH ≥4 over >10 - ≤20 min	7.7 (± 23.8)	70.9 (± 32)	46.2 (± 44.7)	
Electrode 7 pH ≥4 over >10 - ≤20 min	0.5 (± 1.8)	75.3 (± 36.3)	48.4 (± 43)	
Electrode 8 pH ≥4 over >10 - ≤20 min	0 (± 0.2)	43 (± 47.6)	48.7 (± 42.2)	
Electrode 9 pH ≥4 over >10 - ≤20 min	0.4 (± 1.6)	56.4 (± 43.5)	53.4 (± 42.4)	
Electrode 10 pH ≥4 over >10 - ≤20 min	0.2 (± 0.9)	53.1 (± 40.7)	54.5 (± 40)	
Electrode 1 pH ≥4 over >20 - ≤30 min	99 (± 0.7)	99.5 (± 0)	99.2 (± 0.8)	
Electrode 2 pH ≥4 over >20 - ≤30 min	91.1 (± 22.8)	98.8 (± 0.6)	95.9 (± 9.6)	
Electrode 3 pH ≥4 over >20 - ≤30 min	32 (± 36.1)	42.6 (± 36.8)	48.5 (± 45.9)	
Electrode 4 pH ≥4 over >20 - ≤30 min	9.4 (± 26.1)	12.9 (± 14.7)	23.8 (± 37.7)	
Electrode 5 pH ≥4 over >20 - ≤30 min	6.9 (± 25.5)	34.4 (± 33.4)	21.7 (± 39.1)	
Electrode 6 pH ≥4 over >20 - ≤30 min	6.4 (± 22.1)	37.2 (± 30.5)	32.3 (± 47.5)	
Electrode 7 pH ≥4 over >20 - ≤30 min	0.6 (± 2.1)	31.8 (± 33.2)	24.9 (± 45)	
Electrode 8 pH ≥4 over >20 - ≤30 min	0 (± 0)	25.1 (± 37.1)	24.9 (± 45)	
Electrode 9 pH ≥4 over >20 - ≤30 min	0 (± 0)	31.6 (± 28.8)	26.2 (± 44.4)	
Electrode 10 pH ≥4 over >20 - ≤30 min	0 (± 0.2)	35.1 (± 34.5)	25 (± 40)	
Electrode 1 pH ≥4 over >30 - ≤40 min	98.8 (± 1.3)	99.4 (± 0.3)	99.3 (± 0.6)	
Electrode 2 pH ≥4 over >30 - ≤40 min	92 (± 19.3)	98.5 (± 0.8)	96.9 (± 5.9)	
Electrode 3 pH ≥4 over >30 - ≤40 min	42.1 (± 40.4)	39.1 (± 36.5)	46.8 (± 46)	
Electrode 4 pH ≥4 over >30 - ≤40 min	8.3 (± 26.3)	2.2 (± 2.9)	21.2 (± 36.3)	
Electrode 5 pH ≥4 over >30 - ≤40 min	7.1 (± 26.4)	3.8 (± 5.3)	13.8 (± 32.6)	
Electrode 6 pH ≥4 over >30 - ≤40 min	5.7 (± 20.7)	4.9 (± 7.2)	24.1 (± 42.7)	
Electrode 7 pH ≥4 over >30 - ≤40 min	0 (± 0.2)	6 (± 9.6)	16 (± 34.6)	

Electrode 8 pH ≥4 over >30 - ≤40 min	6 (± 22.3)	7.6 (± 8.9)	19 (± 37.1)	
Electrode 9 pH ≥4 over >30 - ≤40 min	1.1 (± 4.1)	10.6 (± 15.4)	19.3 (± 38)	
Electrode 10 pH ≥4 over >30 - ≤40 min	0.1 (± 0.4)	17 (± 22.8)	16.9 (± 33.3)	
Electrode 1 pH ≥4 over >40 - ≤50 min	99.3 (± 0.6)	98.2 (± 2.4)	98.9 (± 0.9)	
Electrode 2 pH ≥4 over >40 - ≤50 min	96.6 (± 5.7)	96.4 (± 6.4)	93 (± 16.1)	
Electrode 3 pH ≥4 over >40 - ≤50 min	40.2 (± 39.8)	23 (± 21.3)	46.6 (± 44.9)	
Electrode 4 pH ≥4 over >40 - ≤50 min	8.9 (± 25.6)	0.9 (± 1.4)	19.3 (± 35.9)	
Electrode 5 pH ≥4 over >40 - ≤50 min	6.4 (± 23.7)	3.3 (± 5.1)	16.9 (± 38.6)	
Electrode 6 pH ≥4 over >40 - ≤50 min	5.4 (± 19.8)	5.4 (± 7.7)	24.9 (± 45)	
Electrode 7 pH ≥4 over >40 - ≤50 min	0.4 (± 1.6)	5.8 (± 9.1)	9.5 (± 28.6)	
Electrode 8 pH ≥4 over >40 - ≤50 min	2.4 (± 8.8)	11.1 (± 17.6)	9.5 (± 28.6)	
Electrode 9 pH ≥4 over >40 - ≤50 min	1.3 (± 4.9)	13.1 (± 16)	16 (± 37.3)	
Electrode 10 pH ≥4 over >40 - ≤50 min	0 (± 0)	14.8 (± 21.6)	14.4 (± 33.7)	
Electrode 1 pH ≥4 over >50 - ≤60 min	98.9 (± 1.2)	99.4 (± 0.3)	99.3 (± 0.5)	
Electrode 2 pH ≥4 over >50 - ≤60 min	96.5 (± 6.2)	98.4 (± 1.5)	97.9 (± 1.6)	
Electrode 3 pH ≥4 over >50 - ≤60 min	49.2 (± 40.3)	14.9 (± 13.2)	38.5 (± 37.4)	
Electrode 4 pH ≥4 over >50 - ≤60 min	12.3 (± 29.9)	19.2 (± 35.4)	16.5 (± 35.7)	
Electrode 5 pH ≥4 over >50 - ≤60 min	7.2 (± 26.6)	17.4 (± 38.4)	16.8 (± 38.6)	
Electrode 6 pH ≥4 over >50 - ≤60 min	9.5 (± 24.6)	18.8 (± 39.9)	25.3 (± 44.5)	
Electrode 7 pH ≥4 over >50 - ≤60 min	0.2 (± 0.7)	21.7 (± 40)	8.3 (± 28.7)	
Electrode 8 pH ≥4 over >50 - ≤60 min	7.2 (± 26.4)	20.1 (± 39.8)	8.3 (± 28.7)	
Electrode 9 pH ≥4 over >50 - ≤60 min	7.1 (± 26.6)	16.9 (± 40.5)	15.7 (± 36.7)	
Electrode 10 pH ≥4 over >50 - ≤60 min	2.3 (± 8.4)	18.6 (± 39.8)	6.3 (± 17.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Percentage of Time that pH ≥3 and pH ≥4 Over the 30 minute intervals at each electrode

End point title	Mean Percentage of Time that pH ≥3 and pH ≥4 Over the 30 minute intervals at each electrode

End point description:

ITT population.

These endpoints were compared between sodium alginate oral suspension and placebo. For calcium carbonate/magnesium carbonate chewable tablets, these endpoints were assessed non-comparatively.

End point type	Secondary

End point timeframe:

Up to 60 minutes post-dose in visit 2 (Period 1) and visit 3 (Period 2)

End point values	Liquid Cohort (Group II): Treatment P	Tablet Cohort (Group I): Treatment B	Liquid Cohort (Group II) - Treatment A	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	6	12	
Units: Percentage of time (%)				
arithmetic mean (standard deviation)				

Electrode 1 pH ≥3 over >0 - ≤30 min	99.5 (± 0.6)	99.8 (± 0)	99.7 (± 0.2)	
Electrode 2 pH ≥3 over >0 - ≤30 min	94.3 (± 15.5)	99.3 (± 0.3)	99.2 (± 0.8)	
Electrode 3 pH ≥3 over >0 - ≤30 min	45.3 (± 38.5)	70.2 (± 23.3)	66.6 (± 31.1)	
Electrode 4 pH ≥3 over >0 - ≤30 min	17.4 (± 28.3)	58.4 (± 17.9)	46.6 (± 26.8)	
Electrode 5 pH ≥3 over >0 - ≤30 min	18.8 (± 27.3)	65.5 (± 22.2)	46.7 (± 30.3)	
Electrode 6 pH ≥3 over >0 - ≤30 min	14.3 (± 25.5)	70.3 (± 19.5)	54.2 (± 32.8)	
Electrode 7 pH ≥3 over >0 - ≤30 min	1.5 (± 3)	65 (± 21.9)	49.9 (± 30.9)	
Electrode 8 pH ≥3 over >0 - ≤30 min	3.7 (± 9.1)	40.5 (± 34)	45 (± 33.6)	
Electrode 9 pH ≥3 over >0 - ≤30 min	0.9 (± 1.5)	47.9 (± 31.2)	48.2 (± 33.4)	
Electrode 10 pH ≥3 over >0 - ≤30 min	0.6 (± 1)	54.3 (± 29.7)	50 (± 27)	
Electrode 1 pH ≥3 over >30 - ≤60 min	99.4 (± 0.8)	99.4 (± 0.6)	99.5 (± 0.4)	
Electrode 2 pH ≥3 over >30 - ≤60 min	96.6 (± 6.5)	98.2 (± 1.7)	96.6 (± 7.1)	
Electrode 3 pH ≥3 over >30 - ≤60 min	48.5 (± 40.2)	37.1 (± 28.1)	47.3 (± 43.5)	
Electrode 4 pH ≥3 over >30 - ≤60 min	10.9 (± 27)	9.2 (± 12.9)	20.8 (± 35.9)	
Electrode 5 pH ≥3 over >30 - ≤60 min	7.2 (± 25.9)	10.5 (± 15.5)	16.5 (± 37.4)	
Electrode 6 pH ≥3 over >30 - ≤60 min	13.1 (± 32.6)	13.4 (± 19.8)	25.3 (± 44.4)	
Electrode 7 pH ≥3 over >30 - ≤60 min	0.3 (± 1)	16.5 (± 23.8)	11.8 (± 29.4)	
Electrode 8 pH ≥3 over >30 - ≤60 min	7.2 (± 26.7)	18.1 (± 22.8)	13.4 (± 30.1)	
Electrode 9 pH ≥3 over >30 - ≤60 min	6.9 (± 25.6)	19.4 (± 19.9)	18.3 (± 37.8)	
Electrode 10 pH ≥3 over >30 - ≤60 min	5 (± 18.2)	21.3 (± 24)	15.4 (± 32.7)	
Electrode 1 pH ≥4 over >0 - ≤30 min	99.4 (± 0.8)	99.8 (± 0)	99.7 (± 0.3)	
Electrode 2 pH ≥4 over >0 - ≤30 min	93.2 (± 18.7)	99.2 (± 0.4)	98.4 (± 3.2)	
Electrode 3 pH ≥4 over >0 - ≤30 min	40.5 (± 37.3)	63.8 (± 26.2)	64.2 (± 32)	
Electrode 4 pH ≥4 over >0 - ≤30 min	16.1 (± 28.3)	51.7 (± 15.1)	44.4 (± 27.2)	
Electrode 5 pH ≥4 over >0 - ≤30 min	15.4 (± 26.3)	60.1 (± 22.4)	44.9 (± 30.3)	
Electrode 6 pH ≥4 over >0 - ≤30 min	10.8 (± 23.2)	61.6 (± 18.2)	53.2 (± 33)	
Electrode 7 pH ≥4 over >0 - ≤30 min	0.9 (± 2)	58.6 (± 22.4)	49.1 (± 31.3)	
Electrode 8 pH ≥4 over >0 - ≤30 min	0.6 (± 1.7)	33.5 (± 35.2)	43.9 (± 33.8)	
Electrode 9 pH ≥4 over >0 - ≤30 min	0.4 (± 0.8)	39.1 (± 27.6)	44.7 (± 30.5)	
Electrode 10 pH ≥4 over >0 - ≤30 min	0.3 (± 0.6)	44.6 (± 30.7)	45.1 (± 24.5)	
Electrode 1 pH ≥4 over >30 - ≤60 min	99.3 (± 0.8)	99.3 (± 0.8)	99.5 (± 0.4)	
Electrode 2 pH ≥4 over >30 - ≤60 min	95.4 (± 9.2)	98.1 (± 1.8)	96.3 (± 7.5)	
Electrode 3 pH ≥4 over >30 - ≤60 min	44 (± 38.6)	25.7 (± 20.8)	44.1 (± 42.2)	
Electrode 4 pH ≥4 over >30 - ≤60 min	9.8 (± 26.7)	7.4 (± 11.3)	19.1 (± 35.6)	
Electrode 5 pH ≥4 over >30 - ≤60 min	6.9 (± 25.7)	8.2 (± 14)	15.9 (± 36.5)	
Electrode 6 pH ≥4 over >30 - ≤60 min	6.9 (± 21.1)	9.8 (± 15.4)	24.8 (± 44.2)	
Electrode 7 pH ≥4 over >30 - ≤60 min	0.2 (± 0.8)	11.2 (± 16.9)	11.3 (± 29.3)	
Electrode 8 pH ≥4 over >30 - ≤60 min	5.2 (± 19.2)	13 (± 18.6)	12.3 (± 29.4)	
Electrode 9 pH ≥4 over >30 - ≤60 min	3.2 (± 11.9)	13.6 (± 18.5)	17.1 (± 37.2)	
Electrode 10 pH ≥4 over >30 - ≤60 min	0.8 (± 2.8)	16.8 (± 21.9)	12.6 (± 27)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to follow-up (Day 7)	
Adverse event reporting additional description:	
Treatment-emergent adverse events (TEAE) for Safety population	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups	
Reporting group title	Adverse Events

Reporting group description: -

Serious adverse events	Adverse Events		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Adverse Events		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 20 (25.00%)		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	2		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Infections and infestations			

Nasopharyngitis subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported