



Clinical trial results:

A multicentre, randomised, double-blind, two arm, parallel group, placebo controlled pivotal study to assess the effect of a sodium alginate liquid suspension as add-on therapy in GORD patients with inadequate response to once daily proton pump inhibitor treatment.

Summary

EudraCT number	2014-003174-17
Trial protocol	GB
Global end of trial date	24 December 2015

Results information

Result version number	v1 (current)
This version publication date	19 November 2017
First version publication date	19 November 2017

Trial information

Trial identification

Sponsor protocol code	GA1405
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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	17 March 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 December 2015
Global end of trial reached?	Yes
Global end of trial date	24 December 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to assess the efficacy of sodium alginate liquid suspension compared with matched placebo liquid in the suppression of GORD symptoms in patients whose symptoms are inadequately controlled by once daily PPI therapy alone.

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	28 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	United Kingdom: 227
Country: Number of subjects enrolled	Germany: 169
Worldwide total number of subjects	396
EEA total number of subjects	396

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)	106
From 65 to 84 years	290

85 years and over	0
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Subject disposition

Recruitment

Recruitment details:

This study was conducted in 19 primary care sites in the United Kingdom (UK) and Germany.

Pre-assignment

Screening details:

A total of 396 patients were screened for the study; 371 patients entered the run-in period and 133 patients were discontinued prior to randomization. Randomized subjects were 263.

One subject from placebo group was lost to follow-up. This subject was excluded from ITT population as it is unknown whether any medication was taken by this subject.

Pre-assignment period milestones

Number of subjects started	396
Intermediate milestone: Number of subjects	Run-in period: 371
Number of subjects completed	263

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Screen failure: 133
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Period 1

Period 1 title	Overall (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Gaviscon® Double Action Liquid

Arm description:

Gaviscon® Double Action 20 ml (2 x 10 ml) liquid sachets by mouth 4 times a day for 7 days

Arm type	Experimental
Investigational medicinal product name	Gaviscon® Double Action Liquid
Investigational medicinal product code	
Other name	sodium alginate liquid suspension
Pharmaceutical forms	Oral suspension in sachet
Routes of administration	Oral use

Dosage and administration details:

Gaviscon® Double Action (sodium alginate 1000 mg, sodium bicarbonate 426 mg and calcium carbonate 650 mg) 20 ml (2 x 10 ml) liquid sachets by mouth 4 times a day for 7 days

Arm title	Placebo
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Arm description:

Placebo 20 ml (2 x 10 ml) liquid sachets by mouth 4 times a day for 7 days

Arm type	Placebo
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Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	Matched placebo liquid
Pharmaceutical forms	Oral suspension in sachet
Routes of administration	Oral use

Dosage and administration details:

Placebo 20 ml (2 x 10 ml) liquid sachets by mouth 4 times a day for 7 days

Number of subjects in period 1^[1]	Gaviscon® Double Action Liquid	Placebo
Started	131	132
Completed	128	130
Not completed	3	2
Adverse event	3	1
Lost to follow-up	-	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: A total of 396 patients were screened for the study; 371 patients entered the run-in period and 133 patients were discontinued prior to randomization. Randomized subjects were 263.

Baseline characteristics

Reporting groups

Reporting group title	Gaviscon® Double Action Liquid
Reporting group description:	
Gaviscon® Double Action 20 ml (2 x 10 ml) liquid sachets by mouth 4 times a day for 7 days	
Reporting group title	Placebo
Reporting group description:	
Placebo 20 ml (2 x 10 ml) liquid sachets by mouth 4 times a day for 7 days	

Reporting group values	Gaviscon® Double Action Liquid	Placebo	Total
Number of subjects	131	132	263
Age categorical Units: Subjects			
Adults (18-64 years)	27	32	59
From 65-84 years	104	100	204
Age continuous Units: years			
arithmetic mean	54.28	52.36	-
standard deviation	± 12.62	± 14.41	-
Gender categorical Units: Subjects			
Female	82	76	158
Male	49	56	105
Race Units: Subjects			
Caucasian (White)	129	132	261
Asian	2	0	2
Height Units: cm			
arithmetic mean	168.56	171.15	-
standard deviation	± 9.6	± 9.82	-
Weight Units: kg			
arithmetic mean	83.75	85.82	-
standard deviation	± 17.5	± 19.63	-
BMI			
BMI - Body mass index			
Units: kg/m2			
arithmetic mean	29.41	29.28	-
standard deviation	± 5.32	± 6.25	-

End points

End points reporting groups

Reporting group title	Gaviscon® Double Action Liquid
Reporting group description:	
Gaviscon® Double Action 20 ml (2 x 10 ml) liquid sachets by mouth 4 times a day for 7 days	
Reporting group title	Placebo
Reporting group description:	
Placebo 20 ml (2 x 10 ml) liquid sachets by mouth 4 times a day for 7 days	

Primary: Number of subjects with Reduction of at least 3 days in HRDQ (heartburn & regurgitation) score >0.7 during 7-day treatment period compared to baseline (7-day run-in period)

End point title	Number of subjects with Reduction of at least 3 days in HRDQ (heartburn & regurgitation) score >0.7 during 7-day treatment period compared to baseline (7-day run-in period)
End point description:	
Intention-to-treat (ITT) population: All subjects in the safety set who were recruited into the study and had at least 1 day of complete HRDQ scores (severity and frequency scores for both Heartburn and Regurgitation) for both the run-in and treatment periods. Subjects were assigned to the treatment groups as randomised. This population was used for summaries of efficacy and baseline data.	
Heartburn Regurgitation and Dyspepsia Questionnaire (HRDQ): HRDQ symptom severity was recorded: 0 (no symptoms), 1 (mild), 2 (moderate) and 3 (severe) and the frequency was scored as 0 (none), 1 (once), 2 (twice), 3 (thrice), 4 (4 or 5 times), 5 (6 – 10 times) and 6 (more than 10 times or constant). In addition, the HRDQ questionnaire required patients to record the duration of their symptoms and whether or not they had experienced night-time symptoms.	
End point type	Primary
End point timeframe:	
Up to Day 7 (treatment period)	

End point values	Gaviscon® Double Action Liquid	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	131	131		
Units: Subjects				
Reduction in HRDQ Score >0.7: Less than 3 days	64	68		
Reduction in HRDQ Score >0.7: 3 days	16	24		
Reduction in HRDQ Score >0.7: 4 days	13	9		
Reduction in HRDQ Score >0.7: 5 days	17	13		
Reduction in HRDQ Score >0.7: 6 days	12	7		
Reduction in HRDQ Score >0.7: 7 days	9	10		
Reduction in HRDQ Score >0.7: 3 to 7 days	67	63		

Statistical analyses

Statistical analysis title	Reduction in HRDQ Score >0.7: Gaviscon vs Placebo
Comparison groups	Placebo v Gaviscon® Double Action Liquid
Number of subjects included in analysis	262
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5939
Method	Regression, Logistic

Secondary: Change in mean daily HRDQ score (heartburn and regurgitation) from baseline (7-day run-in period)

End point title	Change in mean daily HRDQ score (heartburn and regurgitation) from baseline (7-day run-in period)
End point description: ITT population.	
End point type	Secondary
End point timeframe: Up to Day 7 (treatment period)	

End point values	Gaviscon® Double Action Liquid	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	131	131		
Units: unit on a scale				
arithmetic mean (standard deviation)				
Run-in Period	1.79 (± 0.84)	1.64 (± 0.71)		
Treatment Period	0.91 (± 0.8)	0.84 (± 0.67)		
Change from run-in to treatment periods	-0.89 (± 0.8)	-0.8 (± 0.68)		

Statistical analyses

Statistical analysis title	HRDQ Score: Gaviscon vs Placebo
Statistical analysis description: HRDQ Score (Heartburn & Regurgitation)	
Comparison groups	Gaviscon® Double Action Liquid v Placebo
Number of subjects included in analysis	262
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8435
Method	ANCOVA

Secondary: Change in mean daily heartburn and regurgitation score from baseline (7-day run-in period)

End point title	Change in mean daily heartburn and regurgitation score from baseline (7-day run-in period)
End point description:	
ITT population.	
End point type	Secondary
End point timeframe:	
Up to Day 7 (treatment period)	

End point values	Gaviscon® Double Action Liquid	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	131	131		
Units: Unit on a scale				
arithmetic mean (standard deviation)				
Heartburn - Run-in Period	0.94 (± 0.51)	0.85 (± 0.41)		
Heartburn - Treatment Period	0.45 (± 0.45)	0.41 (± 0.34)		
Heartburn - Change from run-in to treatment period	-0.49 (± 0.45)	-0.43 (± 0.39)		
Regurgitation - Run-in period	0.85 (± 0.47)	0.79 (± 0.43)		
Regurgitation - Treatment period	0.46 (± 0.43)	0.43 (± 0.4)		
Regurgitation-Change b/w run-in & treatment period	-0.4 (± 0.42)	-0.36 (± 0.36)		

Statistical analyses

Statistical analysis title	HRDQ Heartburn - Gaviscon vs Placebo
Comparison groups	Gaviscon® Double Action Liquid v Placebo
Number of subjects included in analysis	262
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8537
Method	ANCOVA

Statistical analysis title	HRDQ Regurgitation - Gaviscon vs Placebo
Comparison groups	Gaviscon® Double Action Liquid v Placebo

Number of subjects included in analysis	262
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8409
Method	ANCOVA

Secondary: Change in mean daily frequency of individual symptoms (heartburn & regurgitation) from baseline (7-day run-in period)

End point title	Change in mean daily frequency of individual symptoms (heartburn & regurgitation) from baseline (7-day run-in period)
End point description:	
ITT population.	
End point type	Secondary
End point timeframe:	
Up to Day 7 (treatment period)	

End point values	Gaviscon® Double Action Liquid	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	131	131		
Units: Unit on a scale				
arithmetic mean (standard deviation)				
Heartburn Frequency - Run-in Period	3.98 (± 2.5)	3.46 (± 1.89)		
Heartburn Frequency - Treatment Period	1.97 (± 2.02)	1.81 (± 1.56)		
Heartburn Frequency - Change from baseline	-2.01 (± 1.97)	-1.65 (± 1.62)		
Regurgitation Frequency - Run-in period	3.82 (± 2.53)	3.44 (± 2.18)		
Regurgitation Frequency - Treatment period	2.26 (± 2.36)	2.02 (± 2.08)		
Regurgitation Frequency -Change from baseline	-1.56 (± 1.89)	-1.42 (± 1.44)		

Statistical analyses

Statistical analysis title	HRDQ Heartburn Frequency - Gaviscon vs Placebo
Comparison groups	Gaviscon® Double Action Liquid v Placebo
Number of subjects included in analysis	262
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5847
Method	ANCOVA

Statistical analysis title	HRDQ Regurgitation Frequency - Gaviscon vs Placebo
Comparison groups	Gaviscon® Double Action Liquid v Placebo
Number of subjects included in analysis	262
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8618
Method	ANCOVA

Secondary: Change in mean daily severity of individual symptoms (heartburn & regurgitation) from baseline (7-day run-in period)

End point title	Change in mean daily severity of individual symptoms (heartburn & regurgitation) from baseline (7-day run-in period)
End point description:	
ITT population.	
End point type	Secondary
End point timeframe:	
Up to Day 7 (treatment period)	

End point values	Gaviscon® Double Action Liquid	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	131	131		
Units: Unit on a scale				
arithmetic mean (standard deviation)				
Heartburn Severity - Run-in Period	1.65 (± 0.63)	1.56 (± 0.57)		
Heartburn Severity - Treatment Period	0.94 (± 0.68)	0.92 (± 0.56)		
Heartburn Severity - Change from baseline	-0.71 (± 0.68)	-0.64 (± 0.57)		
Regurgitation Severity - Run-in period	1.53 (± 0.6)	1.45 (± 0.58)		
Regurgitation Severity - Treatment period	0.92 (± 0.65)	0.88 (± 0.61)		
Regurgitation Severity -Change from baseline	-0.61 (± 0.64)	-0.57 (± 0.57)		

Statistical analyses

Statistical analysis title	HRDQ Heartburn Severity - Gaviscon vs Placebo
Comparison groups	Gaviscon® Double Action Liquid v Placebo
Number of subjects included in analysis	262
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7243
Method	ANCOVA

Statistical analysis title	HRDQ Regurgitation Severity - Gaviscon vs Placebo
Comparison groups	Gaviscon® Double Action Liquid v Placebo
Number of subjects included in analysis	262
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.935
Method	ANCOVA

Secondary: Change in mean daily duration of symptoms (heartburn & regurgitation) from baseline (7-day run-in period)

End point title	Change in mean daily duration of symptoms (heartburn & regurgitation) from baseline (7-day run-in period)
End point description:	
ITT population.	
End point type	Secondary
End point timeframe:	
Up to Day 7 (treatment period)	

End point values	Gaviscon® Double Action Liquid	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	131	131		
Units: minutes				
arithmetic mean (standard deviation)				
Run-in period	253.08 (± 295.08)	203.37 (± 244.58)		
Treatment period	136.05 (± 209.04)	126.14 (± 190.68)		
Change from run-in to treatment periods	-117.022 (± 217.499)	-77.231 (± 166.587)		

Statistical analyses

Statistical analysis title	HRDQ Daily Symptoms Duration - Gaviscon vs Placebo
Comparison groups	Gaviscon® Double Action Liquid v Placebo

Number of subjects included in analysis	262
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3304
Method	ANCOVA

Secondary: Change from baseline (7-day run-in period) in patient satisfaction scores at end of study

End point title	Change from baseline (7-day run-in period) in patient satisfaction scores at end of study
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End point description:

ITT population.

Patient satisfaction with medication in controlling their symptoms was assessed in response to the question: 'Thinking back over the past 7 days and the medication you received, how satisfied are you with the control of your symptoms?' The patient had to draw a perpendicular line on a 100 mm Visual Analogue Scale (VAS), with anchors at 0 = 'Very Dissatisfied' and 100 = 'Very Satisfied.'

End point type	Secondary
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End point timeframe:

Up to Day 8 (End of Study visit)

End point values	Gaviscon® Double Action Liquid	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	131	131		
Units: Unit on a scale				
arithmetic mean (standard deviation)				
Run-in period	30.99 (± 21.86)	36.23 (± 20.82)		
Treatment period	61.22 (± 29.93)	63.96 (± 27.96)		
Change from run-in to treatment periods	30.2 (± 35.08)	27.84 (± 28.51)		

Statistical analyses

Statistical analysis title	Patient Satisfaction scores - Gaviscon vs Placebo
Comparison groups	Gaviscon® Double Action Liquid v Placebo
Number of subjects included in analysis	262
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9028
Method	ANCOVA

Secondary: Change in mean reflux disease questionnaire (RDQ) symptom scores for GORD dimension from baseline (7-day run-in period)

End point title	Change in mean reflux disease questionnaire (RDQ) symptom scores for GORD dimension from baseline (7-day run-in period)
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End point description:

ITT population.

RDQ consists of 12 items that describe 3 dimensions for assessment of heartburn, dyspepsia, & regurgitation. Heartburn and regurgitation can be combined into a GORD dimension. Each dimension includes 4 items measuring the frequency and severity of following questions:

- A burning feeling behind your breastbone (heartburn)
- Pain behind your breastbone (heartburn)
- An acid taste in your mouth (regurgitation)
- Unpleasant movement of material upwards from the stomach (regurgitation)
- A burning feeling in the center of the upper stomach (dyspepsia)
- A pain in the center of the upper stomach (dyspepsia)

Response options are scaled with scores 0, 1, 2, 3, 4, 5 for frequencies (Did not have, 1 day, 2 days, 3-4 days, 5-6 days, Daily), whereas for Severity a 6-grade Likert scale is used (0=Did not have, 1=Very mild, 2=Mild, 3=Moderate, 4=Moderately severe, & 5=Severe).

End point type	Secondary
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End point timeframe:

Up to Day 7 (treatment period)

End point values	Gaviscon® Double Action Liquid	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	131	131		
Units: Unit on a scale				
arithmetic mean (standard deviation)				
Run-in period	2.87 (± 1.05)	2.72 (± 0.99)		
Treatment period	1.71 (± 1.17)	1.62 (± 1.16)		
Change from run-in to treatment periods	-1.15 (± 1.14)	-1.1 (± 1.15)		

Statistical analyses

Statistical analysis title	RDQ Scores for GORD Dimension -Gaviscon vs Placebo
Comparison groups	Gaviscon® Double Action Liquid v Placebo
Number of subjects included in analysis	262
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8288
Method	ANCOVA

Secondary: Change in mean RDQ scores for Heartburn and Regurgitation from baseline (7-day run-in period)

End point title	Change in mean RDQ scores for Heartburn and Regurgitation
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from baseline (7-day run-in period)

End point description:

ITT population.

End point type	Secondary
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End point timeframe:

Up to Day 7 (treatment period)

End point values	Gaviscon® Double Action Liquid	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	131	131		
Units: Unit on a scale				
arithmetic mean (standard deviation)				
Heartburn - Run-in Period	2.76 (± 1.36)	2.63 (± 1.3)		
Heartburn - Treatment Period	1.72 (± 1.39)	1.7 (± 1.39)		
Heartburn - Change from baseline	-1.03 (± 1.39)	-0.95 (± 1.32)		
Regurgitation - Run-in period	2.98 (± 1.31)	2.81 (± 1.26)		
Regurgitation - Treatment period	1.7 (± 1.38)	1.55 (± 1.37)		
Regurgitation - Change from baseline	-1.27 (± 1.37)	-1.26 (± 1.35)		

Statistical analyses

Statistical analysis title	RDQ Heartburn - Gaviscon vs Placebo
Comparison groups	Gaviscon® Double Action Liquid v Placebo
Number of subjects included in analysis	262
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8854
Method	ANCOVA

Statistical analysis title	RDQ Regurgitation - Gaviscon vs Placebo
Comparison groups	Placebo v Gaviscon® Double Action Liquid
Number of subjects included in analysis	262
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6107
Method	ANCOVA

Secondary: Change in mean RDQ frequency scores for heartburn and regurgitation from baseline (7-day run-in period)

End point title	Change in mean RDQ frequency scores for heartburn and
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End point description:

ITT population.

End point type Secondary

End point timeframe:

Up to Day 7 (treatment period)

End point values	Gaviscon® Double Action Liquid	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	131	131		
Units: Unit on a scale				
arithmetic mean (standard deviation)				
Heartburn frequency - Run-in Period	2.93 (± 1.56)	2.82 (± 1.52)		
Heartburn frequency - Treatment Period	1.83 (± 1.57)	1.87 (± 1.61)		
Heartburn frequency - Change from baseline	-1.09 (± 1.62)	-0.97 (± 1.56)		
Regurgitation frequency - Run-in period	3.13 (± 1.46)	2.97 (± 1.45)		
Regurgitation frequency - Treatment period	1.81 (± 1.54)	1.64 (± 1.55)		
Regurgitation frequency - Change from baseline	-1.31 (± 1.51)	-1.31 (± 1.58)		

Statistical analyses

Statistical analysis title	RDQ Heartburn frequency - Gaviscon vs Placebo
Comparison groups	Gaviscon® Double Action Liquid v Placebo
Number of subjects included in analysis	262
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7026
Method	ANCOVA

Statistical analysis title	RDQ Regurgitation frequency - Gaviscon vs Placebo
Comparison groups	Placebo v Gaviscon® Double Action Liquid
Number of subjects included in analysis	262
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5541
Method	ANCOVA

Secondary: Change in mean RDQ severity scores for heartburn and regurgitation

from baseline (7-day run-in period)

End point title	Change in mean RDQ severity scores for heartburn and regurgitation from baseline (7-day run-in period)
End point description:	
ITT population.	
End point type	Secondary
End point timeframe:	
Up to Day 7 (treatment period)	

End point values	Gaviscon® Double Action Liquid	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	131	131		
Units: Unit on a scale				
arithmetic mean (standard deviation)				
Heartburn Severity - Run-in Period	2.59 (± 1.29)	2.45 (± 1.2)		
Heartburn Severity - Treatment Period	1.61 (± 1.33)	1.53 (± 1.28)		
Heartburn Severity - Change from baseline	-0.98 (± 1.33)	-0.93 (± 1.24)		
Regurgitation Severity - Run-in period	2.82 (± 1.29)	2.66 (± 1.24)		
Regurgitation Severity - Treatment period	1.58 (± 1.33)	1.45 (± 1.29)		
Regurgitation Severity -Change from baseline	-1.24 (± 1.4)	-1.21 (± 1.28)		

Statistical analyses

Statistical analysis title	RDQ Heartburn Severity - Gaviscon vs Placebo
Comparison groups	Gaviscon® Double Action Liquid v Placebo
Number of subjects included in analysis	262
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8724
Method	ANCOVA

Statistical analysis title	RDQ Regurgitation Severity - Gaviscon vs Placebo
Comparison groups	Gaviscon® Double Action Liquid v Placebo
Number of subjects included in analysis	262
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6732
Method	ANCOVA

Secondary: Change in mean HRDQ scores for number of nights with symptoms from baseline (7-day run-in period)

End point title	Change in mean HRDQ scores for number of nights with symptoms from baseline (7-day run-in period)
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End point description:

ITT population.

End point type	Secondary
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End point timeframe:

Up to Day 7 (treatment period)

End point values	Gaviscon® Double Action Liquid	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	131	131		
Units: Unit on a scale				
arithmetic mean (standard deviation)				
Run-in period	4.07 (± 2.67)	4.25 (± 2.52)		
Treatment period	2.57 (± 2.67)	2.69 (± 2.61)		
Change from run-in to treatment periods	-1.49 (± 2.48)	-1.56 (± 2.42)		

Statistical analyses

Statistical analysis title	HRDQ Night symptoms - Gaviscon vs Placebo
Comparison groups	Gaviscon® Double Action Liquid v Placebo
Number of subjects included in analysis	262
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Poisson regression model

Secondary: Number of subjects with night-time symptoms

End point title	Number of subjects with night-time symptoms
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End point description:

ITT population.

End point type	Secondary
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End point timeframe:

At baseline (7-day run-in period) and Day 7 (treatment period)

End point values	Gaviscon® Double Action Liquid	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	131	131		
Units: Subjects				
Run-in period - Yes	107	115		
Run-in period - No	24	16		
Treatment period - Yes	83	89		
Treatment period - No	48	42		

Statistical analyses

Statistical analysis title	HRDQ subjects count with Night symptoms
Comparison groups	Gaviscon® Double Action Liquid v Placebo
Number of subjects included in analysis	262
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4158
Method	Cochran-Mantel-Haenszel

Secondary: Days free from Heartburn and Regurgitation symptoms

End point title	Days free from Heartburn and Regurgitation symptoms
End point description:	
ITT population.	
Symptom-free day is defined as a day where the respective symptoms (heartburn and regurgitation — all derived from the HRDQ) had a value for frequency of 0.	
End point type	Secondary
End point timeframe:	
Up to Day 7 (treatment period)	

End point values	Gaviscon® Double Action Liquid	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	131	131		
Units: Days				
arithmetic mean (standard deviation)				
Run-in period	0.1 (± 0.49)	0.19 (± 0.5)		
Treatment period	1.45 (± 2.15)	1.45 (± 2.04)		

Change from run-in to treatment periods	1.35 (\pm 2.1)	1.26 (\pm 2)		
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Statistical analyses

Statistical analysis title	HRDQ Symptom free days - Gaviscon vs Placebo
Comparison groups	Gaviscon® Double Action Liquid v Placebo
Number of subjects included in analysis	262
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Poisson regression model

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to Day 8 (visit 3, End of Study)

Adverse event reporting additional description:

Treatment-Emergent Adverse Events (TEAEs) for SAF population.

Safety (SAF) population includes all subjects who were recruited into the study and received at least one dose of the study medication.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18
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Reporting groups

Reporting group title	Overall study
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Reporting group description: -

Serious adverse events	Overall study		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 263 (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	Overall study		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	108 / 263 (41.06%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 263 (0.38%)		
occurrences (all)	1		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 263 (0.38%)		
occurrences (all)	1		
Malaise			

subjects affected / exposed occurrences (all)	2 / 263 (0.76%) 2		
Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all) Throat irritation subjects affected / exposed occurrences (all)	 4 / 263 (1.52%) 4 3 / 263 (1.14%) 3		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	 1 / 263 (0.38%) 1		
Injury, poisoning and procedural complications Accidental overdose subjects affected / exposed occurrences (all) Epicondylitis subjects affected / exposed occurrences (all) Laceration subjects affected / exposed occurrences (all) Overdose subjects affected / exposed occurrences (all)	 4 / 263 (1.52%) 4 1 / 263 (0.38%) 1 1 / 263 (0.38%) 1 1 / 263 (0.38%) 1		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Lethargy subjects affected / exposed occurrences (all)	 20 / 263 (7.60%) 20 1 / 263 (0.38%) 1		
Ear and labyrinth disorders Vertigo			

subjects affected / exposed	2 / 263 (0.76%)		
occurrences (all)	2		
Eye disorders			
Visual impairment			
subjects affected / exposed	1 / 263 (0.38%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	3 / 263 (1.14%)		
occurrences (all)	3		
Abdominal distension			
subjects affected / exposed	3 / 263 (1.14%)		
occurrences (all)	3		
Abdominal pain			
subjects affected / exposed	4 / 263 (1.52%)		
occurrences (all)	4		
Abdominal pain upper			
subjects affected / exposed	8 / 263 (3.04%)		
occurrences (all)	8		
Defaecation urgency			
subjects affected / exposed	1 / 263 (0.38%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	10 / 263 (3.80%)		
occurrences (all)	10		
Dyspepsia			
subjects affected / exposed	1 / 263 (0.38%)		
occurrences (all)	1		
Flatulence			
subjects affected / exposed	6 / 263 (2.28%)		
occurrences (all)	6		
Nausea			
subjects affected / exposed	11 / 263 (4.18%)		
occurrences (all)	11		
Regurgitation			

subjects affected / exposed occurrences (all)	2 / 263 (0.76%) 2		
Skin and subcutaneous tissue disorders Erythema subjects affected / exposed occurrences (all) Hyperhidrosis subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all)	1 / 263 (0.38%) 1 1 / 263 (0.38%) 1 1 / 263 (0.38%) 1		
Renal and urinary disorders Renal failure subjects affected / exposed occurrences (all)	1 / 263 (0.38%) 1		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Osteoarthritis subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all)	2 / 263 (0.76%) 2 1 / 263 (0.38%) 1 1 / 263 (0.38%) 1 2 / 263 (0.76%) 2		
Infections and infestations Bronchitis subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all)	1 / 263 (0.38%) 1 3 / 263 (1.14%) 3		

Sinusitis			
subjects affected / exposed	1 / 263 (0.38%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	1 / 263 (0.38%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 July 2015	<p>The following changes to the study protocol were made:</p> <ol style="list-style-type: none">1. The creation of additional subsections to accommodate the addition of an exploratory endpoint section.2. The clarification of an existing secondary endpoint.3. The reclassification of some secondary endpoints into exploratory endpoints.4. The addition of a new endpoint to newly created exploratory endpoints section.5. Changes to the compliance, calculations and which data to be used.6. Correction to text for classification of AEs.7. Administrative correction to Table 11-1. <p>This amendment was considered to be substantial due to the impact on the scientific integrity of the study that the following changes had:</p> <p>The secondary endpoint was amended to specify the symptoms from which patients had to experience alleviation within the 7-day treatment period.</p> <p>The addition of a new secondary endpoint which specified the symptoms from which patients had to experience alleviation within the 7-day treatment period.</p> <p>Changes made had no impact on the conduct of the study. These were purely in relation to the analysis of data and/or correction to text.</p>

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/28464343>