Clinical trial results:
A randomised, controlled, open-label, single-centre, parallel group, pilot study to investigate the onset of action of a lozenge compared with a caplet in patients with sore throat.

Summary

EudraCT number	2006-006769-17
Trial protocol	GB
Global end of trial date	07 February 2008

Results information

Result version number	v1 (current)
This version publication date	09 March 2018
First version publication date	09 March 2018

Trial information

Trial identification

Sponsor protocol code	TH0612

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Reckitt Benckiser Healthcare International Ltd
Sponsor organisation address	103 - 105 Bath Road, Slough, Berkshire, United Kingdom, SL1 3UH
Public contact	Clinical Research, Clinical Research Director, clinicalrequests@rb.com
Scientific contact	Clinical Research, Clinical Research Director, 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	21 October 2008
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 February 2008
Global end of trial reached?	Yes
Global end of trial date	07 February 2008
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Train a UK centre in the 2-stopwatch technique to evaluate the appropriateness of the 2-stopwatch method in the sore throat indication.

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	02 May 2007
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: 23
Worldwide total number of subjects	23
EEA total number of subjects	23

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)	1
Adults (18-64 years)	22
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was a single-centre study, recruited in United Kingdom. 132 subject were screened, out of 109 were screen failures.

Pre-assignment

Screening details:

Twenty-three subjects entered the study. Eleven subjects were randomised to receive a single Strefen Honey & Lemon lozenge(flurbiprofen) and 12 randomised to receive a single dose of two Ibuprofen caplets.

Period 1

Period 1 title	Overall (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	1 x Strefen Honey & Lemon lozenge(flurbiprofen)

Arm description:

Test : Strefen Honey & Lemon 8.75mg flurbiprofen one lozenge by mouth

Arm type	Experimental
Investigational medicinal product name	Strefen Honey & Lemon lozenge
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Lozenge
Routes of administration	Oral use

Dosage and administration details:

Strefen Honey & Lemon 8.75mg flurbiprofen one lozenge by mouth

Arm title	2 x Ibuprofen Caplets

Arm description:

Reference : Ibuprofen Caplets, 200mg ibuprofen two caplets by mouth

Arm type	Active comparator
Investigational medicinal product name	Ibuprofen Caplets
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Ibuprofen Caplets, 200mg ibuprofen two caplets by mouth

Number of subjects in period 1	1 x Strefen Honey & Lemon lozenge(flurbiprofen	2 x Ibuprofen Caplets
Started	11	12
Completed	11	10
Not completed	0	2
Protocol deviation	-	2

Baseline characteristics

Reporting groups	
Reporting group title	1 x Strefen Honey & Lemon lozenge(flurbiprofen)
Reporting group description:	
Test : Strefen Honey & Lemon 8.75mg flurbiprofen one lozenge by mouth	
Reporting group title	2 x Ibuprofen Caplets
Reporting group description:	
Reference : Ibuprofen Caplets, 200mg ibuprofen two caplets by mouth	

Reporting group values	1 x Strefen Honey & Lemon lozenge(flurbiprofen	2 x Ibuprofen Caplets	Total
Number of subjects	11	12	23
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	33.5	34.8	
standard deviation	± 10.6	± 14.2	-
Gender categorical Units: Subjects			
Female	5	9	14
Male	6	3	9
Race Units: Subjects			
Caucasian	11	12	23
Height Units: cm			
arithmetic mean	171.4	167.2	
standard deviation	± 6.9	± 7.4	-
Weight Units: kg			
arithmetic mean	74.9	80.7	
standard deviation	± 16.2	± 17.4	-

End points

End points reporting groups

Reporting group title	1 x Strefen Honey & Lemon lozenge(flurbiprofen)
Reporting group description: Test : Strefen Honey & Lemon 8.75mg flurbiprofen one lozenge by mouth	
Reporting group title	2 x Ibuprofen Caplets
Reporting group description: Reference : Ibuprofen Caplets, 200mg ibuprofen two caplets by mouth	

Primary: Median Time to first confirmed perceptible sore throat pain relief

End point title	Median Time to first confirmed perceptible sore throat pain relief
End point description: KM median - Kaplan-Meier median Intention-to-treat (ITT) population consisted of all patients who were randomized to the study, who completed the baseline efficacy assessments and who had at least one post-baseline assessment.	
End point type	Primary
End point timeframe: At Baseline (pre-dose), 5, 10, 15, 20, 25, 30, 35, 40, 45, 60, 75, 90, 105 and 120 minutes post-dose	

End point values	1 x Strefen Honey & Lemon lozenge(flurbip	2 x Ibuprofen Caplets		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	12		
Units: minutes				
median (confidence interval 95%)				
Overall	7.2 (2.6 to 22.6)	17.6 (15.0 to 22.9)		

Statistical analyses

Statistical analysis title	Sore throat relief: lozenge Vs Caplets
Comparison groups	1 x Strefen Honey & Lemon lozenge(flurbiprofen) v 2 x Ibuprofen Caplets
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1205
Method	Regression, Cox

Secondary: Median time to meaningful sore throat pain relief

End point title	Median time to meaningful sore throat pain relief

End point description:

KM median - Kaplan-Meier median

ITT population.

End point type	Secondary

End point timeframe:

At Baseline (pre-dose), 5, 10, 15, 20, 25, 30, 35, 40, 45, 60, 75, 90, 105 and 120 minutes post-dose

End point values	1 x Strefen Honey & Lemon lozenge(flurbip	2 x Ibuprofen Caplets		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	12		
Units: minutes				
median (confidence interval 95%)	17.3 (10.2 to 120.7)	61.3 (32.6 to 78.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Median Time to first unconfirmed perceptible sore throat pain relief

End point title	Median Time to first unconfirmed perceptible sore throat pain relief

End point description:

KM median - Kaplan-Meier median

ITT population.

End point type	Secondary

End point timeframe:

At Baseline (pre-dose), 5, 10, 15, 20, 25, 30, 35, 40, 45, 60, 75, 90, 105 and 120 minutes post-dose

End point values	1 x Strefen Honey & Lemon lozenge(flurbip	2 x Ibuprofen Caplets		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	12		
Units: minutes				
median (confidence interval 95%)	4.1 (1.1 to 7.2)	17.6 (16.0 to 22.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline in throat soreness sore throat relief

End point title	Mean change from baseline in throat soreness sore throat relief

End point description:

Changes in throat soreness measured using 11-point ordinal scale where 0 = "Not Sore" and 10 = "Very Sore".

ITT population.

End point type	Secondary

End point timeframe:

At Baseline (pre-dose), 5, 10, 15, 20, 25, 30, 35, 40, 45, 60, 75, 90, 105 and 120 minutes post-dose

End point values	1 x Strefen Honey & Lemon lozenge(flurbip	2 x Ibuprofen Caplets		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	12		
Units: unit on scale				
arithmetic mean (standard deviation)				
Baseline	7.36 (± 0.81)	7.33 (± 0.98)		
Post-dose : 5 Minutes	-1.27 (± 1.62)	-0.25 (± 0.62)		
Post-dose : 10 Minutes	-1.55 (± 1.57)	-0.25 (± 0.62)		
Post-dose : 15 Minutes	-1.82 (± 1.47)	-0.42 (± 0.67)		
Post-dose : 20 Minutes	-1.82 (± 1.54)	-0.75 (± 0.97)		
Post-dose : 25 Minutes	-2.00 (± 1.48)	-1.00 (± 1.04)		
Post-dose : 30 Minutes	-2.00 (± 1.48)	-1.33 (± 1.15)		
Post-dose : 35 Minutes	-2.18 (± 1.40)	-1.55 (± 1.29)		
Post-dose : 40 Minutes	-2.00 (± 1.48)	-1.91 (± 1.14)		
Post-dose : 45 Minutes	-2.00 (± 1.41)	-2.09 (± 1.22)		
Post-dose : 60 Minutes	-2.27 (± 1.85)	-2.64 (± 1.43)		
Post-dose : 75 Minutes	-2.18 (± 1.66)	-3.20 (± 1.40)		
Post-dose : 90 Minutes	-2.09 (± 1.58)	-3.40 (± 1.35)		
Post-dose : 105 Minutes	-2.27 (± 1.56)	-3.90 (± 1.60)		
Post-dose : 120 Minutes	-2.09 (± 1.81)	-3.80 (± 1.87)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline in difficulty in swallowing

End point title	Mean change from baseline in difficulty in swallowing

End point description:

Difficulty in swallowing measured using 100 mm VAS with "Not Difficult" on the left hand side of the 100mm line and "Very Difficult" on the right hand side.

ITT population.

End point type	Secondary

End point timeframe:

At Baseline (pre-dose), 5, 10, 15, 20, 25, 30, 35, 40, 45, 60, 75, 90, 105 and 120 minutes post-dose

End point values	1 x Strefen Honey & Lemon lozenge(flurbip	2 x Ibuprofen Caplets		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	12		
Units: unit on scale				
arithmetic mean (standard deviation)				
Baseline	66.5 (± 6.8)	68.0 (± 6.3)		
Post-dose : 5 Minutes	-10.8 (± 16.1)	-0.3 (± 6.4)		
Post-dose : 10 Minutes	-12.7 (± 15.0)	-0.7 (± 6.8)		
Post-dose : 15 Minutes	-13.9 (± 15.2)	-2.4 (± 9.1)		
Post-dose : 20 Minutes	-13.9 (± 14.1)	-9.1 (± 14.5)		
Post-dose : 25 Minutes	-17.3 (± 14.4)	-11.9 (± 15.0)		
Post-dose : 30 Minutes	-17.4 (± 14.6)	-12.3 (± 16.5)		
Post-dose : 35 Minutes	-17.7 (± 16.0)	-14.5 (± 15.9)		
Post-dose : 40 Minutes	-18.2 (± 16.5)	-19.5 (± 15.8)		
Post-dose : 45 Minutes	-18.6 (± 17.2)	-20.2 (± 16.6)		
Post-dose : 60 Minutes	-18.4 (± 18.8)	-23.4 (± 18.8)		
Post-dose : 75 Minutes	-17.5 (± 17.0)	-29.1 (± 17.2)		
Post-dose : 90 Minutes	-18.2 (± 18.0)	-33.0 (± 16.7)		
Post-dose : 105 Minutes	-20.9 (± 19.5)	-37.1 (± 19.6)		
Post-dose : 120 Minutes	-19.1 (± 22.4)	-38.5 (± 23.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change for sore throat relief at various time points

End point title	Mean change for sore throat relief at various time points

End point description:

Sore throat relief measured using 7 point rating scale where assessed to 7 = complete relief, 6 = almost complete relief, 5 = considerable relief, 4 = moderate relief, 3 = mild relief, 2 = slight relief and 1 = no relief.

ITT population

End point type	Secondary

End point timeframe:

At 5, 10, 15, 20, 25, 30, 35, 40, 45, 60, 75, 90, 105 and 120 minutes post-dose

End point values	1 x Strefen Honey & Lemon lozenge(flurbip	2 x Ibuprofen Caplets		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	12		
Units: unit on scale				
arithmetic mean (standard deviation)				
Post-dose : 5 Minutes	2.36 (± 1.57)	1.17 (± 0.39)		
Post-dose : 10 Minutes	2.73 (± 1.42)	1.17 (± 0.39)		
Post-dose : 15 Minutes	2.91 (± 1.45)	1.42 (± 0.67)		
Post-dose : 20 Minutes	2.91 (± 1.51)	1.75 (± 0.62)		
Post-dose : 25 Minutes	3.0 (± 1.48)	2.0 (± 0.74)		
Post-dose : 30 Minutes	3.09 (± 1.51)	2.33 (± 0.89)		
Post-dose : 35 Minutes	3.09 (± 1.58)	2.45 (± 1.13)		
Post-dose : 40 Minutes	3.0 (± 1.55)	2.73 (± 1.10)		
Post-dose : 45 Minutes	3.09 (± 1.51)	3.0 (± 1.34)		
Post-dose : 60 Minutes	3.27 (± 1.56)	3.55 (± 1.44)		
Post-dose : 75 Minutes	2.91 (± 1.30)	4.10 (± 1.45)		
Post-dose : 90 Minutes	2.91 (± 1.38)	4.10 (± 1.60)		
Post-dose : 105 Minutes	2.64 (± 1.57)	4.30 (± 1.64)		
Post-dose : 120 Minutes	2.91 (± 1.76)	4.30 (± 1.83)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean scores for overall treatment rating

End point title	Mean scores for overall treatment rating

End point description:

Overall Treatment Rating assessed using an 11-point ordinal scale where 0 = “Poor” and 10 = “Excellent”.

ITT population

End point type	Secondary

End point timeframe:

At 120 mins

End point values	1 x Strefen Honey & Lemon lozenge(flurbip	2 x Ibuprofen Caplets		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	12		
Units: unit on scale				
arithmetic mean (standard deviation)	6.27 (± 2.41)	7.80 (± 1.62)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients issued with Strepsils at Discharge

End point title	Number of patients issued with Strepsils at Discharge

End point description:

ITT population

End point type	Secondary

End point timeframe:

At 120 minutes post-dose

End point values	1 x Strefen Honey & Lemon lozenge(flurbip	2 x Ibuprofen Caplets		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	12		
Units: Number of subjects	11	12		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Adverse Events (AEs)

End point title	Number of Subjects With Adverse Events (AEs)

End point description:

Intensity was determined by the Investigator. For symptomatic AEs the following definitions were applied:

Mild = AE does not limit usual activities; the subject may experience slight discomfort.
Moderate = AE results in some limitation of usual activities; the subject may experience significant discomfort.
Severe = AE results in an inability to carry out usual activities; the subject may experience intolerable discomfort or pain.

Relationship to Investigational Medicinal Products (IMP):

Possible = Reasonable suspicion that the AE was caused by the IMP.
Unlikely = Slight, but remote, chance that the AE was caused by the IMP, but the balance of judgment is

that it was most likely not due to the IMP.
Unrelated = No possibility that the AE was caused by the IMP.

End point type	Secondary

End point timeframe:

Up to 12 hours (Visit 1)

Safety population consist of all patients taking at least one dose of study medication.

End point values	1 x Strefen Honey & Lemon lozenge(flurbip	2 x Ibuprofen Caplets		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	12		
Units: Subjects				
Intensity - Mild	0	1		
Intensity - Moderate	0	0		
Intensity - Severe	0	0		
Relationship - Possible	0	1		
Relationship - Unlikely	0	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Up to 12 hours (Visit 1)	
Adverse event reporting additional description: Safety population.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	10.1

Reporting groups	
Reporting group title	1 x Strefen Honey & Lemon lozenge(flurbiprofen)
Reporting group description: -	
Reporting group title	2 x Ibuprofen Caplets
Reporting group description: -	

Serious adverse events	1 x Strefen Honey & Lemon lozenge(flurbiprofen	2 x Ibuprofen Caplets	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	1 x Strefen Honey & Lemon lozenge(flurbiprofen	2 x Ibuprofen Caplets	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal			

disorders Cough subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	1 / 12 (8.33%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 June 2007	The substantial amendments to a clinical trial, dated 20 June 2007, 21 June 2007, 10 October 2007 and 18 October 2007, initiated by the Investigator, documented the study suspension, study recommencement, and a minor change to the Patient Information Sheet, respectively.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
18 June 2007	The temporary halt from 18 June 2007 was due to poor recruitment during the spring/summer season where sore throat of the required intensity was uncommon. The recommencement of the study was in November 2007. The minor change to the Patient Information Sheet included additional side effects (taste perversion and mouth ulcers) of Strefen Honey & Lemon lozeng (flurbiprofen). These changes were made after 7 of 23 subjects had been enrolled and 6 of 21 subjects completed the study.	-

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was stopped prematurely, before the planned number of subjects was recruited. The study was ended after 23 subjects had been enrolled and 21 of the 23 enrolled subjects completed the study.

Notes: