Reckitt Benckiser

1 CLINICAL STUDY REPORT ERRATUM TITLE PAGE

EudraCT/IND Number:	2010-024045-69
Study Number:	TH1017
Study Title:	A multi-centre, randomised, double blind, single dose parallel group, placebo controlled study to investigate the efficacy of Strepsils Plus and Strepsils Extra in the treatment of sore throat due to upper respiratory tract infection.
Study Phase:	IV
Date First Subject Enrolled:	02nd February 2011
Date Last Subject Completed:	01st April 2011
Erratum Report Date:	08th Aug 2014 (Date of Final CSR: 12th Sep 2011)
Chief Investigator:	Dr. Damien McNally, Ormeau Health Centre, 120 Ormeau Road, Belfast BT7 2EB
Study Conduct Statement:	This study was designed in accordance with ICH Good Clinical Practice and the ethical principles contained within the Declaration of Helsinki, as referenced in EU Directive 2001/20/EC and with US Good Clinical Practice Regulations (21 CFR 50, 21 CFR 54, 21 CFR 56, and 21 CFR 312). Documents defined by ICH GCP as "essential documents" will be archived In the RB company archive in Hull, HU8 7DS, UK. The purpose of this erratum is to document non-compliances.

2 UPDATED STUDY SYNOPSIS

<table>
<tr><td>Name of Sponsor/ Company:
Reckitt Benckiser Healthcare International Ltd</td><td rowspan="2">Individual Trial Table Referring to Part of the Dossier

Volume:

Page:</td><td rowspan="2">(For National Authority use only)</td></tr>
<tr><td>Name of Finished Product:
1) Strepsils Plus
2) Strepsils Extra

Name of Active Ingredient(s):
1) 1.2 mg, 2, 4 – dichlororbenzyl alcohol and 0.6 mg amylmetacresol and 10 mg lidocaine hydrochloride
2) 2.4 mg hexylresorcinol</td></tr>
<tr><td colspan="3">Title of Trial: A multi-centre, randomised, double blind, single dose parallel group, placebo controlled study to investigate the efficacy of Strepsils Plus and Strepsils Extra in the treatment of sore throat due to upper respiratory tract infection.</td></tr>
<tr><td colspan="3">Investigator(s): Dr Damien McNally, Dr Paul Conn, Dr Malcolm McCaughey, Dr Michael Redmond, Dr Nigel Hart, Dr Peter Ryan, Dr Gerry McKeague, Dr Sean Haigney</td></tr>
<tr><td colspan="3">Trial Site(s): Multi-Centre study in 8 GP Primary Care sites in Northern Ireland, UK</td></tr>
<tr><td colspan="3">Publication (reference): McNally D, Shephard A, Field E. Randomised, Double-Blind, Placebo-Controlled Study of a Single Dose of an a amylmetacresol/2,4-dichlorobenzyl Alcohol Plus Lidocaine Lozenge or a Hexylresorcinol Lozenge for the Treatment of Acute Sore Throat Due to Upper Respiratory Tract Infection. J Pharm Pharmaceut Sci (www.cspsCanada.org) 15(2) 281 - 294, 2012</td></tr>
<tr><td colspan="2">Studied Period: 3 months
Date first subject enrolled: 02nd February 2011
Date last subject completed: 01st April 2011</td><td>Phase of Development: IV</td></tr>
<tr><td colspan="3">Objectives: The primary objective of the study was to determine the analgesic efficacy of Strepsils Plus and Strepsils Extra in patients with a sore throat due to upper respiratory tract infection (URTI) compared to a placebo lozenge. The analgesic properties were assessed by looking at the change in severity of throat soreness.

The secondary objective was to determine consumer acceptability of this product via responses to a consumer questionnaire.</td></tr>
<tr><td colspan="3">Methodology: Patients with a sore throat due to an URTI either presented opportunistically or following response to advertisements for patients in GP surgeries, community pharmacies and via local media.

Patients were screened at the 8 primary care sites. Eligible patients that met the study inclusion and exclusion criteria were randomized to receive one of the three test products. Within 1 minute of the baseline assessments of Throat soreness (11-point scale) difficulty swallowing (100mm VAS) and Swollen throat (100mm VAS) and a two part consumer questionnaire, patients were blindfolded and dosed with the assigned trial medication according to their randomisation number (single active or placebo lozenge). At 1, 5, 10, 15, 30, 45, 60, 75, 90, 105 and 120 minutes post dose patients completed the throat soreness and difficulty swallowing scales along with a 7-point categorical sore throat relief scale, a 5-point categorical throat numbness scales and a 100mm VAS swollen throat scale. One question regarding speed of numbing sensation was completed at 1 minute post dose, one question concerning the soothing sensation was completed at 5 minutes, three questions concerning the strength, intensity and depth of numbing were completed at 20 minutes post dose and other relief and emotional questions were completed at 60 and 120 minutes post dose. In addition, an overall treatment rating and a global evaluation were completed 120 minutes by the patient. A practitioner's clinical assessment of the study medication was conducted at 120 minutes by the investigator.

Following completion of the two hour assessment, patients left the investigative site with a patient diary to record any concomitant medication or adverse events (AEs) experienced up to 24 hours post dose of the study medication. A follow up telephone call by the site to the patient</td></tr>
</table>

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Name of Active Ingredient(s): 1) 1.2 mg, 2, 4 – dichlororbenzyl alcohol and 0.6 mg amylmetacresol and 10 mg lidocaine hydrochloride 2) 2.4 mg hexylresorcinol	**Page:**	

was made one to three days after completing the study to transcribe into the CRF any concomitant medications or AEs recorded by the patient in their diary.

There is potential for the blinding of the study to have been compromised. Each subject was to be blindfolded and provided with one throat lozenge by a research staff member not subsequently involved with the assessment/oversight of that subject within the centre. Patients were instructed to suck it slowly, moving the throat lozenge around the mouth until dissolved and not to chew or crunch the throat lozenge. Although blindfolding was a requirement of the protocol, the TMF documentation cannot verify that this requirement was adhered to, nor can the delegation of duties confirm how blinding of study staff was maintained.

The placebo throat lozenge used in this study was similar to that used in other Strepsils studies; it was a shaped matched lozenge without colour and with a sweet bland flavour. The intention of this placebo throat lozenge was to control for demulcency so any differences observed would be attributable to the formulations being tested, not just the active ingredients. The placebo throat lozenge was not the same colour as the Strepsils Plus and Strepsils Extra lozenges, which also differed from each other in appearance. In addition the placebo was unintagliated and the active lozenges were intagliated. Further to this the active lozenges were packed into clear blister packs with the placebo lozenge packed into opaque blister packs. In addition patients were made aware of some key product differences in the information sheet. These details and the inability to confirm how blinding was maintained at the sites indicates that the blinding of the study was compromised.

Number of Subjects:	**Planned:**	190
	Randomised:	190
	Analysed:	190 (Safety)
		190 (Full analysis set)
		174 (Per Protocol [PP])

Diagnosis and Main Criteria for Inclusion: Male and Female patients aged between 18 and 75 years of age with a sore throat due to URTI of onset not more than 4 days at the time of dosing were eligible for randomisation to the study. Patients had to have confirmed objective findings of sore throat assessed by the expanded Tonsillopharyngitis Assessment (TPA) scoring at least 5 points on the TPA and had to score at least 6 on the 11 point ordinal Throat Soreness Scale. Further inclusion criteria was a VAS score of >50mm on the difficulty swallowing and >33mm on the swollen throat scales at baseline.

Exclusion criteria excluded patients with conditions that could interfere with the assessment of sore throat analgesic activity and with any contraindications to any of the study medication.

Test Products:

Single oral doses of:

Strepsils Plus Lozenge: intagliated lozenges, pale green in colour with a mentholated flavour containing 1.2 mg, 2, 4 – dichlororbenzyl alcohol and 0.6 mg amylmetacresol and 10 mg lidocaine hydrochloride (Batch No. 3EE2).

Strepsils Extra Blackcurrant Lozenge: intagliated lozenges, reddish purple in colour with a blackcurrant and mild menthol flavour containing 2.4 mg hexylresorcinol (Batch No. 4GG).

Assessment Period: 2 hours

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Reference Therapy: Single dose of a shaped matched non-medicated, unintagliated, sugar based placebo lozenge colourless to slightly yellow in colour with a sweet bland flavour (Batch No. 2254653)

Criteria for Evaluation:

Efficacy: Efficacy was assessed by subjective rating scales. The primary efficacy variable was the change from baseline in severity of throat soreness (using the 11 point throat soreness scale) for the Strepsils Plus and Extra versus the placebo at 2 hours post dose.

There were a number of secondary endpoints. These were the AUC's from baseline to 2 hours for the change from baseline in difficulty swallowing, throat numbness and swollen throat. The change from baseline in difficulty in swallowing and swollen throat at 1, 5, 10, 15, 30, 45, 60, 75, 90, 105 and 120 minutes post dose was assessed as was throat numbness at 1, 5, 10, 15, 30, 45, 60, 75, 90, 105 and 120 minutes post dose. The total sum of pain relief ratings (TOTPAR), defined as the AUC from baseline to 2 hours post first dosing for sore throat relief, was assessed as was sore throat relief at 1, 5, 10, 15, 30, 45, 60, 75, 90, 105 and 120 minutes post dose. Onset of analgesia defined as the times to first reporting 'moderate pain relief' (which is the midpoint on the 7-point sore throat relief scale) was assessed as was the Global evaluation of the Study Medication as a Treatment of Sore Throat (GLOBAL) and Practitioner's Clinical Assessment of the Study Medication as a Treatment of Sore Throat (CLIN) at 2 hours. Responses to questions from the consumer questionnaire were also assessed.

Safety: Safety and tolerability of the lozenges were assessed in terms of the overall proportion of patients who reported adverse events (AEs) and serious adverse events (SAE's) during the 2 hours of observation and in the 24 hour period following administration of the lozenge when patients were asked to complete a patient diary. The information from the diary was obtained by a phone call to the patient by the nurse in a follow up period not exceeding 3 days post dose.

Statistical Methods: All efficacy variables were analysed using the full analysis dataset, which consisted of all patients who were randomised to the study and took study medication. The primary analysis and secondary analysis of the change from baseline in severity of throat soreness from 0 to 2 hours, AUC from baseline to 2 hours for the change from baseline of severity of throat soreness and difficulty in swallowing and the AUC from baseline to 2 hours for throat numbness and sore throat relief were repeated using a per-protocol set.

The primary efficacy variable was analysed using Analysis of Covariance (ANCOVA) with the baseline severity of throat soreness as a covariate and a factors for treatment group and centre.

The secondary AUCs, changes from baseline and overall treatment rating variables were analysed using ANCOVA with baseline severity of throat soreness as a covariate and a factors for treatment group and centre. Covariates for swollen throat and difficulty swallowing were also added to the model for analysis of these variables. The time to onset of moderate pain relief was compared between treatment groups using the Cox-proportional hazards model. Consumer questionnaire responses were analysed using a proportional odds model (non-numeric data) or ANCOVA (numeric ordinal data).

For ease of interpretation the AUC values obtained were divided by the total hours the scale was assessed for reporting purposes.

Safety data were analysed using the safety set which included all patients who took study medication. The proportion of patients reporting treatment emergent AEs was compared

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between treatment groups using the chi-square test.

Treatment group differences were presented with 95% confidence intervals. All AUC analyses were based on actual timings and were calculated using the trapezoidal rule.

Concomitant medications on-going at randomisation were coded using the ATC level 2 categories from the WHO dictionary Enhanced 3.11 Version. Adverse Events were listed and tabulated by treatment, severity, relationship to therapy and primary system organ class according to Version 13.1 of MedDRA.

SUMMARY & CONCLUSIONS

EFFICACY RESULTS:

The treatment groups were matched for demographic variables with the age range being 18-73 years with a mean of 31.6 years. There was an imbalance in gender between the groups; the two active groups had 33% male patients compared with 58% in the placebo group. The majority (98%) of patients were Caucasian.

Strepsils Extra showed clear superiority with statistical significance over placebo for the primary variable of throat soreness at 2 hours and across all efficacy variables in the study. Strepsils Plus also achieved significant efficacy over Placebo at various time points for the efficacy measures and both Strepsils Lozenges showed statistically significant sore throat relief in comparison to placebo. Results for the primary efficacy variable are summarised in Table 1.

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TABLE 1: Primary Efficacy Variable - Change from baseline in throat soreness at 120 minutes post dose

Throat soreness measured on an 11-point scale where 0 = Not sore, 10 = Very sore

	Strepsils Plus lozenge	Strepsils Extra lozenge	Placebo
FULL ANALYSIS SET			
N	64	64	62
Baseline (Mean±sd)	7.16±1.07	7.27±1.21	7.13±1.00
120 minutes post-dose (Mean±sd)	5.41±2.34	5.05±2.62	6.16±1.87
Change from baseline (Mean±sd)	-1.75±2.31	-2.22±2.66	-0.97±1.96
LS mean[a]	-1.78	-2.19	-1.03
Difference between LS means v placebo[b]	-0.75	-1.16	
95% Confidence Interval	-1.54,0.04	-1.95,-0.37	
P value	0.06	0.004**	
PER-PROTOCOL SET			
N	58	58	57
Baseline (Mean±sd)	7.10±1.00	7.40±1.12	7.25±0.93
120 minutes post-dose (Mean±sd)	5.48±2.31	5.12±2.62	6.26±1.89
Change from baseline (Mean±sd)	-1.62±2.09	-2.28±2.66	-0.98±2.03
LS mean[a]	-1.68	-2.22	-1.03
Difference between LS means v placebo[b]	-0.65	-1.19	
95% Confidence Interval	-1.47,0.18	-2.01,-0.36	
P value	0.12	0.005 **	

a Estimated from ANCOVA model with factors for treatment and centre and a covariate for baseline throat soreness

b A negative difference favours the first treatment against second treatment

** Comparison statistically significant at 1% level

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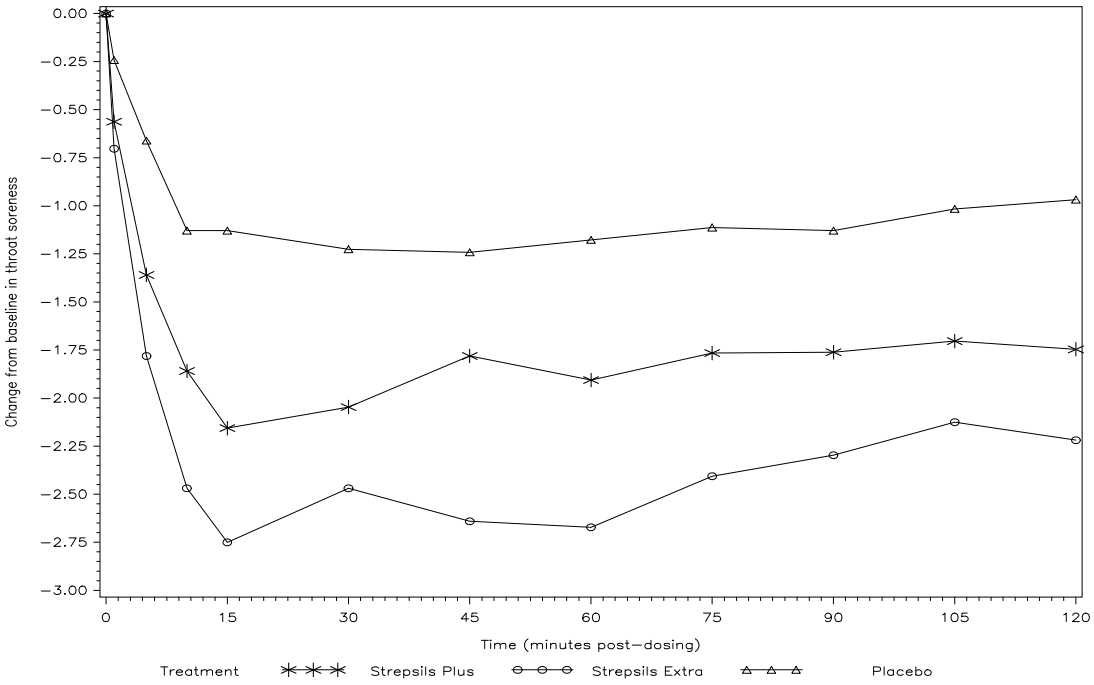
Figure 1: Mean change from baseline in throat soreness from 1-120 minutes post dose – Full analysis set

Throat soreness measured on an 11 point scale where 0=not sure, 10=very sore



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Key secondary efficacy variable data are summarised in Table 2 - 7 – Full analysis set.

TABLE 2: Mean ± sd for change from baseline in throat soreness at 1, 5, 10, 15, 30, 45, 60, 75, 90 and 105 minutes post dose – Full analysis set

Throat soreness measured on an 11-point scale where 0 = Not sore, 10 = Very sore

Minutes post-dose	Strepsils Plus lozenge (n)	Strepsils Extra lozenge (n)	Placebo (n)	Strepsils Plus versus Placebo	Strepsils Extra versus Placebo
0	7.20±1.12 (64)	7.27±1.21 (64)	7.13±1.00 (62)		
1	-0.56±1.21 (64)	-0.70±1.29 (64)	-0.24±0.82 (62)	ns	*
5	-1.36±1.73 (64)	-1.78±1.72 (64)	-0.66±1.01 (62)	*	***
10	-1.86±1.86 (64)	-2.47±2.01 (64)	-1.13±1.71 (62)	*	***
15	-2.16±2.07 (64)	-2.75±2.01 (64)	-1.13±1.61 (62)	**	***
30	-2.05±2.07 (64)	-2.47±1.97 (64)	-1.23±1.71 (62)	*	***
45	-1.78±2.11 (64)	-2.64±2.23 (64)	-1.24±1.91 (62)	ns	***
60	-1.91±2.10 (64)	-2.67±2.30 (64)	-1.18±1.93 (62)	ns	***
75	-1.77±2.14 (64)	-2.41±2.42 (64)	-1.11±1.92 (62)	ns	**
90	-1.76±2.16 (63)	-2.30±2.54 (64)	-1.13±1.94 (62)	ns	**
105	-1.70±2.24 (64)	-2.13±2.58 (64)	-1.02±2.00 (62)	ns	*

ns Comparison not statistically significant
* Comparison statistically significant at 5% level
** Comparison statistically significant at 1% level
*** Comparison statistically significant at 0.1% level

TABLE 3: Mean ± sd (n) for change from baseline in difficulty in swallowing at 1, 5, 10, 15, 30, 45, 60, 75, 90, 105 and 120 minutes post dose – Full analysis set

Difficulty in swallowing measured on 100mm VAS where 0mm = Not difficult, 100mm = Very difficult

Minutes post-dose	Strepsils Plus lozenge (n)	Strepsils Extra lozenge (n)	Placebo (n)	Strepsils Plus versus Placebo	Strepsils Extra versus Placebo
0	72.5±10.5 (64)	73.6±12.1 (64)	70.8±11.9 (62)		
1	-8.0±13.7 (64)	-10.8±16.2 (64)	-4.1±11.4 (62)	ns	*
5	-15.1±17.2 (64)	-19.8±18.8 (64)	-6.4±11.6 (62)	**	***
10	-19.9±20.5 (64)	-25.6±21.3 (64)	-9.0±14.0 (62)	**	***
15	-21.8±21.9 (64)	-29.1±22.0 (64)	-10.1±13.8 (62)	***	***
30	-20.7±22.2 (64)	-28.6±22.2 (64)	-8.8±12.0 (62)	**	***
45	-18.6±21.7 (64)	-29.5±23.2 (64)	-8.7±12.7 (62)	**	***
60	-18.8±22.3 (64)	-29.7±24.2 (64)	-8.6±13.4 (62)	**	***
75	-19.3±23.2 (64)	-28.4±26.0 (64)	-7.4±13.1 (62)	**	***
90	-18.7±23.6 (64)	-26.9±27.4 (64)	-7.6±13.2 (62)	**	***
105	-19.8±23.6 (64)	-26.2±28.2 (64)	--7.4±13.9 (62)	**	***
120	-19.6±25.2 (64)	-27.0±30.2 (64)	-7.0±15.3 (62)	**	***

ns Comparison not statistically significant
* Comparison statistically significant at 5% level
** Comparison statistically significant at 1% level
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TABLE 4: Mean ± sd (n) for change from baseline in swollen throat at 1, 5, 10, 15, 30, 45, 60, 75, 90, 105 and 120 minutes post dose – Full analysis set

Swollen throat measured on a 100mm VAS scale where 0mm = Not Swollen, 100mm = Very Swollen

Minutes post-dose	Strepsils Plus lozenge (n)	Strepsils Extra lozenge (n)	Placebo (n)	Strepsils Plus versus Placebo	Strepsils Extra versus Placebo
0	66.1±16.3 (63)	68.3±18.1 (64)	66.7±15.2 (62)		
1	-2.8±13.1 (63)	-9.1±18.6 (64)	-1.9±11.8 (62)	ns	**
5	-8.3±16.2 (63)	-14.5±19.2 (64)	-4.3±13.4 (62)	ns	***
10	-13.4±18.6 (63)	-20.0±21.2 (64)	-6.7±15.5 (62)	*	***
15	-14.7±21.6 (63)	-23.0±21.9 (64)	-7.3±14.7 (62)	*	***
30	-15.8±20.5 (63)	-24.4±23.9 (64)	-6.2±15.2 (62)	**	***
45	-14.1±21.0 (63)	-24.3±24.0 (64)	-5.7±14.9 (62)	*	***
60	-14.3±21.7 (63)	-24.9±25.4 (64)	-7.1±19.0 (62)	ns	***
75	-14.8±23.1 (63)	-24.2±27.0 (64)	-5.6±15.9 (62)	*	***
90	-16.0±22.8 (63)	-22.8±28.9 (64)	-5.7±16.6 (62)	**	***
105	-15.5±24.1 (63)	-22.6±28.6 (64)	-5.5±17.0 (62)	*	***
120	-15.0±24.9 (63)	-23.1±29.6 (64)	-5.2±18.1 (62)	*	***

ns Comparison not statistically significant
* Comparison statistically significant at 5% level
** Comparison statistically significant at 1% level
*** Comparison statistically significant at 0.1% level

TABLE 5: Mean ± sd (n) for sore throat relief at 1, 5, 10, 15, 30, 45, 60, 75, 90, 105 and 120 minutes post first dose – Full analysis set

Measured on a 7-point scale where 0 = No relief, 1 = Slight relief, 2 = Mild relief, 3 = Moderate relief, 4 = Considerable relief, 5 = Almost complete relief, 6 = Complete relief

Minutes post-dose	Strepsils Plus lozenge (n)	Strepsils Extra lozenge (n)	Placebo (n)	Strepsils Plus versus Placebo	Strepsils Extra versus Placebo
1	1.13±1.29 (64)	1.03±1.05 (64)	0.37±0.71 (62)	***	***
5	1.83±1.30 (64)	1.83±1.11 (64)	0.76±1.00 (62)	***	***
10	2.20±1.37 (64)	2.41±1.28 (64)	0.98±1.22 (62)	***	***
15	2.28±1.34 (64)	2.66±1.39 (64)	1.00±1.20 (62)	***	***
30	2.17±1.50 (64)	2.63±1.41 (64)	0.97±1.06 (62)	***	***
45	1.98±1.52 (64)	2.52±1.53 (64)	0.92±1.11 (62)	***	***
60	1.86±1.55 (64)	2.42±1.64 (64)	0.82±1.02 (62)	***	***
75	1.78±1.59 (64)	2.33±1.75 (64)	0.76±0.99 (62)	***	***
90	1.66±1.60 (64)	2.08±1.78 (64)	0.71±1.03 (62)	***	***
105	1.63±1.65 (64)	1.97±1.80 (64)	0.71±1.12 (62)	***	***
120	1.66±1.64 (64)	1.95±1.89 (64)	0.68±1.11 (62)	***	***

ns Comparison not statistically significant
* Comparison statistically significant at 5% level
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TABLE 6: Mean ± sd (n) for throat numbness at 1, 5, 10, 15, 30, 45, 60, 75, 90, 105 and 120 minutes post dose – Full analysis set

Throat numbness measured on a 5-point scale where 1 = None, 2 = Mild, 3 = Moderate, 4 = Considerable, 5 = Complete

Minutes post-dose	Strepsils Plus lozenge (n)	Strepsils Extra lozenge (n)	Placebo (n)	Strepsils Plus versus Placebo	Strepsils Extra versus Placebo
1	2.08±0.99 (63)	1.84±0.74 (64)	1.63±0.93 (62)	*	Ns
5	2.40±1.04 (63)	2.38±0.90 (64)	1.80±0.98 (61)	***	**
10	2.54±1.08 (63)	2.70±0.91 (63)	1.84±0.97 (61)	***	***
15	2.63±1.03 (64)	2.69±1.05 (64)	1.84±0.96 (62)	***	***
30	2.33±1.11 (64)	2.56±0.97 (64)	1.77±0.80 (61)	**	***
45	2.17±1.09 (64)	2.48±1.15 (64)	1.74±0.85 (62)	*	***
60	2.08±1.19 (64)	2.27±1.22 (63)	1.64±0.78 (61)	*	**
75	1.95±1.12 (64)	2.19±1.22 (64)	1.58±0.80 (62)	*	**
90	1.91±1.16 (64)	2.09±1.28 (64)	1.52±0.78 (62)	*	**
105	1.92±1.17 (64)	2.05±1.28 (63)	1.48±0.78 (62)	*	**
120	1.92±1.21 (64)	2.03±1.36 (63)	1.45±0.76 (62)	*	**

ns	Comparison not statistically significant
*	Comparison statistically significant at 5% level
**	Comparison statistically significant at 1% level
***	Comparison statistically significant at 0.1% level

Name of Sponsor/ Company: Reckitt Benckiser Healthcare International Ltd	**Individual Trial Table Referring to Part of the Dossier**	**(For National Authority use only)**
Name of Finished Product: 1) Strepsils Plus 2) Strepsils Extra	**Volume:**	
Name of Active Ingredient(s): 1) 1.2 mg, 2, 4 – dichlororbenzyl alcohol and 0.6 mg amylmetacresol and 10 mg lidocaine hydrochloride 2) 2.4 mg hexylresorcinol	**Page:**	

TABLE 7: Summary of Additional Key Secondary Efficacy Variables – Full analysis set

Variable	Strepsils Plus	Strepsils Extra	Placebo
AUC from baseline to 2 hours post dose in difficulty swallowing			
Measured on a 100mm VAS where 0mm=not difficult , 100mm = very difficult			
N	64	64	62
Mean + SD	-19.1±20.0	-27.3±21.9	-8.0±11.6
LS mean[d]	-19.3	-27.2	-8.6
Difference between LS means v placebo[b]	-10.7	-18.7	
95% Confidence Interval	-17.1, -4.3	-25.1, -12.2	
P value	0.0012**	<0.0001***	
AUC from baseline to 2 hours post dose for the change in swollen throat			
Measured on a 100mm VAS where 0mm=not swollen, 100mm=very swollen			
N	63	64	62
Mean + SD	-14.4±19.4	-22.8±23.3	-5.9±14.6
LS mean[d]	-14.9	-22.5	-6.2
Difference between LS means v placebo[b]	-8.8	-16.3	
95% Confidence Interval	-15.3, -2.2	-22.9, -9.8	
P value	0.009**	<0.0001***	
AUC from baseline to 2 hours post dose for sore throat relief (TOTPAR)			
Measured on a 7 point scale where 0=no relief and 6 = complete relief			
N	64	64	62
Mean + SD	1.86±1.33	2.28±1.41	0.81±0.95
LS mean[a]	1.90	2.31	0.84
Difference between LS means v placebo[b]	1.06	1.47	
95% Confidence Interval	0.62, 1.50	1.03, 1.91	
P value	<0.0001***	<0.0001***	
AUC from baseline to 2 hours post dose for the change in baseline in throat numbness			
Measured on a 5 point scale where 1= none and 5 = complete			
N	64	64	62
Mean + SD	2.13±0.98	2.30±0.99	1.64±0.74
LS mean[a]	2.11	2.27	1.63
Difference between LS means v placebo[b]	0.49	0.64	
95% Confidence Interval	0.17,0.80	0.33,0.96	
P value	0.0024 **	<0.0001 ***	
Consumer questionnaire: how would you rate this lozenge as a treatment for sore throat			
Asked at 2 hours post dose and measured on an 11 point scale where 0=poor and 10=excellent			
N	64	64	62
Mean + SD	5.38±2.98	5.64±3.06	2.23±2.73
LS mean[a]	5.38	5.66	2.20
Difference between LS means v placebo[b]	3.18	3.45	
95% Confidence Interval	2.15,4.21	2.42,4.49	
P value	<0.0001 ***	<0.0001 ***	

a Estimated from ANCOVA model with factors for treatment and centre and a covariate for baseline throat soreness

b A negative difference favours the first treatment against second treatment

c A positive difference favours the first treatment against second treatment

d Estimated from ANCOVA model with factors for treatment and centre and covariates for baseline throat soreness baseline difficulty swallowing/ baseline swollen throat as appropriate

Name of Sponsor/ Company: Reckitt Benckiser Healthcare International Ltd	**Individual Trial Table Referring to Part of the Dossier**	**(For National Authority use only)**
Name of Finished Product: 1) Strepsils Plus 2) Strepsils Extra	**Volume:**	
Name of Active Ingredient(s): 1) 1.2 mg, 2, 4 – dichlororbenzyl alcohol and 0.6 mg amylmetacresol and 10 mg lidocaine hydrochloride 2) 2.4 mg hexylresorcinol	**Page:**	

Maximum reductions in throat soreness were evident at 15 minutes post dose for both Strepsils Lozenges compared to 45 minutes post dose for placebo.

Maximum mean throat numbness was obtained at 10 minute post dose for the Strepsils Extra lozenge and placebo and 15 minute post dose for Strepsils Plus.

Both Strepsils Lozenges were superior to placebo in providing sore throat relief than placebo with maximum pain relief being achieved at 15 minutes post dose for all 3 treatments.

For the functional element of the consumer questionnaire, statistically significant differences in favour of Strepsils Extra, when compared to placebo, were obtained for improvements in talking ($p=0.005$) and swallowing ($p=0.002$) at one hour post dose. There was no significant improvement for Strepsils Plus v placebo for any of the functional impairments.

There was a statistically significant difference in favour of both Strepsils Lozenges against placebo in patient reported outcomes of; how effective their lozenge was, the depth of numbing, intensity of the numbing, feeling their best overall and how happy they were with their throat. This significant difference was also reflected in the patient's response to feeling less distracted, making patients feel better than before and taking their minds off the pain. Both Strepsils Lozenges were found to offer highly significant soothing over placebo.

Both Strepsils Lozenges were significantly better than placebo ($p<0.0001$) with respect to both the Practitioner Clinical assessment of the study medication and the Patient's Global evaluation of the medication.

SAFETY RESULTS:

There were no significant differences between the treatment groups in the proportion of subjects reporting treatment emergent AEs. There were a total of 7 AEs reported by 6 patients:

Strepsils Extra lozenge group, one patient reported two AEs

Strepsils Plus lozenge group, one patient reported one AE

Placebo group, four patients reporting four AEs

The majority of events were of mild severity with one event classed as severe (placebo – earache). None were considered to be definitely, probably or possibly related to the study medication.

CONCLUSION:

Blinding of the study was compromised and as such, in hindsight, the study cannot be considered double blind. The placebo throat lozenge was designed to control for demulcency so any differences observed would be attributable to the formulations as a whole, not just the active ingredients. As such, the efficacy and safety of both Strepsils Extra and Strepsils Plus was evident in the soothing relief of sore throats due to URTI. Following a single dose, relief was evident from 1 minute post dose with maximal effects at 15 minutes post dose. Strepsils Extra was more efficacious and achieved statistical significance over placebo for all the analgesic variables related to throat soreness, sore throat relief and difficulty in swallowing. Both Strepsils Lozenges demonstrated superiority over placebo consistently over the variables measured. Both Strepsils Lozenges were well tolerated.

Date of the Erratum: 08 Aug 2014

3 TABLE OF CONTENTS

4 LIST OF ABBREVIATIONS AND DEFINITION OF TERMS FOR ERRATUM REPORT

Abbreviation	Abbreviation in Full
ABPI	Association of the British Pharmaceutical Industry
AE	Adverse event
AIDS	Acquired Immune Deficiency Syndrome
AMC	Amylmetacresol BP
ANCOVA	Analysis of covariance
ANOVA	Analysis of variance
AR	Adverse Reaction
AUC	Area under the curve
BNF	British National Formulary
CFR	Code of Federal Regulations
CI	Confidence Interval
CLIN	Practitioners Clinical Assessment of the Study Medication
CPM	Clinical Project Manager
CRF	Case Report Form
CRO	Contract research organisation
CSR	Clinical Study Report
CTA	Clinical Trial Application
CV	Curriculum vitae
DCBA	2,4-Dichlorobenzyl alcohol
DSS	Difficulty Swallowing Scale
EC	Ethics Committee
eCRF	Electronic Case Report Form
EU	European Union
FDA	Food and Drug Administration
GCP	Good Clinical Practice
GLOBAL	Patient Global Evaluation of the Study Medication
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
GP	General Practitioner
HIV	Human Immunodeficiency Virus

Abbreviation	Abbreviation in Full
ICF	Informed Consent Form
ICH	International Conference on Harmonisation
IEC	Independent ethics committee
IMSU	Investigational Material Supplies Unit
IND	Investigational New Drug
IRB	Institutional Review Board
ITT	Intent-to-treat
LS	Least Square
MedDRA	Medical Dictionary for Regulatory Authorities
N	Number
NCR	No carbon required
NHS	National Health Service
NSAID	Non steroidal anti-inflammatory drug
p	Probability
PAIN	Practitioner's Assessment of Pharyngeal Inflammation
PIS	Patient Information Sheet
PK	Pharmacokinetic
QA	Quality Assurance
QC	Quality Control
R&D	Research and Development
RB	Reckitt Benckiser
SAE	Serious adverse event
SD	Standard Deviation
SDV	Source data verification
SMO	Site management organisation
SOP	Standard operating procedure
SwoTS	Swollen Throat Scale
TMF	Trial Master File
TOTPAR	Summed changes from baseline in sore throat pain relief
TPA	Tonsillopharyngitis Assessment
TS	Throat Soreness Scale
UK	United Kingdom (of Great Britain and Northern Ireland)

Abbreviation	Abbreviation in Full
URTI	Upper Respiratory Tract Infection
US	United States (of America)
VAS	Visual Analogue Scale
WCT	Worldwide Clinical Trials
WHO	World Health Organisation

5 INTRODUCTION TO STUDY REPORT ERRATUM

Following production of the original Clinical Study Report (CSR) for TH1017 potential issues relating to Good Clinical Practice (GCP) compliance of the study have been highlighted which were not adequately described in the original CSR. Specifically that the placebo throat lozenge was not matched to the active lozenges in terms of flavour or appearance and that the delegation of duties with respect to blinded vs. unblinded personnel was not clear and cannot be verified from the trial documentation. These findings have prompted a review of the TMF including the previous CSR to identify where information was lacking or incomplete in the original CSR. This document is an erratum to the original CSR and provides additional information concerning the blinding of the study and other key operational details.

Information is presented as amended CSR sections using the same numbering system as it appears in the CSR. This starts from section 5 below, hence two sections numbered 5 being present in this report erratum.

5 CSR SECTION - ETHICS

5.2 Ethical Conduct of the Study

This study was designed in accordance with the Declaration of Helsinki, as referenced in EU Directive 2001/20/EC. It was carried out according to the principles of International Conference on Harmonisation (ICH) GCP and applicable regulatory requirements.

9 CSR SECTION – INVESTIGATIONAL PLAN

9.2 Discussion of Study Design, Including the choice of Control Groups

The methodology used in this study is an accepted and validated analgesic methodology based on the Sore Throat Pain Model described in the literature by Schachtel[1,2,3]. Other indicators of pain such as difficulty in swallowing and a swollen sensation in the throat were also assessed by employment of the Difficulty Swallowing Scale and the Swollen Throat Scale[4, 5]. The methodology has been previously used in a number of studies with Strepsils lozenges and in sore throat studies investigating the analgesic properties of a sore throat lozenge containing the non-steroidal anti-inflammatory (NSAID) drug flurbiprofen[6,7,8]. Differences exist in the

studies on selection of primary endpoint and statistical analyses; namely use of TOTPAR (summed change in sore throat pain relief ratings from baseline (BH5013)), differences in throat soreness at the 2 hour time point (TH0705 and this study) or area under the curve for the change in sore throat ratings from baseline (TH0817).

Sore throat due to Upper Respiratory Tract Infection (URTI) is a common illness for which most patients seek symptomatic relief; it is a minor, non-serious condition. The extent of possible improvement in symptoms is quite small, making comparisons between active treatments difficult. In this study to investigate the analgesic, numbing and consumer acceptability of the two anaesthetic Strepsils variants – Strepsils Plus and Strepsils Extra - the study required participants to have sufficient throat soreness at baseline and used a placebo throat lozenge without flavour or other excipients in order to discriminate between treatments.

Therefore to be eligible for study entry, patients had to have a throat soreness score of 6 or more as scored on the Throat Soreness Scale. In addition to this subjective measure of throat soreness, patients had to undergo an objective Tonsillopharyngitis Assessment (TPA). The TPA ensured that patients had some objective sign of a sore throat and that only patients with acute tonsillopharyngitis were recruited into the study. The TPA consisted of assessments of 7 pertinent features of tonsillopharyngitis, oral temperature, size of tonsils, oropharyngeal colour, number of oropharyngeal enanthems, and size, number and tenderness of the anterior cervical lymph nodes. The TPA provided a score ranging from 0 to 21 points. A minimum score of 5 points was required to confirm the presence of tonsillopharyngitis and permit entry into the study.

The choice of control group was based on the previous studies conducted with Strepsils. The lozenge format itself provides soothing relief through demulcency, sucking a throat lozenge helps to increase saliva production[9.10] and the mucosa remains lubricated[11, 12]. This can be enhanced by the excipients and flavourings added to throat lozenges which provide sensorial effects[9] and in some cases actually further provoke saliva production[13]. The placebo throat lozenge used in this study was similar to that used in other Strepsils studies; a shaped matched lozenge, colourless to slightly yellow in colour and with a sweet but bland flavour. The active lozenges were intagliated, with the placebo unintagliated. The placebo was achieved by omitting the essence pre-mix which contains the AMC/DCBA and flavouring components, and the colours from a standard Strepsils Original formulation. The intention of this placebo throat lozenge was to control for demulcency so any differences observed would be attributable to the formulations as a whole, not just the active ingredients. Each patient was to be blindfolded and provided with one throat lozenge by a research staff member not subsequently involved with the assessment/oversight of that patient. The intention was to ensure the patient and the staff supervising their assessments remained blinded to the treatment they had received. The placebo and this method of blinding were considered adequate controls to which to compare the overall effects of the Strepsils Plus and Strepsils

Extra formulations. However, it should be noted that the active lozenges included in this study included actives (lidocaine hydrochloride and hexylresorcinol) with distinct anaesthetic/numbing properties which were freely available on the UK market where the study was conducted. Any patient therefore that had taken Strepsils plus or Strepsils Extra in the past would probably be aware of the tongue/throat numbing action of the products and hence be aware of whether they had been assigned an active or the placebo group.

9.4 Treatments

9.4.1 Treatments Administered

Patients were randomly allocated to one of three treatment groups. The following medications were supplied:

I. Strepsils Plus lozenge containing 0.6mg amylmetacresol BP, 1.2mg, 4-Dichlorobenzyl alcohol and 10mg Lidocaine Hydrochloride

II. Strepsils Extra lozenge containing 2.4mg Hexylresorcinol

III. Non-medicated sugar based placebo lozenge

Each patient was randomized to receive one of the 3 treatments by allocating them to an assigned number. Numbers were allocated in a sequential manner from lowest to highest at each site. Patients were given the instruction to suck the lozenge slowly and move it around the mouth until it dissolved. The patients were asked not to chew or crunch the lozenge. Patients completed self-assessment forms during the 2 hour observation period.

9.4.2 Identity of Investigational Product(s)

The identities of the medicines supplied in the study were:

I. Strepsils Plus lozenge pale green in colour with a mentholated flavour containing 1.2 mg, 2, 4 – dichlororbenzyl alcohol and 0.6 mg amylmetacresol and 10 mg lidocaine hydrochloride, PA 979/40/1, Batch No. 3EE2

II. Strepsils Extra Blackcurrant Lozenge reddish purple in colour with a blackcurrant and mild menthol flavour containing 2.4 mg hexylresorcinol, PL00063/0392, Batch No. 4GG

III. Shaped matched non-medicated sugar based lozenge (Placebo) colourless to slightly yellow in colour with a sweet bland flavour Batch No. 2254653

The two Strepsils lozenges and the non-medicated sugar based placebo lozenges were manufactured, primary packed, secondary packed and labelled to Good Manufacturing Practice by RB, Nottingham, NG90 2DB. The active lozenges (Strepsils Plus and Strepsils Extra) were packed in transparent blisters and the placebo lozenges were packed into opaque blisters.

All drug supplies were re-packed into patient packs and labelled by the Investigational Material Supplies Unit (IMSU), Reckitt Benckiser Healthcare (UK) Ltd, Dansom Lane, Hull, HU8 7DS. This was a double-blind trial, therefore drug supplies needed to be blinded. However, the two active products and the placebo were labelled differently as Product X, Product Y and Product Z. They were shipped directly from the IMSU to the investigative site.

9.4.6 Blinding

The study was described as double-blind and the intention was that as the lozenges were not colour matched, the dose would be administered to the patient by an independent member of the Clinic staff that was not involved with any other study related procedures pre or post dosing. In addition each patient was to be blindfolded during dosing. This was to enable both patient and staff supervising the efficacy and safety assessments to remain blinded.

However, there were a number of procedural issues that meant blinding of the study was not achieved. The products all differed from each other in terms of appearance and were packed in different blister materials, the active lozenges in transparent blisters the placebo lozenge in opaque blisters. In addition the products were clearly identifiable from the lid foils and were labelled differently as Product X, Product Y and Product Z. Documentation sent to the site staff also identified the different products; the Release Certificate for the investigators provided full product descriptions, individual batch numbers and individual expiry dates for each treatment arm.

Therefore the study was unblinded to a number of people at study sites by the documentation and the appearance of the products - different colours, differing intagliation of the products, different laminate material, product name on the lidding foil. Insufficient information was included in the protocol and subsequently in the TMF on how a study member could act as the "blinded" person at the study sites and delegation of duties logs did not always show a separation of blinded and unblinded duties.

The information sheet stated that the placebo is sugar based only and that both actives contain anaesthetic and also that the treatments can be distinguished from each other. Any subject therefore that had taken Strepsils in the past would probably be aware of the tongue/throat numbing action of the active.

9.8 Changes in the Conduct of the Study or Planned Analysis

9.8.1 Changes in the Conduct of the Study

The study was not double-blind. To ensure that visual differences in the lozenges did not result in data bias, staff administering the investigational products were to be independent of the investigational staff who were involved in the study assessments. The monitoring plan has no specific mention of blinded/unblinded personnel and blinded assessors and best practice was not followed with respect to documenting delegation of responsibilities of the research staff. It is unclear whether the staff

monitoring the study remained blinded throughout the study. However, drug accountability was verified by the monitor(s), it is concluded that the blinding of the monitor(s) checking accountability was not maintained.

13 CSR SECTION - DISCUSSION AND OVERALL CONCLUSIONS

13.1 Discussion

This study was part of the continued Strepsils brand development to support Strepsils products and claims. The primary objective of this study was to determine the analgesic properties of Strepsils Plus and Strepsils Extra anaesthetic throat lozenges in patients with a sore throat due to an URTI. Sample size and choice of primary endpoint were determined on the basis of previous clinical experience with Strepsils lozenges but not the anaesthetic variants. Both variants used in the study (Strepsils Plus and Strepsils Extra) are believed to achieve their analgesic efficacy through an anaesthetic action locally at the site of pain, so in addition to patient reported outcomes related to their throat condition, throat numbness was also evaluated.

Both products demonstrated efficacy in relieving sore throat through multiple independent patient reported outcomes with Strepsils Extra achieving statistically significant superiority compared with the placebo lozenge across all measures. For Strepsils Plus, superiority over placebo was demonstrated but statistical significance was not consistent across all endpoints.

The primary efficacy results from this study are summarised in Table 13.1.1 compared with the equivalent results from a previous study, TH0705, which had the same primary endpoint but investigated the Strepsils Original lozenge. For the primary efficacy variable, the change at 120 minutes post dose from baseline in throat soreness (using the 11-point Throat Soreness Scale) the results are broadly consistent with the results seen in TH0705. In the current study there were LS mean reductions from baseline of -2.19, -1.78, and -1.03 for Strepsils Extra, Strepsils Plus and placebo throat lozenges respectively. The LS mean differences between active and placebo were statistically significant (-1.16, 95% CI -1.95, -0.37, p=0.004) for Strepsils Extra, but only of borderline statistical significance for Strepsils Plus (-0.75, 95% CI - 1.54, 0.04).

There was no significant centre differences observed for the primary endpoint and recruitment was capped at 33 patients at any one centre therefore it is unlikely that the centre contributed to the differences noted. 16 patients were excluded from the per-protocol analysis as they had not met the initial inclusion criteria and the decision was made to increase the total of patients randomized from 180 to 190 to give 174 evaluable patients. The actual variability observed during the study was 2.24 compared to 1.78 that was predicted and on which the sample size calculation was based. As a consequence the study power was less than expected.

Table 13.1.1 Comparison of Primary Efficacy Variable – Change in Throat Soreness at 120 minutes post dose

Throat soreness measured on a 11-point scale where 0=Not sore, 10 = Very sore

Study	Parameter	Placebo Lozenge	Strepsils Plus	Strepsils Extra	Strepsils Original
TH1017	N	62	64	64	
	Female: Male	26:36	43:21	43:21	
	Mean Age (yrs) ± SD	31.5 ± 11.7	32.4 ± 15.8	30.9 ± 12.8	
	BSL Throat Soreness ± SD	7.1 ± 1.0	7.2 ± 1.1	7.3 ± 1.2	
	Mean 120 mins post-dose Throat Soreness ± SD	6.2 ± 1.9	5.4 ± 2.3	5.1 ± 2.6	
	Mean Change from BSL ± SD	-0.97 ± 1.96	-1.75 ± 2.31	-2.22 ± 2.66	
	LS Mean	-1.03	-1.78	-2.19	
	Difference		-0.75	-1.16	
	95% CI		-1.54, 0.04	-1.95, -0.37	
	P Value		0.06	0.004	
TH0705	N	155			155
	Female: Male	105:50			105:50
	Mean Age (yrs) ± SD	35.9 ± 14.2			36.3 ± 14.0
	BSL Throat Soreness ± SD	7.2 ± 1.2			7.1 ± 1.1
	Mean 120 mins post-dose Throat Soreness ± SD	6.3 ± 1.8			5.1 ± 2.1
	Mean Change from BSL ± SD	-0.88 ± 1.50			-2.07 ± 2.02
	LS Mean	-0.85			-2.06
	Difference				-1.21
	95% CI				-1.59, -0.82
	P value				<0.0001

Given that this study was investigating short acting local anaesthetic products the selection of primary endpoint (efficacy at a single 2 hour time point post dose) was probably not the most representative candidate of product efficacy. It is clear that the numbing effect of both products decreases over 2 hours with a more marked reduction observed with Strepsils Plus than Strepsils Extra, in line with the short action of lidocaine hydrochloride. A more representative measure of efficacy is probably the AUC from baseline to 2 hours post-dose for the change from baseline in Throat Soreness. These data are summarised in Table 13.1.2 along with comparable data from other Strepsils Studies.

Table 13.1.2 Comparison of AUC from Baseline to 2 hours post-dose for the change from Baseline in Throat Soreness

Throat soreness measured on a 11-point scale where 0=Not sore, 10 = Very sore

Study	Parameter	Placebo Lozenge	Strepsils Plus	Strepsils Extra	Strepsils Variant
TH1017	N	62	64	64	
	Female: Male	26:36	43:21	43:21	
	Mean Age (yrs) ± SD	31.5 ± 11.7	32.4 ± 15.8	30.9 ± 12.8	
	BSL Throat Soreness ± SD	7.1 ± 1.0	7.2 ± 1.1	7.3 ± 1.2	
	Mean AUC 0 – 2 hrs ± SD	-1.09 ± 1.64	-1.80 ± 1.84	-2.38 ± 1.94	
	LS Mean	-1.18	-1.85	-2.39	
	Difference		-0.66	-1.21	
	95% CI		-1.28, -0.05	-1.82, -0.59	
	P value		0.03	0.0001	
TH0705[a]	N	155			155
	Female: Male	105:50			105:50
	Mean Age (yrs) ± SD	35.9 ± 14.2			36.3 ± 14.0
	BSL Throat Soreness ± SD	7.2 ± 1.2			7.1 ± 1.1
	Mean AUC 0 – 2 hrs ± SD	-0.73 ± 1.14			-1.97 ± 1.49
	LS Mean	-0.69[a]			-1.94[b]
	Difference				-1.26[b]
	95% CI				-1.54, -0.97[b]
	P value				<0.0001[b]
TH0817[c]	N	74		74	77
	Female: Male	43:31		45:29	45:32
	Mean Age (yrs) ± SD	32.6 ± 13.2		32.4 ± 14.7	30.3 ± 12.2
	BSL Throat Soreness ± SD	6.81 ± 1.57		6.81 ± 1.24	6.91 ± 1.02
	Mean AUC 0 – 2 hrs ± SD	1.00 ± 1.61		2.07 ± 1.47	1.83 ± 1.50
	LS Mean	-0.98		-2.06	-1.78
	Difference			-1.08	-0.80
	95% CI			-1.56, -0.60	-1.27, -0.33
	P value			<0.0001	0.001

[a] Strepsils Variant – Strepsils Original
[b] Results for 154 patients/group
[c] Strepsils Variant – Strepsils Warm

Although mean AUCs were comparable to those observed in the other Strepsils studies (TH0705 & TH0817) there was a greater placebo response in the present study and greater variability which reduced the active-control difference particularly for Strepsils Plus. Strepsils Plus is most similar to the other Strepsils variants used in the other studies in that it too contains AMC/DCBA as well as lidocaine hydrochloride. On the other hand Strepsils Extra only contains hexylresorcinol. The design of the study and choice of control were based on investigating the effects of the whole Strepsils products not just the active ingredients and hence these factors may have affected the results seen. The lack of flavour, smell and colour coupled with the facts the information provided to patients stated the active products contained anaesthetic ingredients, and maintenance of blinding procedures at sites cannot be verified, is considered to have compromised the blinding of the study. So results should be viewed as those obtained from an open study.

There were a number of secondary endpoints assessed in the study, difficulty in swallowing, throat numbness, swollen throat and sore throat relief. Strepsils Extra and Strepsils Plus both demonstrated effectiveness which started within the first 1 to 10 minutes. In addition both patient and doctor global assessments at 2 hours rated both Strepsils Lozenges significantly higher than placebo.

The additional benefits of both Strepsils Lozenges were apparent in the consumer questionnaire responses which demonstrated significant effects over all patient reported outcomes of reported effectiveness, depth and intensity of numbing and how patients felt overall and with their throat. Both Strepsils produced prominent soothing effects.

The maximum reduction in throat soreness was evident at 15 minutes post dose for both active lozenges and the Kaplan-Meier time to moderate pain relief was estimated as 12.5 minutes for Strepsils Extra and 30 minutes for Strepsils Plus.

There were no significant safety issues highlighted by this study.

13.2 Conclusion

Blinding of the study was compromised and as such, in hindsight, the study cannot be considered double blind. The placebo throat lozenge was designed to control for demulcency so any differences observed would be attributable to the formulations as a whole, not just the active ingredients. As such, the efficacy and safety of both Strepsils Extra and Strepsils Plus was evident in the soothing relief of sore throats due to URTI. Following a single dose relief was evident from 1 minute post dose with maximal effects at 15 minutes post dose. Strepsils Extra was more efficacious and achieved statistical significance over placebo for all the analgesic variables related to throat soreness, sore throat relief and difficulty in swallowing. Both Strepsils Lozenges demonstrated superiority over placebo consistently over the variables measured. Both Strepsils Lozenges were well tolerated.

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Reckitt Benckiser

CHIEF INVESTIGATOR'S SIGNATURE

Study Number: TH1017

Report Title: A multi-centre, randomised, double blind, single dose parallel group, placebo controlled study to investigate the efficacy of Strepsils Plus and Strepsils Extra in the treatment of sore throat due to upper respiratory tract infection.

Phase: IV

Chief Investigator:

By my signature below, I hereby state that I have read this report and confirm that, to the best of my knowledge, it accurately describes the conduct and results of the study. I agree its conclusions and ~~wish~~/do not wish to make an additional statement regarding the safety of the product under test.

[redacted] [redacted]

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