The study listed may include approved and non-approved uses, formulations or treatment regimens. The results reported in any single study may not reflect the overall results obtained on studies of a product. Before prescribing any product mentioned in this Register, healthcare professionals should consult prescribing information for the product approved in their country.

Study No.: TOC100224

Title: A Randomised, Observer-blind, Multi-centre, Non-inferiority, Comparative, Phase III Study of the Safety and Efficacy of Topical 1% SB-275833 Ointment, Applied Twice Daily for 5 Days, versus Topical 2% Sodium Fusidate Ointment Applied Three Times Daily for 7 Days in the Treatment of Adult and Paediatric Subjects with Impetigo

Rationale: Impetigo is a highly contagious common bacterial skin infection that is commonly treated with antibacterial agents. However, the emergence and spread of antibiotic resistance in hospital and community pathogens has significantly eroded the utility of established antibacterial agents, creating a need for new antibiotics with modes of action distinct from those of established agents. SB-275833 Ointment, 1%, is currently being developed as a topical antibiotic for bacterial skin infections including impetigo, secondarily-infected traumatic lesions (SITL) and secondary infected dermatoses (SID). This study supports the use of SB-275833 Ointment, 1%, in adults and children for the treatment of impetigo.

Phase: III

Study Period: 23 April 2005 - 07 September 2005

Study Design: Randomised, observer-blind, multi-centre, non-inferiority, comparative study

Centres: This study was conducted in 42 centres in nine countries.

Indication: Impetigo

Treatment: Subjects received one of two treatment regimens (2:1) randomisation: topical SB-275833 Ointment, 1%, twice daily for 5 days or topical sodium fusidate ointment, 2%, three times daily for 7 days.

Objectives: To compare the efficacy and safety of topical applications of SB-275833 Ointment, 1%, given twice daily for 5 days with topical sodium fusidate ointment, 2%, three times daily for 7 days in the treatment of impetigo in adult and paediatric subjects.

Primary Outcome/Efficacy Variable: The primary efficacy endpoint was the clinical response (clinical success or clinical failure) to study medication at End of Therapy, two days after treatment (Day 7 [Visit 2] for SB-275833 Ointment, 1%, and Day 9 [Visit 3] for sodium fusidate ointment, 2%) in the Per Protocol Clinical (PPC) population.
The hypothesis to be tested by the primary endpoint was that the clinical efficacy of SB-275833 Ointment, 1%, at End of Therapy was non-inferior to that of sodium fusidate ointment, 2%, in the treatment of subjects with impetigo.

Secondary Outcome/Efficacy Variables: The secondary efficacy endpoints were as follows:

- Clinical response at Day 7; Visit 2 (2 days after treatment for SB-275833 Ointment, 1%, and on-therapy for sodium fusidate ointment, 2%).
- Clinical response at Day 9; Visit 3 (4 days after treatment for SB-275833 Ointment, 1%, and 2 days after treatment for sodium fusidate ointment, 2%).
- Clinical response at Follow-Up (Day 14; Visit 4).
- Assessment of lesion(s) area at End of Therapy (Day 7 [Visit 2] for SB-275833 Ointment, 1%, Day 9 [Visit 3] for sodium fusidate ointment, 2%) and Follow-Up (Day 14; Visit 4)
- Microbiological response at End of Therapy (Day 7 [Visit 2] for SB-275833 Ointment, 1%, Day 9 [Visit 3] for sodium fusidate ointment, 2%).
- Microbiological response at Follow-Up (Day 14; Visit 4).
- Number and percent of subjects who had methicillin resistant *Staphylococcus aureus* (MRSA), mupirocin resistant *S. aureus* (mupRSA) or fusidic acid resistant *S. aureus* (fusRSA) isolated at baseline and by clinical response at End of Therapy (Day 7 [Visit 2] for SB-275833 Ointment, 1%, Day 9 [Visit 3] for sodium fusidate ointment, 2%).
- Number and percent of subjects who had various pathogens including MRSA, mupRSA and fusRSA isolated at baseline by clinical response at Follow-Up.

Statistical Methods: This was a non-inferiority trial with 90% power, a non-inferiority margin of 10% and a one-sided type 1 error rate of 2.5%. A 2:1 randomisation scheme of SB-275833 Ointment, 1%: sodium fusidate Ointment, 2%, was employed. A conclusion of non-inferior efficacy of SB-275833 Ointment, 1%, was drawn if the lower limit of the 95% confidence interval for the treatment difference was greater than or equal to –10%.
Four subject populations were defined for the analysis of clinical efficacy and bacteriology data, and one population was defined for the safety analyses, as follows:

- Intent to Treat Clinical (ITTC): All randomised subjects who took at least one dose of study medication.
- Intent to Treat Bacteriology (ITTB): All ITTC subjects who had evidence of a bacterial infection at baseline.

- Per Protocol Clinical (PPC): Subjects from the ITTC population who adhered to the protocol (did not violate the protocol).
- Per Protocol Bacteriology (PPB): Subjects from the ITTB population who adhered to the protocol (did not violate the protocol).
- Safety Population: All subjects who took at least one dose of study medication, (i.e., the ITTC population).

Study Population: Subjects aged ≥9 months with a clinical diagnosis of primary impetigo (bullous or non-bullous), defined as a lesion or a group of lesions characterised by red spots or blisters without crusts, which later progress to lesions that ooze and form yellow or honey-coloured crusts surrounded by an erythematous margin; no more than 10 discrete localised impetigo lesions (lesion(s) with a maximum area of 100cm^2 for either a single lesion or multiple lesions) suitable for topical treatment; and Skin Infection Rating Scale Score (SIRS) of at least 8. Subjects were excluded from the study if they had a previous hypersensitivity to either ointment any component of the ointment, they had an underlying skin disease or skin trauma with clinical evidence of secondary infection, they had signs and symptoms of systemic infection, they had a bacterial skin infection which in the opinion of the investigator could not be appropriately treated by a topical antibiotic or they had received a systemic antibacterial, steroid, or applied any topical therapeutic agent directly to the impetigo lesion(s), less than 24 hours prior to study entry.

Number of Subjects	SB-275833	Sodium fusidate
Planned, N	347	173
Randomised, N	346	173
Randomised and Treated, N	345	172
Completed, n (%)	319 (92%)	157 (91%)
Total Number Subjects Withdrawn, N (%)	26 (8%)	15 (9%)
Withdrawn due to Adverse Events n (%)	1 (<1%)	3 (2%)
Withdrawn due to Lack of Efficacy or Disease Progression n (%)	9 (3%)	7 (4%)
Withdrawn for other reasons n (%)	16 (5%)	5 (3%)
Demographics	SB-275833	Sodium fusidate
N (ITTC Population)	345	172
Females: Males	167:178	72:100
Mean Age, years (SD)	17.8 (19.4)	14.4 (15.7)
Paediatric (<18 years), n (%)	233 (68%)	126 (73%)
Adult, n (%)	112 (32%)	46 (27%)
Race, n (%)		
White – Caucasian/European heritage, n (%)	140 (41%)	65 (38%)
African American/African heritage, n (%)	92 (27%)	48 (28%)
Asian – Central/South Asian heritage, n (%)	85 (25%)	44 (26%)
Other, n (%)	28 (8.1%)	15 (8.7%)
Primary Efficacy Results:	SB-275833	Sodium fusidate
Clinical Response at End of Therapy (PPC Population)	N=317	N=150
Success rate, %	99.1	94.0
Difference in success rate	5.1	
95% confidence intervals	1.1, 9.0	
Secondary Efficacy Results:		
Clinical Response at Follow up (PPC population)	N=308	N=143
Success rate, %	96.4	93.7
Difference in success rate	2.7	
95% confidence intervals	-1.8, 7.2	
Assessment of Lesion Area (PPC population)		
End of therapy, mean % change from baseline	85.3	76.9
Follow up, mean % change from baseline	95.6	77.3
Microbiological Response at End of Therapy (PPB population)	N=242	N=114
Success rate, %	98.3	93.9
Difference in success rate	4.5	
Microbiological Response at Follow up (PPB population)	N=235	N=107
Success rate, %	96.6	93.5
Difference in success rate	3.1	

Clinical Response at End of Therapy by Baseline Pathogen (PPC population)		
All pathogens	N=325	N=155
Success rate, %	98.8	91.6
Difference in success rate	7.2	
MRSA	N=8	N=2
Success rate, %	100.0	100.0
Difference in success rate	0	
mupRSA	N=6	N=3
Success rate, %	100.0	66.7
Difference in success rate	33.3	
fusRSA	N=9	N=7
Success rate, %	100.0	57.1
Difference in success rate	42.9	
Clinical Response at Follow up by Baseline Pathogen (PPC population)		
All pathogens	N=318	N=146
Success rate, %	95.6	90.4
Difference in success rate	5.5	
MRSA	N=8	N=2
Success rate, %	100.0	100.0
Difference in success rate	0.0	
mupRSA	N=6	N=3
Success rate, %	100.0	66.7
Difference in success rate	33.3	
fusRSA	N=6	N=4
Success rate, %	100.0	75.0
Difference in success rate	25.0	

Safety Results: Adverse events (AEs) were collected during the treatment and follow-up period (serious adverse events [SAEs] though were recorded from consent to fulfil international regulatory reporting requirements). All AEs and SAEs occurring during this period were followed until resolution, until the condition stabilised, until the event was otherwise explained, or until the subject was lost to Follow-Up.

Most Common AEs (Greater than or equal to 1%) in Either Treatment Group

Preferred Term	Number (%) of Subjects SB-275833 N=345	 Sodium fusidate N=172
Any Adverse Event	56 (16%)	25 (15%)
Application site irritation	6 (2%)	0
Headache	5 (1%)	0
Excoriation	2 (<1%)	4 (2%)
Diarrhea	2 (<1%)	2 (1%)
Urinary tract infection	0	4 (2%)
Arthropod bite	0	2 (1%)

Serious Adverse Events (SAEs) – On- therapy n(%)[considered by the investigator to be related]	SB-275833 N=345	Sodium fusidate N=172
Abnormal co-ordination	1 (0.3%) [0]	0

Conclusion:

- SB-275833 Ointment, 1%, twice daily for 5 days is non-inferior to sodium fusidate ointment, 2%, three times daily for 7 days in the treatment of subjects with impetigo.
- End of therapy results suggest superior efficacy of SB-275833 Ointment, 1% over sodium fusidate ointment, 2%.
- SB-275833 Ointment, 1%, was effective at eradicating the key pathogens associated with impetigo, including *S. aureus* and *S. pyogenes*.
- SB-275833 Ointment, 1%, was effective at eradicating drug-resistant *S. aureus*.
- The safety profile of SB-275833 Ointment, 1%, was similar to that for sodium fusidate ointment, 2%. The overall rate of AEs and the overall number of subjects with laboratory values of clinical concern were low.

Publications: No Publications

Date updated: 05-Dec-2007