

INITIAL INFORMATION

ORIG → EDG, DSERB

- 7 MAY 2001

Page

Centre Number	Subject Number	Subject Initials

SERIOUS ADVERSE EXPERIENCE (SAE)

Person Reporting SAE (Please print clearly)		
Serious Adverse Experience (Please print clearly)	Eye Problems	→ Specify reason(s) for considering this a serious AE. Mark all that apply.
Onset Date and Time	24 APR 00 11:15 Day Month Yr 24hr:min	(1) <input type="checkbox"/> fatal
End Date and Time (If ongoing please leave blank)		(2) <input type="checkbox"/> life threatening
Outcome If subject died, please complete Form D	<input type="checkbox"/> Resolved <input checked="" type="checkbox"/> Ongoing <input type="checkbox"/> Died	(3) <input type="checkbox"/> disabling/incapacitating
Experience Course	<input type="checkbox"/> Intermittent → No. of episodes <input type="checkbox"/> <input checked="" type="checkbox"/> Constant	(4) <input type="checkbox"/> results in hospitalisation (excluding elective surgery or routine clinical procedures)
Intensity (maximum)	<input checked="" type="checkbox"/> Mild <input type="checkbox"/> Moderate <input type="checkbox"/> Severe	(5) <input type="checkbox"/> hospitalisation prolonged
Action Taken with Respect to Investigational Drug	<input checked="" type="checkbox"/> None <input type="checkbox"/> Dose reduced <input type="checkbox"/> Dose increased <input type="checkbox"/> Drug interrupted/restarted <input type="checkbox"/> Drug stopped	(6) <input type="checkbox"/> congenital abnormality
Relationship to Investigational Drug	<input type="checkbox"/> Not related <input type="checkbox"/> Unlikely <input checked="" type="checkbox"/> Suspected (reasonable possibility) <input type="checkbox"/> Probable	(7) <input type="checkbox"/> cancer
Corrective Therapy If 'Yes', record details in the Concomitant Medication section	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	(8) <input type="checkbox"/> overdose
Was subject withdrawn due to this specific SAE?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	(9) <input checked="" type="checkbox"/> Investigator considers serious or a significant hazard, contraindication, side effect or precaution
		Did the SAE abate? <input type="checkbox"/> Yes <input type="checkbox"/> No
		If study medication was interrupted, stopped or dose reduced: Was study medication reintroduced (or dose increased)? <input type="checkbox"/> Yes <input type="checkbox"/> No
		If yes, did SAE recur? <input type="checkbox"/> Yes <input type="checkbox"/> No
		→ Assessment The SAE is probably associated with: <input type="checkbox"/> Protocol design or procedures (but not to study drug) Please specify _____
		<input type="checkbox"/> Another condition (eg, condition under study, intercurrent illness) Please specify _____
		<input type="checkbox"/> Another drug Please specify _____

PRE-REG CT

NON-ADAP TREAT

WHD
WHD 2/4/01

INITIAL INFORMATION

2800

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Centre Number	Subject Number	Subject Initials					
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SERIOUS ADVERSE EXPERIENCE (SAE) (cont)

Relevant Laboratory Data
Please provide relevant abnormal laboratory data below

Test	Date	Value	Units	Normal Range				
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Remarks (Please provide a brief narrative description of the SAE, attaching extra pages eg, hospital discharge summary if necessary)

- ① Soldier saw an "x" whilst staring at black spot of Amstar Test. Unable to fully assess due to dilated pupils. No macular abnormality
- ② mild epithelial whorl seen on cornea. POSS
- ③ Visual acuity pre deployment 6/6 6/6 unchanged post deployment 6/6 6/6
For follow up ophthalmological assessment.

VISION ABNORMAL

If applicable, was randomisation code broken at investigational site? No Yes

Randomisation / Study Medication No. [REDACTED]

Investigator's Signature: [REDACTED]
(confirming that the above data are accurate and complete)

Date

01	MAY	01
Day	Month	Year

Please PRINT Name [REDACTED]

Please PRINT Name	<table border="1" style="width: 100%; height: 20px;"> <tr><td style="width: 25%;"></td><td style="width: 25%;"></td><td style="width: 25%;"></td><td style="width: 25%;"></td></tr> </table> Day Month Year				

FAX

- 7 MAY 2001

To ADRAC
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Company
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Fax 02 6232 8392
.....
From [REDACTED]
.....
Tel [REDACTED]
.....
E-mail
.....
Date 07-May-2001 Pages including cover 12
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CC
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Subject Clinical Trial Serious Adverse Event (local ID#
.....
2806 to 2810)
.....

SmithKline Beecham (Australia)
Pty Ltd
ABN 73 008 399 415
300 Frankston Road
Private Mail Bag 34
Dandenong Vic 3175
Australia
Tel: 613 9213 4444
Fax 613 9706 5883
www.gsk.com

Dear Sir / Madam

The attached fax contains five cases for reporting to you in this investigator driven study.

Study: 252263/033

Study Title: A randomised, ~~double-blind~~ ^{SECRET} comparative study to evaluate the safety, tolerability and effectiveness of tafenoquine and mefloquine for the prophylaxis of malaria in non-immune Australian soldiers deployed to East Timor.

Study Drug: Tafenoquine, This Study has been unblinded

Relationship to study Drug (causality): Suspected

Please note full documentation of the Safety Report has been sent to the TGA under separate cover. To follow as an attachment is a summary of the Safety Report as background information.

Should you have any enquires regarding this case, please do not hesitate to contact me on [REDACTED] or directly on [REDACTED]

Yours sincerely
[REDACTED]
[REDACTED]

- 7 MAY 2001

CONFIDENTIAL

Letter to the Regulatory Authorities

TO WHOM IT MAY CONCERN

Dear Sirs

Summary

The purpose of this Safety Report is to inform Regulatory Agencies, Ethics Committees and Investigators of preliminary safety findings related to the monitoring for the effects of phospholipidosis in a Phase III Tafenoquine clinical study.

These data are from a subset of subjects (n = 33/99) in a Phase III study (Study 252263/033) investigating the safety, tolerability and effectiveness of tafenoquine in the prophylaxis of malaria in non-immune Australian soldiers deployed to East Timor.

Ophthalmological (corneal examination, visual acuity, visual field) and lung function testing (diffusing capacity of carbon monoxide – D_LCO) data are presented on the first 33 soldiers within this subset, 26 of whom were receiving tafenoquine and 7 of whom were receiving mefloquine. After 6 months weekly dosing corneal changes (a vortex keratopathy) have been seen in 25 of 26 tafenoquine subjects, but in none of the 7 mefloquine subjects. Amsler Grid examinations suggest mild visual field changes in 4 tafenoquine subjects, but not mefloquine subjects. Minor visual acuity changes are reported across both treatment groups. All examinations were normal at baseline.

The changes considered to be clinically significant are the 4 tafenoquine subjects with Amsler Grid changes (subjects 17, 18, 22, 24 in Appendix B), and single tafenoquine subject (subject 14) with more central corneal changes in a Lasik-corrected eye and a reduction in visual acuity. These have been reported as SAEs by the Investigator.

Similar corneal changes (vortex keratopathy) have been observed with other cationic amphiphilic agents. However given the requirement to establish the reversibility of these changes off study drug, and more fully understand the associated visual field and visual acuity changes, GlaxoSmithKline have voluntarily suspended all tafenoquine dosing across both the adult and paediatric programmes.