INITIAL INFORMATION ORIG → EDG, BSER #0810

- 7 MAY 2001 163375

Centre Number	Subject Number	Subject Initials	Page
	[redacted]	[redacted]	

SERIOUS ADVERSE EXPERIENCE (SAE)

Person Reporting SAE (Please print clearly) [redacted]

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 (Day Month Yr) N/A (24hr:min)	[1] ☐ fatal [2] ☐ life threatening [3] ☐ disabling/incapacitating [4] ☐ results in hospitalisation (excluding elective surgery or routine clinical procedures) [5] ☐ hospitalisation prolonged [6] ☐ congenital abnormality [7] ☐ cancer [8] ☐ overdose [9] ☒ Investigator considers serious or a significant hazard, contraindication, side effect or precaution
End Date and Time (If ongoing please leave blank)	Day Month Yr 24hr:min	
Outcome If subject died, please complete Form D ←	☐ Resolved ☒ Ongoing ☐ Died	
Experience Course	☐ Intermittent → No. of episodes ☐ ☒ Constant	
Intensity (maximum)	☒ Mild ☐ Moderate ☐ Severe	
Action Taken with Respect to Investigational Drug POSS	☒ None ☐ Dose reduced ☐ Dose increased ☐ Drug interrupted/restarted ☐ Drug stopped	Did the SAE abate? ☐ Yes ☐ No **If study medication was interrupted, stopped or dose reduced:** Was study medication reintroduced (or dose increased)? ☐ Yes ☐ No If yes, did SAE recur? ☐ Yes ☐ No
Relationship to Investigational Drug	☐ Not related ☐ Unlikely ☒ Suspected (reasonable possibility) ☐ Probable	→ **Assessment** The SAE is probably associated with: ☐ Protocol design or procedures (but not to study drug) *Please specify* ______ ☐ Another condition (eg, condition under study, intercurrent illness) *Please specify* ______ ☐ Another drug *Please specify* ______
Corrective Therapy *If 'Yes', record details in the Concomitant Medication section* ←	☐ Yes ☒ No	
Was subject withdrawn due to this specific SAE ?	☐ Yes ☒ No	

PRE-REG CT

NON - ABRAC TRIAL

Noted 24/4/01

INITIAL INFORMATION

#2810

Page

Centre Number	Subject Number	Subject Initials
	[redacted]	[redacted]

[redacted] 15/0.

SERIOUS ADVERSE EXPERIENCE (SAE) (cont)

Relevant Laboratory Data
Please provide relevant abnormal laboratory data below

Test	Date	Value	Units	Normal Range
	Day Month Yr			
	Day Month Yr		- 7 MAY 2001	
	Day Month Yr			
	Day Month Yr			

Remarks *(Please provide a brief narrative description of the SAE, attaching extra pages eg. hospital discharge summary if necessary)*

DESC

① Soldier saw "black spot mid left bottom" on Amsler Test but unable to fully assess due to dilated pupils.

② Possible slight deposit right and left at macular. ② DSZ

③ Whorls on both corneas

④ Visual acuity was unchanged pre/post deployment 6/6 6/6

VISION ABNORMAL

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

Randomisation / Study Medication Number: 1 4 1 0 3

Investigator's Signature: Leon Benrose

(confirming that the above data are accurate and complete)

Date: 0 1 | MAY | 0 1 (Day Month Year)

Please PRINT Name [redacted]

[redacted] Day Month Year

FAX

- 7 MAY 2001

GlaxoSmithKline

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

To ADRAC

Company

Fax 02 6232 8392

From [redacted]

Tel [redacted]

E-mail

Date 07-May-2001 **Pages including cover** 12

CC

Subject **Clinical Trial Serious Adverse Event (local ID# 2806 to 2810)**

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, 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]

- 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 Invstigators 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.