

**APPENDIX I: POSTMARKETING SURVEY**

## Postmarketing observational survey

### System organ classes for which all and possibly related TEAEs were most commonly reported in Study 5001

MedDRA System organ class	Telithromycin N=34929 (%)
<b>All TEAEs <sup>a</sup></b>	
Subjects with TEAEs	728 (2.1%)
Gastrointestinal disorders	441 (1.3)
Nervous system disorders	118 (0.34)
Infections and infestations	75(0.2)
Eye disorders	66 (0.2)
Skin and subcutaneous tissue disorders	53 (0.15)

a- based on the 5 most frequently affected SOC's in all patients

### System organ classes for which all serious TEAEs were most commonly reported in Study 5001

MedDRA system organ class	Telithromycin N=34929 (%)
<b>Subjects with serious TEAEs <sup>a</sup></b>	<b>32 (0.09)</b>
Gastrointestinal disorders	17 (0.05)
Eye disorders	13 (0.04)
Infections and infestations	13 (0.04)
Nervous system disorders	12 (0.03)
Respiratory, thoracic and mediastinal disorders	10 (0.03)

a- based on the 5 most frequently affected SOC's in all patients

**Hepatic Events.**

There were a total of 23 subjects with hepatic adverse events in Study 5001. None of these cases were considered serious by the investigator.

**All hepatic adverse events in Study 5001  
Number (% of subjects)**

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Preferred Term	TEL(n=34929)
<b>Subjects with hepatic TEAEs</b>	<b>23 (0.07)</b>
ALT increased	17
AST increased	10
Transaminases increased	3
Liver function test abnormal	1
GGT increased	1

**Visual Adverse Events**

There were a total of 64 subjects with 82 visual adverse events. A total of 15 subjects had serious visual events. The adverse events by preferred term are outline by total events in Table 19.

**All Visual adverse events in Study 5001  
Number (%) of subjects**

Preferred Term	TEL(n=34929)
<b>Subjects with visual TEAEs</b>	<b>64 (0.18%)</b>
Vision blurred	34 (0.1)
Visual disturbance NOS	28 (0.08)

Preferred Term	TEL(n=34929)
Photopsia	6 (0.02)
Visual acuity reduced	1 (0.0)
Accommodation disorder	5 (0.01)
Diplopia	4(0.01)
Hallucination NOS	2 (0.0)
Visual brightness	1 (0.0)

The table below provides an outline of the 15 subjects who experienced serious visual events..

Event ID	Positive Dechallenge	Outcome	SA Comment
200215125DE	Yes	Recovered	Sudden onset of blurred vision affecting near sight about 3 hours after intake of TEL. Patient was completely unable to work. Treatment with TEL was discontinued immediately.
200210735DE	Yes	Recovered	Patient with history of cataract and blurred vision for weeks developed visual disturbance of double images that created moderate impairment in patient's activity.
200121340DE	Yes	Recovered	Immediately after each intake of TEL, patient developed blurred vision (near-sight

			only) and flickering before her eyes that persisted for 3 or 4 hours.
200121953DE	Yes	Recovered	About 25 minutes after intake of TEL patient developed blurred vision, bilateral strabismus and difficulty focusing affecting patients far-sight. Events impaired patient's daily activities lasting for 3 to 4 hours.
200210062DE	Yes	Sequelae	On the first day of treatment with TEL, this far-sighted patient developed blurred vision affecting his near-sight; he could not read.
200210522DE	Unknown	Recovered	On the third day of treatment, about 1 hour after each intake of TEL, patient experienced blurred vision affecting both near and far sight lasting about 4 or 5 hours; she could not drive.
200211294DE	Yes	Recovered	Patient experienced blurred vision about 30 minutes after each intake of TEL that lasted 2 hours each

			episode. Event affected her daily activities including driving.
200211925DE	Yes	Recovered	After first dose of TEL patient developed vertigo with nausea that resolved several hours after discontinuation of TEL. Events severely impaired patient's activities.
200212357DE	Yes	Recovered	About 30 minutes after intake of TEL, patient developed severe cephalgia and visual disorder affecting near and far sight that lasted for 1-2 hours and impaired patient's activities including driving.
200311125DE	Unknown	Recovered	Patient developed blurred vision after 1 <sup>st</sup> intake of Ketek. Patient's vision normalized after 8 hours
200121092DE	Yes	Recovered	Visual disturbance persisted for 2.5 hours. Ketek discontinued.
200121593DE	Yes	Recovered	After the first intake of Ketek the patient's underlying myasthenia gravis/muscular weakness aggravated. The patient was hospitalized.

			Treatment with Ketek was discontinued and the symptoms resolved.
200121384DE	Yes	Recovered	The patient developed hallucinations and nightmares. Symptoms increased on day 3 so that the patient was hospitalized. The event was ongoing. Treatment with Ketek was discontinued.
200121952DE	Yes	Recovered	The patient suffered from hallucinations at night (ships). Ketek was withdrawn and he was medicamentously treated and recovered then
200214068DE	Yes	Recovered	29 year old male who developed blurred vision after 1 <sup>st</sup> dose, which lasted 3 hours. Subject recovered without requiring treatment.

TEL = telithromycin

### ***Syncopal events***

There was 1 syncopal event in Study 5001. It was coded as depressed level of consciousness and was not serious and considered unrelated to telithromycin.

### ***Myasthenia gravis***

There was one reported case of myasthenia gravis, which was considered serious and related by the investigator.

This case involved a 40 year-old female with a history of hypertension, cardiac dysrhythmia and myasthenia gravis pseudoparalytica who developed a myasthenic crisis after first dose of telithromycin. Concomitant medications included pyridostigmine and bisoprolol. Symptoms included dyspnea, dizziness and visual disorder requiring hospitalization. Ketek was discontinued and she was treated with prednisone and theophylline since symptoms were also consistent with allergic reaction. Her symptoms improved and was discharged the following day.