FOI 057-1112 DOCUMENT 2.

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Attention: Ms Jovi Bacud-van der Kallen,
Clinical Evaluation Unit 1

* Copy to ADRAC for Australian ADRAC
* Copy to ADEC for information.
DC 27/2/06

13 February 2006

Dear Ms Bacud-van der Kallen,

Re: Clozaril (clozapine) – revision to haematological monitoring schedule
Clin File No.: 2004/051517

We refer to your letter dated 16 January 2006 regarding changes to the frequency of blood monitoring in the US prescribing information (US PI) for Clozaril (clozapine).

1. The reasons for the major changes to the US monitoring schedule

In summary, the US PI was amended to reduce blood monitoring frequency. Prior to 1997, the US PI recommended weekly monitoring of white blood cells (WBC) and absolute neutrophil counts (ANC) throughout continuous treatment. In 1997 the FDA Psychopharmacological Advisory Committee (PDAC) recommended that the monitoring schedule after 6 months be reduced to every 2 weeks. In 2003 there was yet another PDAC meeting, to discuss whether monitoring frequency should be further reduced. Data from 3 registries (US, UK & Ireland, and Australia) were submitted to the PDAC in 2003. Based on this data, the PDAC recommended that the monitoring schedule should be reduced to at least every 4 weeks, but did not specify a particular point in time when this should happen.

It wasn't until January 2005, that the FDA formally requested the label changes based on the recommendation of the PDAC and these changes were made by Novartis US in a labelling revision dated 12 May 2005.

2. Whether Novartis Australia intends to include similar changes to the Australian PI for Clozaril. Please provide justification if you do not intend to amend the Australian monitoring schedule.

The approved US PI now stipulates WBC and ANC monitoring weekly for the first 6 months of continuous treatment, followed by 6 months of counts every 2 weeks, followed by at least monthly monitoring thereafter throughout treatment (providing WBC counts remain acceptable, WBC ≥3000/mm^3, ANC ≥2000/mm^3).

call.

In Australia, the approved PI stipulates WBC and ANC monitoring weekly for the first 18 weeks of continuous treatment, followed by at least monthly monitoring thereafter throughout treatment (providing WBC counts remain acceptable, WBC ≥3000/mm^3, ANC ≥2000/mm^3).

In summary, the US PI has always differed from the Australian PI in terms of blood monitoring frequency. [redacted]

Please do not hesitate to contact me if you require any further information.

Yours sincerely
Novartis Pharmaceuticals Australia Pty Limited

Monique Baldwin
Ref: MB06/018