



Australian Government

Department of Health



Deputy Secretary

Colleen Bebbington
Coroner's Registrar
Coroners Court of Victoria
65 Kavanagh Street
SOUTHBANK VIC 3006

Dear Ms Bebbington

Re: Investigation into the death of Kathy Jelbart (COR REF - 2016 006193)

I am writing to provide an update regarding our response to Coroner Mr John Olle's recommendation:

1. that TPMT genotyping for the common alleles should be mandatory for patients prior to the commencement of thiopurine containing medications.

As forecast in my letter dated 30 January 2018 the TGA has since reviewed the use of TPMT testing in association with the use of thiopurine medicines.

The TGA review found that all thiopurines are associated with a risk of potentially fatal myelosuppression, and that this risk is increased in individuals with a low-functioning variant of the TPMT gene. However, there is no clear evidence that TPMT testing improves patient outcomes, as TPMT activity does not predict toxicity in all patients (most episodes of thiopurine myelotoxicity occur in patients with a normal-functioning TPMT gene), therefore ongoing white blood cell monitoring is still required. There are currently no regulatory controls on the availability of thiopurines (all are reimbursed through the PBS as general benefits) which would allow for the enforcement of mandatory TPMT testing. It was therefore concluded that the introduction of a new regulatory mechanism would require more robust evidence for the benefits of TPMT testing.

Advice was sought from the TGA's expert advisory committee, the Advisory Committee on Medicines (ACM). The ACM agreed with the findings of the TGA review, and further advised that the Product Information (PI) documents for thiopurines should be updated to include:

- TPMT testing should be strongly recommended but not mandatory
- haematological monitoring of patients on thiopurines is the critical issue, particularly early in the treatment period and in elderly patients
- early recognition and empiric treatment of suspected infections or sepsis in patients receiving thiopurines is essential
- recognition that TPMT testing is widely available via pathology laboratories and genetic testing services.

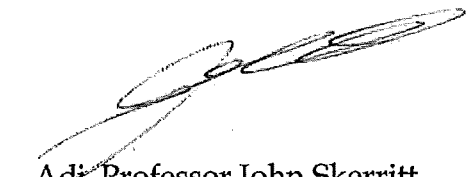
The committee further advised that a boxed warning in the PI was not warranted for this issue.

The sponsor of all three innovator thiopurine medicines available in Australia has now updated the PI documents to include above information. Sponsors of generic thiopurine medicines are now also required to update their PI to ensure they reflect these updates.

The TGA is writing to relevant medical specialty groups to alert them to the above information, including the importance of education for patients taking thiopurine medications.

Thank you for notifying the TGA of the Coroner's recommendation.

Yours sincerely



Adj. Professor John Skerritt
Health Products Regulation Group

17 September 2019