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Medicines & Healthcare products Regulatory Agency

MHRA
Regulating Medicines and Medical Devices

Mr Zafar Siddique
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Your reference: RJB

9th July 2015

Dear Mr Saddique

Regulation 28 Report Coroners and Justice Act 2009 – Bridget May Cahill.

Thank you for following up on our response to the correspondence from your predecessor Dr Balmain concerning the death of Bridget May Cahill (letter dated 22nd July 2014 and the subsequent post-mortem report dated 26th August 2014). He raised the concern that a person who is prescribed morphine and has less than the amount prescribed for them, can nevertheless suffer an overdose. He asked whether:

- attention needs to be given to the maximum dose that can be recommended and
- whether it is, or should be, subject to factors such as body weight, any co-morbidities and any other factors and
- whether attention should be directed towards the possibility of buildup of morphine in the body for those involved in long-term therapy.

He also considered that MHRA was in a position to take action to prevent other deaths in similar circumstances.

We have carefully reviewed the findings of the post mortem report, considered the pharmacokinetics and pharmacodynamics of morphine in the light of current prescribing advice in the Summary of Product Characteristics (SmPC) for morphine and a detailed discussion is attached as Annex 1. The summary of our view is as follows:

1. Does attention need to be given to the maximum dose that can be recommended?

This case does not prompt a review of the maximum permitted dose given the interindividual range of dose needed to achieve analgesia and the tolerance that is expected to develop as a result of chronic morphine administration.

2. Should the maximum dose be subject to factors such as body weight and any co morbidities?

In our view no, for the same reasons explained above. The prescribing information already advises on circumstances in which dosage may need to be reduced i.e. in the elderly, patients with moderate-severe renal or hepatic impairment, or where sedation is undesirable.

3. Should attention be directed towards the possible build-up of morphine in the body for those involved in long-term therapy?

   Although build up could be expected in the elderly as a result of reduced renal function, the evidence in this case does not support an excessive accumulation of the metabolites, as would have been expected (since the metabolites depend primarily on renal function for their elimination, while this is not the case for morphine, which is mainly metabolised).

   The elderly are known to be particularly sensitive to the effects of many CNS-acting agents and perhaps this is the more important contributing factor in this case. The case highlights the importance of careful titration and review of opioid dosing at regular intervals, as recommended in current treatment guidelines.

Finally, I sincerely apologise for the oversight which resulted in us not issuing out response within the required timeframe. Should you have any further queries about our analysis please contact me again.

Yours sincerely

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Chief Executive, MHRA

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