BMJ Group

16 September 2024

Caroline Topping
HM Coroner's Court
Station Approach
Woking
Surrey GU22 7AP

Dear Ms Topping

Re: Regulation 28 Report - Action to Prevent Future Deaths - Jessica Maizy Anne De Souza

As CEO of BMJ Publishing Group Limited (**BMJ Group**), I write to respond to the above report sent by email to me on 26 July 2024. We were very sorry to learn about the death of Miss de Souza and the circumstances surrounding her illness and would like to express our deepest sympathies to her family.

We have considered the matters of concern listed in the report and set out BMJ Group's response below.

First of all, we would like to make clear that BMJ Best Practice is an online clinical decision support tool (https://bestpractice.bmj.com/) to be used as a source of reference material by medical professionals. The clinical content on BMJ Best Practice is live and can be updated at any time in response to changes in the evidence landscape - and in line with our processes. We have reviewed the content that is (according to our internal records) likely to have been online at the time of Miss de Souza's hospital admission in Summer 2022.

The first matter of concern that references BMJ Group (ii) states:
The clinicians relied on the BNF and BMJ Best Practice Bipolar Disorder in Adults and the BNF to support their decision to prescribe aripiprazole as prophylaxis for both polarities as a monotherapy

The second matter of concern that references BMJ Group (iv) states:
The BMJ refers to aripiprazole being used as a monotherapy to treat bipolar disorder, though does advise that it is more effective in preventing mania than depression.

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The BMJ Best Practice 'Bipolar Disorder in Adults' topic, at the time (and still does) discusses the complex nature of bipolar disorder and the many factors to consider and monitor during treatment. It outlines the different phases in terms of acute mania, acute depression and patients with mixed features, as well as maintenance treatment, and the differing treatment options and considerations during each phase. It is the duty of the treating doctor to take all of this into account when deciding on treatments.

We note that aripiprazole was used during the admission for an acute episode of mania, and continued following stabilisation and discharge. In the 'Bipolar Disorder in Adults' topic management approach section narrative, options are discussed for maintenance treatment. General comments in the content at the time said that "*Monitoring and enhancing adherence is a routine part of long-term bipolar disease management*" and that "*Effective therapies that maximise adherence share common characteristics: education, self-monitoring, recurrence prevention, managing adverse effects, identifying and managing stressors, and addressing belief systems and attitudes to illness*".

More specific information, under the heading 'Bipolar I' stated that "*Lithium has the strongest evidence for prevention of recurrence in bipolar disorder compared with other agents, and remains the treatment of choice for long-term maintenance therapy. It is effective against relapse of both manic and depressive symptoms and appears to have an antisuicidal effect. Other first-line options include quetiapine (as an adjunct to lithium or divalproex sodium, or as monotherapy), divalproex sodium, lamotrigine, asenapine, and aripiprazole (as an adjunct to lithium or divalproex sodium, or as monotherapy as an oral or monthly injectable preparation). Quetiapine is effective in preventing manic, depressive, and mixed episodes and so may be particularly useful as maintenance treatment for patients with mixed features. Monotherapy with asenapine or aripiprazole is more effective in preventing mania than depression. Lamotrigine is more effective in preventing depression than mania, but is also indicated for prevention of recurrence for any mood disorder*."

Aripiprazole is discussed as one of the treatment options, and as noted in the Regulation 28 notice, the BMJ Best Practice topic stated that monotherapy with aripiprazole is more effective in preventing mania than depression. Lithium is stated in the topic to be first line, and quetiapine is also highlighted as a useful option for patients with mixed features. Given that the content points to other agents possibly being preferable, the prescribing clinicians would have made the selection for aripiprazole knowing full details of the clinical context which might have included any previous medications used for treatment, potential adverse effects, or other medical conditions. The BMJ Best Practice website states that:

"As a medical professional you retain full responsibility for the care and treatment of your patients and you should use your own clinical judgement and expertise when using this product.

This content is not intended to cover all possible diagnosis methods, treatments, follow up, drugs and any contraindications or side effects. In addition, since such standards and practices in medicine change as new data become available, you should consult a variety

of sources. We strongly recommend that you independently verify specified diagnosis, treatments and follow-up and ensure it is appropriate for your patient within your region. In addition, with respect to prescription medication, you are advised to check the product information sheet accompanying each drug to verify conditions of use and identify any changes in dosage schedule or contraindications, particularly if the drug to be administered is new, infrequently used, or has a narrow therapeutic range. You must always check that drugs referenced are licensed for the specified use and at the specified doses in your region"

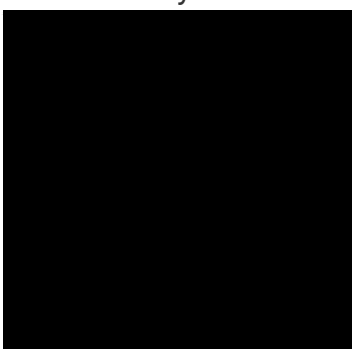
The content in BMJ Best Practice discussed the multiple factors to consider in the context of the treatment options available to the clinicians: aripiprazole is stated to be an option, and the decision that this was the best option for an individual patient remains that of the prescribing clinician.

The BMJ Best Practice topic discusses that treatment should be reviewed regularly and it may have been that on clinical review after a period of time, the treatment would have been adjusted or changed which might have been clinically appropriate. However the report describes how the planned follow-up did not take place.

In updates since 2022, the topic discusses in more detail the differences between guidelines, and incorporates the NICE guideline in greater detail but there has been no substantive change to the content that is relevant to the report. In keeping with our processes, we will continue to review and update this topic with subject matter experts and will incorporate new evidence into the content as appropriate.

We hope this response adequately addresses the matters of concern that reference BMJ Best Practice but please let me know if you require any further information.

Yours sincerely



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CEO