Medicines & Healthcare products
Regulatory Agency

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Ms K Skerrett
His Majesty's Senior Coroner for Gloucestershire
Gloucestershire Coroners Court
By Email: [redacted]

Reference: [redacted]

12 February 2025

Dear Ms Skerrett,

Regulation 28 Report into the death of Thomas Henry Robin Kingston

Thank you for your Regulation 28 Report relating to the death of Thomas Henry Robin Kingston. I would like to offer my sincere condolences to Mr Kingston's family on their tragic loss.

In the Matters of Concern section of the report relating to Mr Kingston you ask the Medicines and Healthcare products Regulatory Agency (MHRA) whether there is adequate communication about the risks of suicide associated with the Selective Serotonin Reuptake inhibitor (SSRI) medicines and whether the current guidance to persist with SSRI medicine or switch to an alternative SSRI is appropriate when no benefit has been achieved and/ or especially when any adverse side effects are being experienced.

May I start by outlining the current information with SSRI antidepressant medicines regarding the risk of suicidal behaviour. The product information for all SSRI medicines contains warnings about the risk of suicidal behaviour. These warnings were introduced following UK and European reviews of the evidence of such a risk which were started in 2003 and concluded that the risk of suicidal acts and behaviour is increased with the use of sertraline, citalopram, escitalopram, paroxetine, venlafaxine, and mirtazapine in young patients (under 25 years of age).

The product information for all SSRIs warns that the risk of suicidal behaviour is considered to be greatest in the early stages of antidepressant treatment. This is likely to be related to antidepressants being effective only after a few weeks of taking the medicine and depression itself being associated with an increased risk of suicidal behaviour.

There are no marked differences in suicidal risk between the different antidepressants within the SSRI class of medicines. The product information for all SSRIs recommends that close supervision of patients and particularly those at high risk should accompany drug therapy especially in early treatment and following dose changes. Patients (and caregivers of patients) should be alerted about the need to monitor for any clinical worsening, suicidal behaviour or thoughts and unusual changes in behaviour and to seek medical advice immediately if these symptoms present.

The current warnings in the SSRI medicines' Patient Information Leaflets (PILs), including citalopram and sertraline, were subject to user testing and section two contains a bold headline on "**Thoughts of suicide and worsening of your depression or anxiety disorder**". Use of emboldened text and bullet points are used throughout the PIL to highlight key safety information and action for people who experience thoughts of self-harm. There is also advice in the PIL to inform family and friends about a diagnosis of depression or anxiety as it is recognised people with depression may not have insight into their own behaviour and in some patients leaflets this is emboldened.

To supplement this information, the MHRA has informed healthcare professionals in the UK about the risk of suicidal behaviour associated with antidepressants via articles in the MHRA's bulletin Drug Safety Update in April 2008[1] and published guidance for prescribers on the MHRA website in December 2014 to summarise key safety messages[2].

The British National Formulary (BNF) states, "the use of antidepressants has been linked with suicidal thoughts and behaviour; children, young adults, and patients with a history of suicidal behaviour are particularly at risk. Where necessary patients should be monitored for suicidal behaviour, self-harm, or hostility, particularly at the beginning of treatment or if the dose is changed." The information in the product information and the BNF should form the basis of a discussion between the doctor and patient when deciding on the most appropriate medicine for them.

Despite all the currently available information about the risk and benefits of SSRI antidepressants designed to supplement and support the clinical conversation and monitoring of patients by the healthcare professionals prescribing antidepressants, the MHRA is aware that some patients and families have ongoing concerns about the effectiveness of the current warnings in the patient information leaflets.

In 2022, the MHRA sought the advice of the Commission on Human Medicines (CHM) on the need to convene an Expert Working Group (EWG) to review how the risk of suicidal behaviours is communicated in the patient leaflets to establish if this can be improved or if it would be more helpful for patients to receive this information in different formats within the regulatory framework. The first meeting of the EWG was held on 4 July 2024. Round table meetings involving patient charities and families of those bereaved by suicide will be held in March 2025. The membership and remit of the EWG can be found here Commission on Human Medicines - GOV.UK.

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[1] https://www.gov.uk/drug-safety-update/antidepressants-suicidal-thoughts-and-behaviour

[2] https://www.gov.uk/government/publications/ssris-and-snris-use-and-safety/selective-serotonin-reuptake-inhibitors-ssris-and-serotonin-and-noradrenaline-reuptake-inhibitors-snris-use-and-safety

The considerations of the EWG are anticipated to complete in 2025. We will communicate to healthcare professionals, patient groups and relevant voluntary organisations any updates on how the risk of suicidal behaviours associated with antidepressants is presented in the antidepressant PILs following the conclusions of the EWG and subsequent CHM advice.

Secondly in your letter you also ask about the guidance around the use of SSRIs, particularly if no benefit has been seen or adverse reactions have been reported. Clinical guidance issued by the National Institute for Health and Care Excellence (NICE) (Clinical Guideline NG222) on depression in adults recommends that if a person with depression is started on antidepressants and is considered to be an increased suicide risk or is between 18 and 25 years (because of the potential increased prevalence of suicidal thoughts in the early stages of antidepressant treatment for this group) they should be reviewed after one week of starting antidepressants or after increasing the dose and again after this as often as needed, but no later than four weeks after the appointment at which the antidepressant was started.

Clinical Guideline 90 advises prescribers to follow a stepped-care model in which to organise the provision of services and supports patients, carers and practitioners in identifying and accessing the most effective interventions; the least intrusive and most effective intervention is provided first. More details of this stepped-care model can be found at https://www.nice.org.uk/guidance/cg90/resources/depression-in-adults-recognition-and-management-pdf-975742636741

NICE guidelines advise healthcare professionals that if a person's depression has had no or a limited response to treatment with antidepressant medication alone, and no obvious cause can be found and resolved, to discuss further treatment options with the person and make a shared decision on how to proceed based on their clinical need and preferences.

Finally I should add that your report of Mr Kingston's adverse reaction to SSRI medicines has been added to the Yellow Card database (reference number ADR 34440796), which is the UK's system for collecting and monitoring information on suspected Adverse Drug Reactions.

Should you have any further questions, please do not hesitate to contact my office:
[redacted]

Yours sincerely

[redacted]

[redacted]
Chief Executive
Medicines and Healthcare products Regulatory Agency
E: [redacted]