Leyden Delta
Unit 5 | Chase Industrial Estate | Alton Road
Ross-on-Wye | HR9-5WA | United Kingdom

Att Chistopher Morris, Area Coroner
Coroner's Court
1 Mount Tabor Street
Stockport SK1 3AG

Tuesday, September 10, 2024

RE: Leyden Delta's response to your request related to the Regulation 28 Report into the death of Sasha Drysdale

Dear Sir,

We are writing to you in response to your letter dated 18 July 2024, pertaining to your Regulation 28 Report in relation to the death of Ms Sasha Drysdale. In that letter you raised concerns about the safety of clozapine and a potential link between clozapine and Acute Myeloid Leukaemia (**AML**). You suggested that further research is needed and requested that Leyden Delta provide you with an action plan which will address actions to prevent future deaths. Whilst we understand that Zaponex® manufactured by Leyden Delta was not prescribed to Ms Drysdale, we respond below accordingly.

As you are aware, medicines are licensed by the regulatory authority, the Medicines and Healthcare products Regulatory Agency (**MHRA**) in the UK. The decision to grant a licence is based on evidence from safety and efficacy studies and the therapeutic need, in terms of clinical efficacy of the product and/or lack of alternative treatment options. In cases where the benefits of a medicine are deemed to outweigh the risks for individual patients and/or for the public health (a positive outcome of the risk/ benefit assessment) a licence is granted.

The initial and continued licensing of clozapine reflects the MHRA's informed view of the medication's safety and efficacy in this context. Details of the evidenced risks and benefits of Zaponex® (clozapine) are provided in its product information.
Once a product is allowed to the market, pharmaceutical legislation also requires companies to continuously monitor the safety profile of their products and to inform the Regulatory Authority and to take action when changes to the benefit/risk profile become apparent.

Once a medicine is allowed to be placed on the market, the MHRA is principally responsible for continuously monitoring the safety profile of the medicine. This is known as pharmacovigilance. Patients, health professionals and pharmaceutical companies all contribute to pharmacovigilance activities. The MHRA will take action when changes to the benefit/risk profile become apparent based on its monitoring of multiple information sources, including spontaneous adverse drug reaction reporting schemes, clinical and epidemiological studies and reviews of worldwide published medical literature.

Leyden Delta, as the marketing authorisation holder for Zaponex, has a pharmacovigilance and risk management system in place with processes for the continuous collection and evaluation of safety information. Leyden Delta takes proactive steps in conjunction with the regulatory authority when changes to the benefit/risk profile emerge.

In respect of the concern raised, concerning a potential for clozapine to cause AML, it is the considered position of Leyden Delta that there is no causal link between clozapine and AML. Neither we, nor the MRHA have identified such a link through pharmacovigilance. Upon receipt of your letter, Leyden Delta has additionally sought the expert opinion of their Consultant Haematologist,

Professor Dr T.J.M. de Witte of Radboud Medical University, Nijmegen. Prof. de Witte has advised that based on his assessment of the clinical information of case reports from Leyden Delta's safety database and a review of scientific literature, he could not see convincing evidence for a causal relation between clozapine and AML.

Leyden Delta will continue to comply with its pharmacovigilance obligations and operating procedures for monitoring the safety profile of Zaponex. In particular we encourage, and will carefully review, any further research into clozapine (and indeed, AML) and we will not hesitate to take appropriate action should changes to the medicine's safety profile emerge.

We trust that this response is of assistance, and we would be happy to respond to any questions you may have.

Yours faithfully,

[redacted]

Medical Director