Irish Pain Society Statement on the EMA's Review of Metamizole-Containing Products (Article 107i of Directive 2001/83/EC)

The European Medicines Agency (EMA) has initiated a review of metamizole-containing medications due to concerns that existing measures to mitigate the known risk of agranulocytosis may be inadequate.

Metamizole, also known as dipyrone, is a non-opioid analgesic and antipyretic widely used in Germany, Spain, and South America for managing post-operative pain, cancer pain, migraine, and fever[1,2,3,4]. Introduced commercially in 1922[2], metamizole has never been licensed in Ireland, and it remains unclear if any manufacturer has sought marketing authorisation in Ireland.

Safety concerns, particularly the risk of agranulocytosis, have led to the withdrawal of metamizole from markets in the United States and several European countries. Although rare, the risk of agranulocytosis was considered by these jurisdictions to be too high relative to the availability of alternative analgesics with comparable efficacy but better safety profiles[4].

Epidemiological data suggest that populations in the United Kingdom, Ireland, and Scandinavian countries may be more susceptible to this adverse effect of agranulocytosis[5]. Consequently, it is recommended that metamizole use in these populations be closely monitored, including regular blood counts to detect early signs of agranulocytosis. The epidemiological data, however, are based on small sample sizes, and the cause of increased toxicity remains uncertain, necessitating further research.

In countries where metamizole is approved, guidelines typically emphasise caution due to the associated risk of agranulocytosis. For instance, in the Netherlands, a controlled access program is in place to mitigate these risks[6], requiring the marketing authorisation holder to provide educational materials to both patients and healthcare providers about the potential for agranulocytosis and the importance of monitoring.

The use of metamizole as an analgesic and antipyretic is marked by significant geographic variation. Despite its clinical efficacy being comparable to other

analgesics, the associated risks warrant caution. While no specific regional increase in risk has been identified, it is advisable to emphasise potential risks, particularly for populations from Ireland, the UK, and Scandinavian countries. This should be reflected in the product literature, though current data may not be sufficient to fully support this.

The Irish Pain Society recommends caution in prescribing metamizole and urges healthcare professionals to be aware of the risks of agranulocytosis, which may be higher in certain populations. Ongoing epidemiological research is essential to better understand the risk factors for agranulocytosis, including genetic predispositions, dosage, duration, and route of administration, to optimise the safe use of metamizole in clinical practice.

References

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