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TO
EMA

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Statement from the Board of the German Pain Society on EMA's review of metamizole-containing products according to Article 107i of Directive 2001/83/EC

In Germany, metamizole plays a crucial role in both acute and chronic pain management. It is one of the most commonly used non-opioid analgesics. In a survey of more than 2000 anesthesiologists and pain specialists, 93.8% reported using metamizole, 54.0% used NSAIDs, 41.8% used COX-2 inhibitors, and 49.2% acetaminophen (Reist et al). For chronic pain, 76.7% of respondents prescribed metamizole in combination with other non-opioids, 19.9% used metamizole alone and only 2.9% denied using metamizole. Based on the annual report of the largest health insurance company, metamizole is the second most frequently used active pharmaceutical Ingredients in Germany

(<https://www.barmer.de/resource/blob/1247494/f995023b563dfa99436f1b7615bb984/0/dl-praesentation-arzneimittelreport-2023-s-h-data.pdf>). The German guideline for the treatment of acute pain stated with the highest grade of recommendation: "NSAIDs, COX-2 inhibitors and metamizole have equally good analgesic quality and should be preferred over the weaker-acting paracetamol." (Deutsche Gesellschaft für Anästhesiologie und Intensivmedizin 2021).

Metamizole is used extremely frequently in palliative medicine. Therefore, as a supplement to international guidelines on tumor pain therapy, which often ignore metamizole, metamizole was included in the German recommendations for tumor pain therapy as an equivalent alternative to NSAIDs and paracetamol (https://www.dgpalliativmedizin.de/images/stories/LL_Palliativmedizin_Kurzversion_1.1.pdf).

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A meta-analysis conducted in this context concluded: “Dipyrone can be recommended for the treatment of cancer pain as an alternative to other non-opioids either alone or in combination with opioids. It can be preferred over non-steroidal anti-inflammatory drugs due to the presumably favorable side effect profile in long-term use, but comparative studies are not available for long-term use.” (Gaertner et al 2017).

The German scientific and clinical community is aware of the risks of metamizole, particularly the risk of agranulocytosis. Expert groups therefore made several recommendations to raise awareness of and deal with these risks (Stamer et al 2017, Stamer et al 2019). They summarized their recommendations as follows: “The medical staff shall be aware of the symptoms and course of action when agranulocytosis is suspected. Patients shall be informed about the risks and benefits of dipyrone and about potential alternatives.”, but also emphasized: “The expert group concluded that dipyrone has a relatively positive risk-benefit ratio compared to other nonopioid analgesics” (Stamer et al 2019).

The German Pain Society fully agrees with this point of view. In particular, it points out that a limited availability of metamizole will most likely lead to an increase in significantly less controlled and largely over-the-counter consumption of NSAIDs, which is likely to pose significantly greater health risks than through controlled and strictly prescribed intake is to be expected from metamizole. An additional risk is the increased prescription of opioids; if NSAIDs are contraindicated, and metamizole is not available, the prescription of opioids will most likely rise tremendously as shown in the US.

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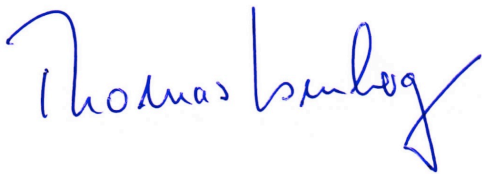
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Kind regards,



Thomas Isenberg
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