Supplementary material

Box 1. Incidence and risk of metamizole-induced agranulocytosis (MIA) [1–3]

- 6.2/1 mln/year (IAAAS report)
- 0.96/1 mln/year (Berlin Case-Control Surveillance Study)
- 0.46–1.63/1 mln/person — days of use (Switzerland report)

1. Risks of agranulocytosis and aplastic anemia. A first report of their relation to drug use with special reference to analgesics. The International Agranulocytosis and Aplastic Anemia Study. JAMA. 1986; 256(13): 1749–1757, indexed in Pubmed: 3747087.
2. Huber M, Andersohn F, Sarganas G, et al. Metamizole-induced agranulocytosis revisited: results from the prospective Berlin Case-Control Surveillance Study. Eur J Clin Pharmacol. 2015; 71(2): 219–227, doi: 10.1007/s00228-014-1777-8, indexed in Pubmed: 25378038.
3. Blaser LS, Tramonti A, Egger P, et al. Hematological safety of metamizole: retrospective analysis of WHO and Swiss spontaneous safety reports. Eur J Clin Pharmacol. 2015; 71(2): 209–217, doi: 10.1007/s00228-014-1781-z, indexed in Pubmed: 25401171.

Box 2. Symptoms of metamizole-induced agranulocytosis (MIA)

- Fever
- Sore throat
- Exhaustion
- Additional mucosal inflammation (aphthous stomatitis, pharyngitis, tonsillitis, proctitis)
- Sepsis
- Pneumonia

Box 3. Key messages

- Metamizole is an important non-opioid analgesic used in multimodal analgesia of postoperative pain.
- More studies are needed to establish its efficacy in postoperative pain treatment and the optimal administration regimens for specific surgical procedures.
- Assessment of the preemptive effectiveness of metamizole should be further evaluated.
- The neuroprotective activity of metamizole should be further evaluated.
- Studies of gender differences in metamizole efficiency should be performed.
- Serious adverse reactions including the risk of agranulocytosis, DILI, and allergic reactions have to be considered before initiating therapy with metamizole.