

# Safety Profile of Meloxicam: Analysis of Adverse Event Reports in the Czech Republic

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## Abstract

**INTRODUCTION:** Meloxicam is a preferential cyclooxygenase-2 inhibitor widely prescribed for rheumatic diseases. Given its long clinical use, further assessment of its safety profile remains relevant.

**AIM OF STUDY:** This study aimed to evaluate the safety profile of meloxicam in the Czech Republic using national pharmacovigilance data, and to compare reported adverse events (AEs) with findings from the WHO VigiAccess database.

**METHODS:** We analyzed all meloxicam-related AEs reported to the State Institute for Drug Control (SÚKL) between January 2015 and December 2020, as well as related data extracted from the World Health Organization's pharmacovigilance VigiAccess database. AEs were classified according to MedDRA terminology. National drug utilization data were obtained from SÚKL to provide an estimate of meloxicam exposure, expressed in defined daily doses (DDD).

**RESULTS:** Over six years, 24 AE reports were identified in the Czech Republic (population 10.7 million). During the same period, meloxicam consumption reached 71,512,140 DDD, corresponding to 4.64 DDD/1000 inhabitants/day. The most frequently reported AEs were hypersensitivity reactions (10 cases), followed by gastrointestinal events (4 cases), nervous system disorders (4 cases), and isolated cardiovascular toxicity (1 case of heart failure).

**CONCLUSION:** In the context of national exposure, only a limited number of meloxicam-related AEs were reported.

## OBJECTIVES

Meloxicam is a COX-2 inhibitor with anti-inflammatory, analgesic, and antipyretic effects, used for rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, and juvenile idiopathic arthritis (Engelhardt *et al.* 1995). Available for over 30 years, it remains widely used for pain management but may cause adverse events requiring careful monitoring, especially in vulnerable patients.

Like other non-steroidal anti-inflammatory drugs (NSAIDs), meloxicam can cause gastrointestinal (GI) adverse events (Sohail *et al.* 2023). For non-selective NSAIDs, these are largely mediated by inhibition of COX-1, which compromises mucosal protection and increases the risk of ulceration and bleeding. By contrast, meloxicam preferentially inhibits COX-2, and clinical trials (MELISSA, SELECT) have shown that it is associated with fewer GI complications than non-selective NSAIDs such as diclofenac and piroxicam (Hawkey *et al.* 1998; Dequeker *et al.* 1998). Nevertheless, meloxicam does not eliminate the risk entirely, and

elderly patients or those taking concomitant medications remain vulnerable to peptic ulcer disease and GI bleeding (Zullo *et al.* 2007).

It should also be noted that the comparative trials used the lowest available dose of meloxicam (7.5 mg), while diclofenac and piroxicam were administered at higher, near-maximal doses for their indications.

Studies of older adults have shown that chronic NSAID use increases the risk of peptic ulcer disease (Bekker *et al.* 2018). The risk of peptic ulcer complications is increased three- to fivefold in older adults using NSAIDs (Griffin, 1998). Several studies have found that age is an independent predisposing factor for gastrointestinal bleeding, with the risk being significantly increased in patients aged >65 years and further increased in those aged >75 years (Zullo *et al.* 2007).

Beyond GI toxicity, meloxicam may also cause hypersensitivity reactions ranging from mild skin eruptions to severe immune-mediated syndromes. Oxicams, as a class, have been implicated in rare but serious reactions such as Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), conditions with high

**Tab. 1.** Characteristics of patients experiencing adverse events

	Age (years)	Sex	Serious	Med.	Physician adjudicated
Exanthem, itching, somnolence, weakness, dizziness, fatigue	72	F	N	Y	N
Itching rash	61	F	N	Y	N
Acute urticarial	42	F	Y	Y	Y
Generalized macular rash, swollen hand	62	F	N	N	Y
Erythema	64	F	N	Y	Y
Maculopapular rash, facial edema, swollen fingers	54	F	Y	N	Y
Rash	66	F	Y	N	Y
Facial exanthem	70	F	Y	N	Y
Drug rash	60	NA	Y	N	Y
Facial edema	NA	F	Y	N	Y
Anemia, dyspepsia, hepatobiliary disorders, decreased appetite, weight loss, peptic ulcer	86	F	Y	Y	N
Peptic ulcer	82	F	Y	N	Y
Peptic ulcer with perforation	71	M	Y	Y	Y
Aphthous stomatitis	51	F	Y	Y	Y
Cerebral hypoxia, hyperkalemia, heart failure	58	F	Y	Y	N
Fatigue, dizziness, nightmare, sleepiness	43	F	Y	Y	N
Somnolence, weakness, dizziness, fatigue	72	F	N	Y	N
Dizziness, vertigo	51	F	N	N	Y
Tinnitus	NA	M	Y	Y	N
Squamous cell tonsillar cancer	NA	M	Y	Y	Y
Eye pain, wart, laryngeal edema, profuse sweating	77	F	N	Y	N
Thyroid disorders, blood pressure changes	74	F	Y	Y	N

F, female; M, male; NA, not available; Med., chronic medication use

morbidity and mortality (Harr & French 2012; Yang et al. 2016). The risk is highest during the first weeks of treatment; should such a reaction occur, meloxicam should be stopped immediately (Drugs.com 2024, Rasul et al. 2012; Rosseli, et al. 2020).

Cardiovascular safety is another important consideration. NSAIDs have been linked to an increased risk of myocardial infarction, a concern particularly associated with COX-2 inhibition (Dalal et al. 2017). Studies and meta-analyses indicate that cardiotoxicity is a class effect, with risk varying among individual NSAIDs. (Varga et al. 2017). In general, cardiovascular safety of meloxicam is comparable with that of other NSAIDs (García Rodríguez et al. 2004; McGettigan & Henry, 2011).

Meloxicam is currently recommended by the UK's National Institute for Health and Care Excellence (NICE) for initial pharmacological treatment and symptom control in selected rheumatic diseases. (NICE 2020). Clinical trials conducted shortly after its introduction into clinical use demonstrated clear benefits compared to other NSAIDs. However, recent studies specifically focusing on meloxicam are lacking. Therefore, this study aimed to evaluate the safety profile of meloxicam in the Czech Republic using national pharmacovigilance data and to compare reported adverse events with international findings from the WHO Vigibase database.

## METHODS

The analysis was carried out using notifications and/or reports of all AEs related to meloxicam use and received by the State Institute for Drug Control (Státní ústav pro kontrolu léčiv, SÚKL), the Czech regulatory authority, as well as data from the World Health Organization's pharmacovigilance Vigibase database.

To classify AEs, we used the clinically validated international dictionary of medical terminology, Medical Dictionary for Regulatory Activities (MedDRA) version 25.0, with the AEs subsequently grouped according

to this system, assessed and analysed to determine the incidence of AEs and to categorize them.

National drug utilization data for meloxicam (2015–2020) were retrieved from the State Institute for Drug Control database, which reports deliveries of medicinal products by ATC code and route of administration (SÚKL 2020). Consumption was expressed in defined daily doses (DDD) according to the WHO ATC/DDD methodology; both total dispensed DDD and DDD/1000 inhabitants/day are reported by SÚKL. For this study, the overall value of DDD/1000 inhabitants/day was calculated as the mean of the annual figures.

## RESULTS

### Meloxicam adverse events reported in the Czech Republic

Over the six-year study period between 1 January 2015 and 31 December 2020, SÚKL, the regulatory authority of the Czech Republic (a country with a population of 10.7 million), received a total of 24 reports of meloxicam-related AEs. One report in which meloxicam was a component of combination therapy involving a total of 23 medications (19 suspicious ATC classes) was excluded because of missing relevant data.

During 2015–2020, a total of 71,512,140 DDD of meloxicam were dispensed in the Czech Republic (SÚKL 2020), corresponding to an average of 4.64 DDD per 1000 inhabitants per day. Relative to this level of exposure, the number of reported adverse events was very low, approximately 0.34 reports per one million DDD.

In 3 of the remaining 23 reports, patients' ages were unavailable, whereas the mean age of the remaining 20 individuals was 64.25 years (median, 64 years). Men were involved in only 3 cases. Patient characteristics are listed in Table 1, categorized AEs in Table 2.

### *Hypersensitivity reactions (skin and vascular-induced reactions)*

Among notifications of AEs clearly related to meloxicam use, particular note should be taken of the incidence of hypersensitivity reactions (10 cases), of which number 8 were physician-adjudicated. Six of the 10 adverse events were very serious, specifically drug-induced exanthem, facial exanthem, rash, maculopapular rash, acute urticaria and facial edema, with the other AEs being non-serious and including erythema, generalized macular rash (with swollen hand), itching rash and skin itching with exanthem.

### *Gastrointestinal disorders*

Over the study period, SÚKL received 4 reports of gastrointestinal AEs, of this number, 3 involved peptic ulcer. Two cases, both involving female patients aged 80+, were treated by concomitant ibuprofen and paracetamol. One of the cases was physician-adjudicated; both were considered critical AEs.

**Tab. 2.** Categorized adverse effects reported to SÚKL after meloxicam use

Adverse effect (or system affected)	Number (%)
Backache	1 (4.4)
Heart failure	1 (4.4)
Hyperkalemia	1 (4.4)
Renal pain	1 (4.4)
Tinnitus	1 (4.4)
Central nervous system	4 (17.3)
Gastrointestinal tract	4 (17.3)
Hypersensitivity reactions	10 (43.5)
<b>Total</b>	<b>23 (100)</b>

A 71-year-old man developed acute peptic ulcer classified as a serious AE. Other reported AEs related to the gastrointestinal tract included aphthous stomatitis as a serious physician-adjudicated AE experienced by a 57-year-old female.

#### *Nervous system disorders*

Mention should be made of AEs on the nervous system (4 cases). One case involved somnolence, weakness, dizziness and fatigue as non-serious AEs reported by a 72-year-old female complaining also of itchy skin with apparent exanthem. Another case involved fatigue, sleepiness, dizziness and nightmare, all assessed as serious AEs, in a 43-year-old female. The third case of an AE, very serious and affecting the central nervous system, was cerebral hypoxia experienced by a 59-year-old female presenting with hyperkalemia and heart failure. The fourth report included complaints of non-serious vertigo and dizziness.

#### *Others*

The AEs reported by one patient included tinnitus with moderate symptoms, low back pain, characterized by a sensation of marked discomfort in the back region, kidney pain, heart failure and hyperkalemia.

#### *Adverse events of meloxicam co-administered with another drug*

Some of the reported AEs cannot be unequivocally related to meloxicam use because of concomitant use with other medicinal products.

## DISCUSSION

Our analysis registered three cases of peptic ulcer associated with meloxicam combined, in two cases, with another NSAID (specifically ibuprofen) or paracetamol. Gastrointestinal toxicity of NSAIDs is primarily due to inhibition of COX-1-mediated prostaglandin synthesis, which compromises mucosal protection and can lead to ulcer formation. It is critical to avoid concomitant use of meloxicam and another NSAID, including the over-the-counter ones; it is also recommended to provide peptic protection by proton pump inhibitors. Individuals should be educated about this when prescribing and dispensing meloxicam.

All three patients developing peptic ulcers were elderly persons. While meloxicam is often considered to carry a lower gastrointestinal risk compared to other NSAIDs due to its preferential COX-2 inhibition, the incidence of gastrointestinal events remains clinically relevant, especially in older adults, those with a history of gastrointestinal disorders, or those taking concurrent medications such as corticosteroids or other NSAIDs. (Sohail *et al.* 2023).

NSAIDs are commonly used in geriatric population and should be prescribed for the shortest duration possible in the lowest effective dose, and with careful

surveillance to monitor gastrointestinal, renal, and cardiovascular toxicity.

The most frequent notifications/reports of AEs following meloxicam use over the research period related to hypersensitivity reactions (10 cases). Hypersensitivity reactions to meloxicam, though relatively uncommon, can occur and range from mild to severe. These reactions are primarily mediated by an immune response to the drug, leading to symptoms such as skin rashes, urticaria, angioedema and, in rare cases, SJS/TEN. Since hypersensitivity reactions to meloxicam are typically unpredictable and may occur upon first or repeated exposure, patients should be informed about early signs such as rash, swelling, or breathing difficulties. Any such symptoms should prompt immediate discontinuation of the drug and medical evaluation (Drugs.com 2024).

Heart failure was the only cardiovascular event reported to SÚKL over the evaluation period. NSAIDs cardiovascular toxicity has raised significant concerns, especially with prolonged use or in high-risk patient populations. The risk is particularly heightened in individuals with preexisting cardiovascular conditions, such as hypertension, heart failure, or a history of myocardial infarction (Minhas *et al.* 2023).

To assess meloxicam's safety, we compared our data with the WHO VigAccess database. Gastrointestinal AEs were most frequent, followed by general disorders, with skin and subcutaneous reactions third.

Comparison with VigAccess showed differences. In the WHO pharmacovigilance database, gastrointestinal disorders represent the most frequently reported adverse events (22% of records), followed by general disorders (16%) and skin reactions (14%). By contrast, in our Czech cohort, hypersensitivity reactions were the most common, while gastrointestinal events ranked second. Several explanations are possible. First, the low absolute number of Czech reports (n = 24) limits direct comparability with the large international database, where the volume of reports reflects global exposure. Second, underreporting patterns may differ between countries, with physicians more likely to recognize and report acute hypersensitivity reactions than other complications in routine practice.

The main limitation is the relatively small number of adverse event reports and by the general limitations of spontaneous reporting systems, including underreporting, reporting bias, and incomplete clinical details. However, these data remain valuable for signal detection, highlighting patterns of clinically relevant events such as hypersensitivity reactions and peptic ulcers.

## CONCLUSION

In this nationwide pharmacovigilance analysis, 24 adverse events associated with meloxicam were reported over six years in the Czech Republic, despite widespread use. Hypersensitivity reactions, including

angioedema, represented the most common events, followed by gastrointestinal complications such as peptic ulcer. Cardiovascular toxicity was rarely reported. These findings indicate that meloxicam remains generally safe in routine clinical practice, but vigilance is warranted, especially when prescribing to elderly patients or in combination with other NSAIDs. Continuous monitoring and comparison with international databases are essential to better characterize the drug's safety profile across populations.

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## REFERENCES

- Bekker A, Kloepping C, Collingwood S (2018). Meloxicam in the management of post-operative pain: Narrative review. *J Anaesthesiol Clin Pharmacol.* **34**(4): 450–457.
- Dalal D, Dubreuil M, Peloquin C, Neogi T, Zhang Y, Choi H, et al. (2017). Meloxicam and risk of myocardial infarction: a population-based nested case-control study. *Rheumatol Int.* **37**(12): 2071–2078.
- Dequeker J, Hawkey C, Kahan A, Steinbruck K, Alegre C, Baumelou E, et al. (1998). Improvement in gastrointestinal tolerability of the selective cyclooxygenase (COX)-2 inhibitor, meloxicam, compared with piroxicam: results of the Safety and Efficacy Large-scale Evaluation of COX- inhibiting Therapies (SELECT) trial in osteoarthritis. *Br J Rheumatol.* **37**(9): 946–951.
- Drugs.com. 2024. Meloxicam Monograph. Revised January 2024. Available from: <https://www.drugs.com/monograph/meloxicam.html> [Accessed 25 May 2024].
- Engelhardt G, Homma D, Schlegel K, Utzmann R, Schnitzler C (1995). Anti-inflammatory, analgesic, antipyretic and related properties of meloxicam, a new non-steroidal anti-inflammatory agent with favourable gastrointestinal tolerance. *Inflamm Res.* **44**(10): 423–433.
- García Rodríguez LA, Varas-Lorenzo C, Maguire A, González-Pérez A (2004). Nonsteroidal Antiinflammatory Drugs and the Risk of Myocardial Infarction in the General Population. *Circulation.* **109**(24): 3000–3006.
- Griffin MR (1998). Epidemiology of Nonsteroidal Anti-inflammatory Drug–Associated Gastrointestinal Injury. *Am J Med.* **104**(3): 235–295.
- Harr T & French LE (2012). Stevens-Johnson syndrome and toxic epidermal necrolysis. *Chem Immunol Allergy.* **97**: 149–66.
- Hawkey C, Kahan A, Steinbruck K, Alegre C, Baumelou E, Begaud B, et al. (1998). Gastrointestinal tolerability of meloxicam compared to diclofenac in osteoarthritis patients. International MELISSA Study Group. Meloxicam Large-scale International Study Safety Assessment [published erratum appears in *Br J Rheumatol* 1998 Oct;37(10): 1142]. *Br J Rheumatol.* vol. **37**(9): 937–945.
- McGettigan P & Henry D (2011). Cardiovascular Risk with Non-Steroidal Anti-Inflammatory Drugs: Systematic Review of Population-Based Controlled Observational Studies. *PLoS Medicine.* **8**(9): e1001098
- Minhas D, Nidhaan A, Husni ME. (2023). Recommendations for the use of nonsteroidal anti-inflammatory drugs and cardiovascular disease risk: Decades later, any new lessons learned? *Rheum Dis Clin North Amem.* **49**(1): 179–191.
- National Institute for Health and Care Excellence (NICE). 2020. Rheumatoid arthritis in adults: diagnosis and management. NICE guideline [NG100]. London: NICE. Available from: <https://www.nice.org.uk/guidance/ng100>
- Rasul S, Farhat F, Endailalu Y, Tabassum Khan F, Poddar V (2012). Mycoplasma pneumoniae Induced Stevens Johnson Syndrome: Rare Occurrence in an Adult Patient. *Case Rep Med.* **2012**: 430490.
- Roselli J, Innocenti T, Lynch E, Parisio L, Apolito P, Mello T, et al. (2020). Stevens–Johnson Syndrome and Herpes Simplex Type 1 Infection during Adalimumab Therapy for Crohn’s Disease. *Case Rep Gastrointest Med.* **2020**: 3875024.
- Sohail R, Mathew M, Patel KK, Reddy SA, Haider Z, Naria M, et al. (2023). Effects of non-steroidal anti-inflammatory drugs (NSAIDs) and gastroprotective NSAIDs on the gastrointestinal tract: A narrative review. *Cureus.* **15**(4): e37080.
- State Institute for Drug Control (SÚKL). 2020. Deliveries of medicinal products in the Czech Republic – by active substances [Internet]. Available from: <https://sukl.gov.cz/prumysl/leciva>
- Varga Z, Sabzwari SRA, Vargova V (2017). Cardiovascular Risk of Nonsteroidal Anti-Inflammatory Drugs: An Under-Recognized Public Health Issue. *Cureus.* **9**(4): e1144.
- Yang M, Lee J, Kim J, Kim G, Kim B, Kim J, et al. (2016). Incidence of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis: A Nationwide Population-Based Study Using National Health Insurance Database in Korea. *PLOS ONE.* **11**(11): e0165933.
- Zullo A, Hassan C, Campo SM, Morini S (2007). Bleeding Peptic Ulcer in the Elderly. *Drugs Aging.* **24**(10): 815–828.