

# Metamizole and risk of hepatotoxicity –comparative cohort study of incidence of hepatic events in patients treated with metamizole vs. patients treated with paracetamol in IMS Disease Analyzer Germany between January 2009 and December 2018 (Metamizole and hepatotoxicity)

**First published:** 18/10/2019

**Last updated:** 02/04/2024

Study

Finalised

## Administrative details

### **EU PAS number**

EUPAS31864

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### **Study ID**

31865

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**DARWIN EU® study**

No

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### Study countries

 Germany

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### Study description

Metamizole is a medication with analgesic, antipyretic, spasmolytic, and weak anti-inflammatory effects, used for acute and chronic pain management, and in some countries, fever management. Cases of drug-induced liver injury (DILI) have been reported in association with metamizole treatment, however the evidence from epidemiological studies is very limited (one case-control only). This study aims to quantify the incidence of hepatic events in patients treated with metamizole compared to patients treated with paracetamol or NSAIDs (chosen as an active comparator).

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### Study status

Finalised

## Research institutions and networks

### Institutions

[European Medicines Agency \(EMA\)](#)

**First published:** 01/02/2024

**Last updated:** 01/02/2024

**Institution**

### Contact details

### **Study institution contact**

Hedelmalm Karin Karin.Hedenmalm@ema.europa.eu

Study contact

[Karin.Hedenmalm@ema.europa.eu](mailto:Karin.Hedenmalm@ema.europa.eu)

### **Primary lead investigator**

Hedelmalm Karin

Primary lead investigator

## Study timelines

### **Date when funding contract was signed**

Planned: 01/06/2018

Actual: 01/06/2018

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### **Study start date**

Planned: 01/01/2019

Actual: 01/04/2019

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### **Data analysis start date**

Planned: 15/04/2019

Actual: 15/06/2019

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### **Date of final study report**

Planned: 01/01/2020

Actual: 01/01/2020

## Sources of funding

- EMA

## Study protocol

[Study-protocol -IMS DE-Metamizole\\_DILI 4 september 2019.pdf](#) (233.46 KB)

## Regulatory

### **Was the study required by a regulatory body?**

Yes

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### **Is the study required by a Risk Management Plan (RMP)?**

Not applicable

## Methodological aspects

### Study type

### Study type list

#### **Study topic:**

Human medicinal product

Disease /health condition

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#### **Study type:**

Non-interventional study

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**Scope of the study:**

Assessment of risk minimisation measure implementation or effectiveness

**Data collection methods:**

Secondary use of data

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**Main study objective:**

This study aims to quantify the incidence of hepatic events in patients treated with metamizole compared to patients treated with paracetamol.

## Study Design

**Non-interventional study design**

Cohort

Other

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**Non-interventional study design, other**

Comparative study

## Study drug and medical condition

**Study drug International non-proprietary name (INN) or common name**

METAMIZOLE

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**Medical condition to be studied**

Drug-induced liver injury

## Population studied

## **Short description of the study population**

The study focused on incident users of metamizole and paracetamol from 1 January 2009 to 31 December 2018.

Patients with less than 365 days of observation and those with a history of cancer, HIV, viral hepatitis, liver disease, or Budd-Chiari syndrome was excluded from the study.

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## **Age groups**

- Adults (18 to < 46 years)
  - Adults (46 to < 65 years)
  - Adults (65 to < 75 years)
  - Adults (75 to < 85 years)
  - Adults (85 years and over)
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## **Special population of interest**

Hepatic impaired

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## **Estimated number of subjects**

600000

# Study design details

## **Outcomes**

Drug-induced liver injury, classified as a composite outcome of various hepatic terms (see protocol). in case of sufficient data, we will analyse separately toxic liver disease (ICD 10 code K71), hepatic failure not elsewhere classified (ICD 10 code K72) and other hepatic events (ICD 10 codes K75-K76).

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## **Data analysis plan**

A comparative cohort will be created, where the relative risk will be calculated with the Cox Proportional Hazards models. All variables will be recorded at baseline and not integrated as time-dependent. The analysis will be adjusted for age (continuous), gender and the identified confounders that will show an effect on the risk estimate (significant association in univariate models and more than 10% change in risk estimate). Missing data will be dealt with through list-wise deletion (complete case analysis).

## Documents

### Study publications

[Hedenmalm K, Pacurariu A, Slattery J, Kurz X, Candore G, Flynn R. Is there an i...](#)

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## Data management

### ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

## Data sources

### Data source(s), other

IQVIA Disease Analyzer Germany

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### Data sources (types)

## Use of a Common Data Model (CDM)

### **CDM mapping**

No

## Data quality specifications

### **Check conformance**

Unknown

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### **Check completeness**

Unknown

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### **Check stability**

Unknown

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### **Check logical consistency**

Unknown

## Data characterisation

### **Data characterisation conducted**

No