# International Platform of Registered Systematic Review and Meta-analysis Protocols



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A Systemic Review and Network Meta-Analysis of Cardiovascular Safety of Benzbromarone, Febuxostat, and Allopurinol in Patients with Gout

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# ADMINISTRATIVE INFORMATION

Support - No funding was received for this research.

Review Stage at time of this submission - Preliminary searches.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202460049

**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 13 June 2024 and was last updated on 13 June 2024.

### **INTRODUCTION**

Review question / Objective The objective of this research is to assess the cardiovascular safety of benzbromarone, febuxostat, and allopurinol in gout patients.

**Condition being studied** Gout is caused by hyperuricemia and is associated with cardiovascular diseases. Treatment for hyperuricemia primarily involves urate-lowering medications. Some trials showed higher cardiovascular mortality rates with febuxostat compared to allopurinol. However, data are limited about the cardiovascular safety of benzbromarone compared to febuxostat and allopurinol.

### **METHODS**

**Participant or population** The population included adult patients ( $\geq$  18 years) with the diagnosis of gout.

Intervention Benzbromarone.

Comparator Febuxostat or allopurinol.

**Study designs to be included** RCTs and comparative observational studies were both included.

**Eligibility criteria** Inclusion criteria were randomized controlled trials (RCTs) and cohort studies including adult patients with the diagnosis of gout, with urate-lowering medications. The outcome was the incidence of major adverse cardiovascular events.

Information sources PubMed and EMBASE.

Main outcome(s) The outcome was the incidence of major adverse cardiovascular events.

**Quality assessment / Risk of bias analysis** We applied Cochrane risk of bias tool to appraise the methodological quality.

**Strategy of data synthesis** Network metaanalyses with random-effects models.

**Subgroup analysis** Subgroup analysis of RCTs versus observational trials was also performed to evaluate the potential heterogeneity.

**Sensitivity analysis** Sensitivity analysis was performed to elucidate overlapping of population.

Country(ies) involved Taiwan.

**Keywords** febuxostat, allopurinol, benzbromarone, cardiovascular, gout.

#### **Contributions of each author**

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