# Use of NSAIDs and risk of critical adverse outcomes in patients with COVID-19

### Synopsis

During the ongoing coronavirus disease (COVID-19) pandemic, case reports have described patients with no comorbidities who developed severe COVID-19 after using non-steroidal anti-inflammatory drugs (NSAIDs) in the early stage of their disease. Based on these reports, the World Health Organisation issued a warning against the use of NSAIDs in COVID-19 patients. While this warning was later retracted and the European Medicines Agency stated that there is currently no scientific evidence to support such a warning, considerable uncertainty persists as to whether NSAID use can be considered safe in patients with COVID-19.

There are biologically plausible mechanisms through which NSAIDS could increase the risk of severe and fatal COVID-19. Specifically, NSAIDs may cause an upregulation of angiotensin-converting enzyme 2 (ACE2) receptors, a receptor that is used by the virus to bind to epithelial cells of the lung and other organs.

Given the potential health impact of discontinuing or withholding NSAIDs in patients with COVID-19, studies are needed to determine the impact of NSAIDs on the prognosis of COVID-19. We therefore propose to determine the association between NSAID use and critical adverse outcomes following hospitalization for COVID-19.

The study population includes hospitalised patients with verified COVID-19. We will investigate the association between current use of NSAIDs and the risk of critical adverse outcomes including admission to an intensive care unit, mechanical ventilation and death.

#### Priority

The research project will address several of the prioritized research aims including addressing an acute research question with limited preexisting evidence, providing evidence on rational use of drugs during COVID-19, is of public health importance because of the prevalent use of NSAIDs and potential severe adverse outcomes.

### Research group

The research group consists of researchers from the pharmacoepidemiology unit at Clinical Pharmacology and Pharmacy, University of Southern Denmark, researchers from Department of Clinical Epidemiology at Aarhus University, and researchers from Statens Serum Institut. The research project will be led by professor Anton Pottegård. The group has substantial documented research experience in academic, industry, and regulatory pharmacoepidemiological drug-safety studies.

## **Conflicts of Interest**

Anton Pottegård reports participation in research projects funded by Alcon, Almirall, Astellas, Astra-Zeneca, Boehringer-Ingelheim, Novo Nordisk, Servier and LEO Pharma, all with funds paid to the institution where he was employed (no personal fees) and with no relation to the current proposal.

Conflict of interest statement from other researchers involved in the project will be identified and submitted as soon as possible.