

COVID-19 rapid evidence summary: acute use of non- steroidal anti-inflammatory drugs (NSAIDs) for people with or at risk of COVID-19

Evidence summary

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www.nice.org.uk/guidance/es23

Key messages

The content of this evidence review was up-to-date on 24 March 2020. See [summaries of product characteristics \(SPCs\)](#), [British national formulary \(BNF\)](#) or the [MHRA](#) or [NICE](#) websites for up-to-date information.

In March 2020, the French Health Ministry issued advice to avoid using non-steroidal anti-inflammatory drugs (NSAIDs) to treat symptoms of COVID-19 because these medicines might aggravate the infection. In response to these concerns, the [MHRA issued a Central alerting system \(CAS\) alert](#) in which the NHS England Medical Director, Professor Stephen Powis, advised using paracetamol in preference to ibuprofen in people with confirmed or suspected COVID-19, while acknowledging there is limited evidence that ibuprofen is either safe or harmful in these people. In view of the current lack of clarity the Commission on Human Medicines (an advisory body of the MHRA) and NICE were asked to review the evidence.

The purpose of this review is to assess the best available evidence to determine:

- If there is any increased risk of developing COVID-19 due to acute use of NSAIDs.
- If acute use of NSAIDs can lead to an increased risk of developing more severe symptoms of COVID-19.

This review does not consider people who are taking NSAIDs long-term for existing chronic conditions.

A literature search identified 156 references, which were screened using their titles and abstracts. Thirteen references were obtained and assessed for relevance; however, none were suitable for inclusion. This means that no evidence from published scientific studies was found to determine whether acute use of NSAIDs is related to increased risk of developing COVID-19 or increased risk of a more severe illness.

The available evidence suggests that, although the anti-inflammatory effects of NSAIDs reduce acute symptoms (such as fever), they may either have no effect on, or worsen, long-term outcomes, possibly by masking symptoms of worsening acute respiratory tract infection. Further evidence is needed to confirm this, and to determine whether these results also apply to infections such as COVID-19.

Likely place in therapy

NHS England has developed a [commissioning policy](#) for acute use of NSAIDs for people with or at risk of COVID-19.

Factors for decision making

Effectiveness and safety

The searches performed for the evidence review found no evidence to determine if there is any increased risk of developing COVID-19 due to acute use of NSAIDs, or if acute use of NSAIDs can lead to an increased risk of developing more severe symptoms of COVID-19. Therefore, with the agreement of NHS England, indirect evidence relating to the acute use of NSAIDs for other acute respiratory tract infections was summarised. Formal searches and critical appraisal were not conducted for this extension to the original question.

Discussion and limitations of the evidence

Concerns over using NSAIDs for COVID-19 were raised by the French Health Ministry after 4 people with COVID-19 and no underlying health problems reportedly developed serious symptoms after using these medicines ([Day 2020](#)). On 14 March 2020, the French Health Minister issued advice to avoid using NSAIDs for COVID-19 based on a [2019 evaluation by the French National Agency for Medicines and Health Products Safety](#), which suggested that infection due to chickenpox (varicella) and some bacterial infections could be made worse by ibuprofen and ketoprofen.

On 18 March 2020, the [EMA issued a press release](#) stating there is currently no scientific evidence establishing a link between ibuprofen and worsening of COVID-19. The EMA is monitoring the situation closely and will review any new information that becomes available on this issue in the context of the pandemic.

[A CEBM review on NSAIDs in acute respiratory infection](#) (not including COVID-19) concluded that NSAIDs do not significantly reduce total symptoms or duration of respiratory infections. Also, there are long-standing and well-recognised gastrointestinal and renal safety concerns with all NSAIDs, and evidence confirming an increased risk of cardiovascular events with many NSAIDs, including COX-2 inhibitors and some traditional NSAIDs such as diclofenac and high-dose ibuprofen (2,400 mg daily or more).

The CEBM advises that there is a need for caution when using NSAIDs for acute respiratory infections. Pre-existing medications and conditions need to be considered when deciding whether to use NSAIDs for symptomatic acute respiratory infections. Clinicians should follow advice in the [BNF](#) and the [NICE clinical knowledge summary on issues around prescribing NSAIDs](#). When considering an NSAID, individual risk factors for adverse effects should be taken into account, including any contraindications, drug interactions, medical history, and any monitoring requirements. The lowest effective dose of an NSAID should be used for the shortest period required to control symptoms and the need for long-term treatment should be reviewed periodically. The [MHRA advises](#) that naproxen and low-dose ibuprofen (up to 1,200 mg per day) are considered to have the most favourable thrombotic cardiovascular safety profiles of all NSAIDs.

The [EMA advises](#) that, when starting treatment for fever or pain in COVID-19, patients and healthcare professionals should consider all available treatment options, including paracetamol and NSAIDs. Each medicine has its own benefits and risks which are reflected in its product information, and which should be considered along with EU national treatment guidelines, most of which recommend paracetamol as a first treatment option for fever or pain. In line with EU national

treatment guidelines, patients and healthcare professionals can continue using NSAIDs (like ibuprofen) as per the approved product information. Current advice includes that these medicines are used at the lowest effective dose for the shortest possible period. Patients who have any questions should speak to their doctor or pharmacist. There is currently no reason for patients taking ibuprofen to interrupt their treatment. This is particularly important for patients taking ibuprofen or other NSAIDs for chronic diseases.

Conclusion

At this time, policy decisions on whether NSAIDs should be used for treating symptoms of COVID-19 will need to take into account data extrapolated from studies involving the use of NSAIDs for other acute respiratory tract infections, together with pharmacoepidemiological studies.

See the [full evidence review](#) for more information.

Commissioned by NHS England.

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