



The following information resources have been selected by the National Health Library and Knowledge Service Evidence Virtual Team in response to your question. The resources are listed in our estimated order of relevance to practicing healthcare professionals confronted with this scenario in an Irish context. In respect of the evolving global situation and rapidly changing evidence base, it is advised to use hyperlinked sources in this document to ensure that the information you are disseminating to the public or applying in clinical practice is the most current, valid and accurate.

YOUR QUESTION

Is it safe to use ibuprofen in the pharmacological treatment of a patient with COVID-19?

What does the Health Protection Surveillance Centre (HSPC) say?

[Healthcare Worker COVID-19 Close Contact Information Leaflet¹](#)

There are no contraindications for ibuprofen use on the HPSC website. However, it is noted that ibuprofen might mask COVID-19 symptoms and should be avoided in cases when an individual has been or is believed to have been in contact with someone infected with COVID-19, or for healthcare workers returning to Ireland after 16th March 2020.

It advocates the following: "Avoid the use of anti-pyretics – for example paracetamol, ibuprofen – while undertaking monitoring in case they mask symptoms."

What does the World Health Organization say?

[Could ibuprofen worsen disease for people with COVID-19?²](#)

The following is the WHO's answer to the following question: Could ibuprofen worsen disease for people with COVID-19?

- WHO does not recommend against the use of ibuprofen
- WHO are consulting with physicians treating COVID-19 patients and are not aware of reports of any negative effects of ibuprofen, beyond the usual known side effects that limit its use in certain populations
- WHO is not aware of published clinical or population-based data on this topic

What does the European Medicines Agency (EMA) say?

EMA gives advice on the use of non-steroidal anti-inflammatories for COVID-19³

EMA is aware of reports, especially on social media, which raise questions about whether non-steroidal anti-inflammatory medicines (NSAIDs) such as ibuprofen could worsen coronavirus disease (COVID19). There is currently no scientific evidence establishing a link between ibuprofen and worsening of COVID-19. EMA is monitoring the situation closely and will review any new information that becomes available on this issue in the context of the pandemic.

In May 2019, EMA's safety committee (PRAC) started a review of the non-steroidal anti-inflammatory medicines ibuprofen and ketoprofen following a survey by the French National Agency for Medicines and Health Products Safety which suggested that infection due to chickenpox and some bacterial infections could be made worse by these medicines. The product information of many NSAIDs already contains warnings that their anti-inflammatory effects may hide the symptoms of a worsening infection. The PRAC is reviewing all available data to see if any additional measure is required. In line with EU national treatment guidelines, patients and healthcare professionals can continue using NSAIDs such as 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, based on the above. This is particularly important for patients taking ibuprofen or other NSAID medicines for chronic diseases. Further to the ongoing PRAC safety review on ibuprofen and ketoprofen, EMA highlights the need for epidemiological studies to be conducted in a timely manner to provide adequate evidence on any effect of NSAIDs on disease prognosis for COVID-19. The Agency is reaching out to its stakeholders and is ready to actively support such studies, which could be useful in guiding any future treatment recommendations.



What does the Food and Drug Administration (US) say?

FDA advises patients on use of non-steroidal anti-inflammatory drugs (NSAIDs) for COVID-19 ⁴

FDA is aware of news reports stating the use of non-steroidal anti-inflammatory drugs such as ibuprofen could worsen coronavirus disease (COVID-19). These news reports followed a March 11, 2020 letter in the *Lancet* medical journal which hypothesized that an enzyme is increased by NSAIDs and could aggravate COVID-19 symptoms.

At this time, FDA is not aware of scientific evidence connecting the use of NSAIDs such as ibuprofen with worsening COVID-19 symptoms. The agency is investigating this issue further and will communicate publicly when more information is available. However, all prescription NSAID labels warn that "the pharmacological activity of NSAIDs in reducing inflammation, and possibly fever, may diminish the utility of diagnostic signs in detecting infections."

For those who wish to use treatment options other than NSAIDs, there are multiple over-the-counter and prescription medications approved for pain relief and fever reduction. FDA suggests speaking to your health care professional if you are concerned about taking NSAIDs and rely on these medications to treat chronic diseases.

What do the Centers for Disease Control and Prevention (CDC) say?

Check and Report Everyday (CARE) ⁵

The CDC document *Check and Report Everyday (CARE)* does not contraindicate ibuprofen, but notes the following:

before you take your temperature wait at least 6 hours after taking medicines that can lower your temperature such as paracetamol or Ibuprofen.



What does the Health Service Executive (HSE) say?

Advice about Anti-Inflammatory medication and COVID-19 ⁶

As of Monday 16 March 2020, the HSE is advising anyone with COVID-19 to continue to take any medication you were already taking, unless you are told not to by a healthcare professional. This includes anti-inflammatories such as ibuprofen, naproxen or diclofenac. HSE advice regarding treatment of symptoms of COVID-19 is unchanged.

The HSE continues to advise, notwithstanding the recent controversy about Ibuprofen, that ibuprofen may help with symptoms of COVID-19 such as pain or fever and that anti-inflammatory medication may be continued by people with COVID-19, unless advised otherwise by their healthcare professional. The HSE notes that paracetamol is usually recommended as the first-line treatment for most people but ibuprofen may be prescribed by the patient's healthcare professional to help with COVID-19 symptoms such as pain or fever.

What does the National Health Service (NHS) say?

Self-isolation if you or someone you live with has symptoms: Coronavirus (COVID-19) ⁷

There is currently no strong evidence that ibuprofen can make coronavirus (COVID-19) worse. But until we have more information, take paracetamol to treat the symptoms of coronavirus unless your doctor has told you paracetamol is not suitable for you. If you are already taking ibuprofen or another non-steroidal anti-inflammatory on the advice of a doctor, do not stop taking it without checking first.

BMJ Best Practice

Coronavirus 2019 (COVID-19)⁸

Some clinicians have suggested that non-steroidal anti-inflammatory drugs such as ibuprofen could worsen COVID-19 or have a negative impact on disease outcome based on anecdotal reports. There is currently no strong evidence to support this. The European Medicines Agency, the US Food and Drug Administration, and the WHO do not recommend avoiding NSAIDs in COVID-19 when clinically indicated. However, NHS UK recommends paracetamol as the drug of choice until there is more information available.

Ibuprofen is not recommended in pregnant women – especially in the third trimester – or children <3 months of age. Age cut-offs vary by country.

In the BMJ Best Practice treatment algorithm for suspected or confirmed COVID-19 ["Initial and Acute Treatment"], dosages of 300-600 mg orally every 6-8 hours to a max of 2400 mg per day as required for adults are indicated for ibuprofen as an adjunct antipyretic or analgesic treatment but it is noted that routine antipyretic treatment for fever is not supported by evidence in acute respiratory infections.

UpToDate

Coronavirus Disease 2019 (COVID-19)⁹

UNCERTAINTY ABOUT NSAID USE: Some clinicians have suggested the use of non-steroidal anti-inflammatory drugs early in the course of disease may have a negative impact on disease outcome. These concerns are based on anecdotal reports of a few young patients who received NSAIDs early in the course of infection and experienced severe disease. In light of these concerns, some providers are using acetaminophen in place of NSAIDs for reduction of fever. However, there have been no clinical or population-based data that directly address the risk of NSAIDs. The European Medicines Agency and the WHO do not recommend that NSAIDs be avoided when clinically indicated.

What does the international literature say?

Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection?¹⁰

This letter explained that human pathogenic coronaviruses bind to their target cells through ACE-2 receptors. It went on to say that ACE-2 expression “can” be increased by ibuprofen. “Consequently, the increased expression of ACE-2 would facilitate infection with COVID-19.” It must be noted, however, that this is an hypothesis only. The article also suggested that patients with diabetes and those with cardiovascular conditions being treated with ACE inhibitors and/or angiotensin II type-1 receptor blockers (ARBs) may be at increased risk of severe illness if they are infected with COVID-19.

Covid-19: ibuprofen should not be used for managing symptoms, say doctors and scientists¹¹

Scientists and senior doctors have backed claims by France’s Health Minister that people showing symptoms of COVID-19 should use paracetamol [acetaminophen] rather than ibuprofen, a drug they said might exacerbate the condition. Jean-Louis Montastruc, Professor of Medical and Clinical Pharmacology at the Central University Hospital in Toulouse, said that such deleterious effects from NSAIDs would not be a surprise given that since 2019, on the advice of the National Agency for the Safety of Medicines and Health Products, French health workers have been told not to treat fever or infections with ibuprofen.

Some experts in the UK have backed this sentiment. Paul Little, Professor of Primary Care Research at the University of Southampton, said that there was good evidence “that prolonged illness or the complications of respiratory infections may be more common when NSAIDs are used — both respiratory or septic complications and cardiovascular complications.” He added: “The finding in two randomised trials that advice to use ibuprofen results in more severe illness or complications helps confirm that the association seen in observational studies is indeed likely to be causal. Advice to use paracetamol is also less likely to result in complications.”

Charlotte Warren-Gash, Associate Professor of Epidemiology at the London School of Hygiene and Tropical Medicine, said: “For COVID-19, research is needed into the effects of specific NSAIDs among people with different



underlying health conditions. In the meantime, for treating symptoms such as fever and sore throat, it seems sensible to stick to paracetamol as first choice."

Misguided drug advice for COVID-19¹²

The French Health Minister Olivier Véran claimed on Twitter that anti-inflammatory drugs such as ibuprofen or cortisone could aggravate the infection of COVID-19. However, scientific evidence does not indicate that nonsteroidal anti-inflammatory drug (NSAID) consumption puts patients who otherwise might have mild or asymptomatic infection by severe acute respiratory syndrome–coronavirus 2 (SARS-CoV-2) — the virus that causes COVID-19 — at risk of more severe disease. People taking NSAIDs for other reasons should not stop doing so for fear of increasing their COVID-19 risk. Given that the elderly appear to comprise the predominant at-risk group for severe COVID-19 at this time, an association between NSAIDs and the disease may merely reflect reverse causality — ie infection makes you more susceptible to adverse effects of NSAIDs on the infection.



SOURCES*

Produced by the members of the National Health Library and Knowledge Service Evidence Team.† Current as at 30 March 2020. This evidence summary collates the best available evidence at the time of writing. Emerging literature or subsequent developments in respect of COVID-19 may require amendment to the information or sources listed in the document. Although all reasonable care has been taken in the compilation of content, the National Health Library and Knowledge Service Evidence Team makes no representations or warranties expressed or implied as to the accuracy or suitability of the information or sources listed in the document. This evidence summary is the property of the National Health Library and Knowledge Service and subsequent re-use or distribution in whole or in part should include acknowledgement of the service.

The following PICO(T) was used as a basis for the evidence summary:

	COVID-19 PATIENTS
	IBUPROFEN

Resources consulted: WHO, ECDC, HPSC, NHS, HSE, BMJ Best Practice, EMA, FDA, UpToDate, EMBASE, Medline, Google Scholar and Google.

The following search strategy was used:

"covid-19" OR coronavirus OR "wuhan virus" OR "2019-ncov" OR "severe acute respiratory syndrome coronavirus 2" OR "2019 novel coronavirus" OR "2019 new coronavirus" AND ibuprofen (and all brand name variants)

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