

## GUIDANCE FROM THE CCS COVID-19 RAPID RESPONSE TEAM

March 20, 2020

### **UPDATED - COVID-19 and concerns regarding use of cardiovascular medications, including ACEi/ARB/ARNi, low-dose ASA and non-steroidal anti-inflammatory drugs (NSAIDs)**

*(French version to follow)*

The Canadian Cardiovascular Society and the Canadian Heart Failure Society make the following recommendations:

1. Patients taking an angiotensin-converting enzyme inhibitor (ACEi), angiotensin receptor blocker (ARB) or angiotensin receptor-neprilysin inhibitor (ARNi) for heart failure or hypertension should continue taking it unless otherwise advised by their physician.
2. **NEW March 20<sup>th</sup>** Patients with confirmed or suspected COVID-19 infection should not stop taking an ACEi/ARB/ARNi unless there is a compelling reason to do so (such as symptomatic hypotension or shock, acute kidney injury, or hyperkalemia).
3. **NEW March 20<sup>th</sup>** Patients taking low-dose acetylsalicylic acid (ASA, Aspirin™) for heart disease should continue taking it unless otherwise advised by their physician. This applies to children, adolescents and adults.
4. **NEW March 20<sup>th</sup>** Confirmed or suspected COVID-19 infection is **not** an indication to stop low-dose ASA.
5. **NEW March 20<sup>th</sup>** There is no clinical evidence regarding non-steroidal anti-inflammatory drugs (NSAIDs) use in patients with or at risk of COVID-19 infection; however, patients with heart failure or hypertension should preferentially choose acetaminophen over NSAIDs for fever or pain to avoid decompensation of these cardiovascular conditions.

### **Rationale**

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- There is no evidence that ACEi/ARB/ARNi or low-dose ASA increase risk of or susceptibility to COVID-19 infection.
- There is no evidence that ACEi/ARB/ARNi or low-dose ASA worsen outcomes in patients with confirmed or suspected COVID-19 infection.
- Cessation of ACEi/ARB/ARNi medications in stable patients with heart failure or hypertension can lead to uncontrolled hypertension and increased hospitalizations for heart failure with an unnecessary increase in health care utilization, exposing patients to risk of contracting the coronavirus, and straining valuable inpatient hospital resources.
- Cessation of low-dose ASA in stable patients with a valid indication for this therapy increases the risk of major cardiovascular events, including myocardial infarction, stroke or death, which would necessitate hospitalization.

## Background

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There are reports in the news and on social media that certain cardiovascular medications may increase the risk of COVID-19 infection or worsen outcomes in those with confirmed or suspected COVID-19 infections. On March 14<sup>th</sup>, a report from the French government reported that serious adverse events were noted among people with confirmed or suspected COVID-19 infection who took the NSAID ibuprofen. This message was spread further by the news and social media, with concerns extended to other NSAIDs, including acetylsalicylic acid (ASA). Importantly, this was based on unconfirmed anecdotes.

There is currently no clinical evidence regarding NSAID use (including ASA) in patients with or at risk of COVID-19 infection. There is insufficient mechanistic evidence for how NSAIDs, including ASA, would impact outcomes in COVID-19. One study in diabetic rats suggested that ibuprofen increases the expression of the angiotensin-converting enzyme-2 (ACE2) in myocardial tissue<sup>1</sup>. The COVID-19 virus (also known as SARS-CoV-2) is known to use ACE2 for entry into target cells<sup>2</sup>. Conversely, one study in dogs suggests that the NSAID indomethacin may have antiviral activity against the coronavirus responsible for the 2003 SARS outbreak<sup>3</sup>. It is important to stress that these are preclinical data only, and do not provide reliable guidance for clinical management.

## Additional resources

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- European Medicines Agency (EMA) press release from March 18, 2020 on NSAIDs for COVID-19: <https://www.ema.europa.eu/en/news/ema-gives-advice-use-non-steroidal-anti-inflammatories-covid-19> [accessed March 19 2020]
- Medscape article on NSAIDs in COVID-19: <https://www.medscape.com/viewarticle/926940> [accessed March 19 2020]
- World Health Organization (WHO) Official Twitter post from March 18, 2020 on ibuprofen in COVID-19: <https://twitter.com/WHO/status/1240409217997189128?s=20> [accessed March 19 2020]
- Preclinical evidence and recommendations on Acei, ARB, ARNi and COVID-19: <http://www.nephjc.com/news/covidace2>

## References

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1. Qiao W, Wang C, Chen B, et al. Ibuprofen attenuates cardiac fibrosis in streptozotocin-induced diabetic rats. *Cardiology*. 2015;131(2):97-106. doi:10.1159/000375362
2. Hoffmann M, Kleine-Weber H, Krüger N, Müller M, Drosten C, Pöhlmann S. The novel coronavirus 2019-nCoV uses the SARS-coronavirus receptor ACE2 and the cellular protease TMPRSS2 for entry into target cells. *bioRxiv*. January 2020:2020.01.31.929042. doi:10.1101/2020.01.31.929042
3. Amici C, Di Caro A, Ciucci A, et al. Indomethacin has a potent antiviral activity against SARS coronavirus. *Antivir Ther (Lond)*. 2006;11(8):1021-1030.

We will continue to provide updates as information becomes available.

Stay connected and stay healthy, to best support our patients.

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