

From the Chief Medical Officer
Dr Michael McBride



Department of
Health

An Roinn Sláinte

Mánnystrie O Poustie

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HSS(MD) 91/2020

FOR ACTION

Chief Executives of HSC Trusts/Health and Social Care Board/Public Health Agency
Chief Executive, RQIA (for distribution to independent hospitals)

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Our Ref: HSS(MD) 91/2020

Date: 23 December 2020

Dear Colleague

COVID-19 THERAPEUTIC ALERT – THERAPEUTIC ANTICOAGULATION (HEPARIN) IN THE MANAGEMENT OF SEVERE COVID-19 (SARS-CoV-2) POSITIVE PATIENTS

ACTIONS FOR HEALTHCARE PROFESSIONALS

Clinicians should:

Continue to follow the NICE COVID-19 rapid guideline: reducing the risk of venous thromboembolism in over 16s with COVID-19 ([link](#)). Further consideration should be given to managing the hypercoagulable state in patients receiving renal replacement therapy, clinical guidance remains the same ([link](#)).

HSC Trusts are asked to:

Ensure front line clinical teams and pharmacy teams are aware of the UK-wide recommendation that a therapeutic dose of heparin is not offered to COVID-19 positive patients unless otherwise eligible for anti-coagulation under standard indications, or as part of a clinical trial.

Summary

Therapeutic dose of either unfractionated heparin (UFH) or subcutaneous low molecular weight heparin (LMWH) should **not** be offered in the treatment of patients with COVID-19, unless there is a standard indication for therapeutic anti-coagulation, such as the acute management of acute deep vein thrombosis or pulmonary emboli, or as part of a clinical trial.

Continue to use pharmacological VTE prophylaxis in COVID-19 pneumonia, unless contraindicated, with a standard prophylactic dose (for acutely ill medical patients) of low molecular weight heparin (LMWH). See NICE guidance ([link](#)).

Further Information

Thromboprophylaxis with small doses of heparin (LMWH or UFH) reduces the rate of hospital-associated venous thromboembolism (VTE) in critically ill patients by about 50% (Alhazzani et al¹). However hospitalised patients with COVID-19 pneumonia requiring critical care admission (known as severe COVID-19 infection) appear to have high rates of hospital-associated VTE despite standard thromboprophylaxis. The inflammatory state of COVID-19 pneumonia results in a profound prothrombotic state, due to multiple mechanisms including cytokines leading to increased production of coagulation proteins by the liver (Levi & Hunt²).

REMAP-CAP (in collaboration with the ACTIV-4 and ATTACC trials) has reported that a therapeutic dose of heparin does not improve clinical outcome in the management of severe³ COVID-19 in the critical care setting, unless otherwise recommended for other indications. The trial compared outcomes for severe COVID-19 positive patients in critical care treated with either a therapeutic dose, or a prophylactic dose (in line with local guidelines) as standard of care. Recruitment to the branch of the REMAP-CAP trial evaluating therapeutic anticoagulation in severely ill patients has now been stopped, on the advice of their Data and Safety Monitoring Committee.

The research has found evidence of higher rates of major bleeding with therapeutic heparin than standard thromboprophylaxis.

The recommendation will be reviewed as further evidence becomes available, including from the moderate⁴ patient arm of the REMAP-CAP trial, which remains open to recruitment.

Product details

Heparin is available as either a solution for intravenous infusion (unfractionated), or a solution for injection (low molecular weight heparin, LMWH or unfractionated). NICE's COVID-19 guidance recommends consideration of an intermediate dose (twice prophylactic dose) of heparin in patients on advanced respiratory support (defined as any ventilatory support via an endotracheal or tracheostomy tube, or extracorporeal respiratory support). This is an off-label use, and guidance has not changed in light of these trial results.

¹ Heparin thromboprophylaxis in medical-surgical critically ill patients: a systematic review and meta-analysis of randomized trials. Alhazzani W, Lim W, Jaeschke RZ, Murad MH, Cade J, Cook DJ. **Crit Care Med**. 2013 Sep;41(9):2088-98. doi: 10.1097/CCM.0b013e31828cf104

² Thrombosis and coagulopathy in COVID-19: An illustrated review. Levi M, Hunt BJ. *Res Pract Thromb Haemost*. 2020 Jul 11;4(5):744-751. doi: 10.1002/rth2.12400. eCollection 2020 Jul

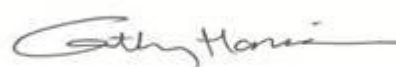
³ Severe state, defined within the REMAP-CAP trial as receiving organ failure support in an ICU

⁴ Moderate state, defined within the REMAP-CAP trial as either not being admitted to an ICU, or admitted to ICU but not receiving organ support

Yours sincerely



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MRS CATHY HARRISON
Chief Pharmaceutical Officer

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