

COVID-19 Therapeutic Alert

CEM/CMO/2020/042

23 December 2020

Therapeutic Anticoagulation (Heparin) in the Management of Severe COVID-19 (SARS-CoV-2 Positive) Patients

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 thromboses 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](#)).

Action

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](#)).

NHS acute trusts / health boards / hospitals 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.

Background Information

Thromboprophylaxis with small doses of heparin (LMWH or UFH) reduces the rates of hospital-associated venous thromboembolism (VTE) in critically ill patients by about 50% (Alhazzani et al¹). However hospitalised patients with COVID-19 pneumonia requiring

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

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 inflammatory 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 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 domain 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 subcutaneous injection (low molecular weight heparin 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 the guidance has not changed in light of the REMAP-CAP trial results.

Distribution

NHS Trusts (NHS boards in Scotland and Wales)
Regional Medical Directors
Regional Chief Pharmacists
Lead/Senior Pharmacists and Regional Procurement Pharmacy Leads
Trust/Hospital Medical Directors and Chief Pharmacists to circulate to medical, pharmacy and nursing staff managing COVID-19 patients

Enquiries

England

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 a ICU, or admitted to ICU but not receiving organ support

Enquiries from NHS trusts in England should in the first instance be directed to the trust pharmacy team who will escalate issues to the Regional Chief Pharmacist and national teams if required.

Further information can also be requested from the dedicated email address:
england.spoc-c19therapeutics@nhs.net.

Northern Ireland

Enquiries from hospitals in Northern Ireland should in the first instance be directed to your hospital pharmacy team who will escalate issues to the Regional Pharmaceutical Procurement Service or Pharmaceutical Directorate at the Department of Health if required. Further information can be obtained by contacting
RPHPS.Admin@northerntrust.hscni.net

Scotland

Enquiries from Scotland should in the first instance be directed to the Health Board Director of Pharmacy who will escalate issues to either NHS National Procurement or the Scottish Government's Medicines Policy Team if required. Contact should be made using the following emails: nss.nhssmedicineshortages@nhs.scot or medicines.policy@gov.scot

Wales

Enquiries in Wales should in the first instance be directed to the health board's Chief Pharmacist who will escalate issues to the Pharmacy and Prescribing Team at Welsh Government if required. Enquiries to the Welsh Government should be directed to:
COVID-19.Pharmacy.Prescribing@gov.wales.