



From the UK CMOs and Medical Director of NHS England.  
16 June 2020

CEM/CMO/2020/026

Dear colleagues,

### **Dexamethasone in COVID-19**

The RECOVERY trial in COVID-19 has provided initial results of the dexamethasone arm [https://www.recoverytrial.net/files/recovery\\_dexamethasone\\_statement\\_160620\\_final.pdf](https://www.recoverytrial.net/files/recovery_dexamethasone_statement_160620_final.pdf)

Dexamethasone 6 mg once per day (either by mouth or by intravenous injection) for ten days was compared with 4321 UK patients randomised to usual care alone. Dexamethasone reduced deaths by one-third in ventilated patients (rate ratio 0.65 [95% confidence interval 0.48 to 0.88];  $p=0.0003$ ) and by one fifth in other patients receiving oxygen only (0.80 [0.67 to 0.96];  $p=0.0021$ ).

There was no benefit among those patients who did not require respiratory support (1.22 [0.86 to 1.75;  $p=0.14$ ).

Normally we would advise waiting for the full paper before changing practice, to ensure final analysis and peer review do not lead to different conclusions. However, given this clear mortality advantage, with good significance, and with a well known medicine which is safe under these circumstances we consider it is reasonable for practice to change in advance of the final paper.

Please find more information below.

Best wishes,

Dr Frank Atherton  
Chief Medical Officer for  
Wales

Dr Gregor Smith  
Chief Medical Officer for  
Scotland

Dr Michael McBride  
Chief Medical Officer for  
Northern Ireland

Professor Stephen Powis  
National Medical Director  
NHS England and NHS  
Improvement

Professor Chris Whitty  
Chief Medical Officer for  
England

# COVID-19 Therapeutic Alert

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## **Dexamethasone in the treatment of COVID-19**

Implementation and management of supply for treatment in hospitals

### Summary

#### **For immediate action**

Dexamethasone has been demonstrated to have a clear place in the management of hospitalised patients with COVID-19.

There were no excess harms identified in using this dose of dexamethasone in this patient population. Dexamethasone was not used in pregnant women.

Clinicians should therefore consider dexamethasone for the management of hospitalised patients with COVID-19 who require oxygen or ventilation.

#### **Out of hospital treatment is not appropriate.**

There is no current or anticipated constraint on supply of the medicine in the UK.

### Clinical Guidance

The approach to utilisation of dexamethasone in COVID-19 is informed by the extensive experience of the use of the medicine for other indications and the information from the RECOVERY trial on the groups of patients where a clinical benefit was demonstrated.

Dexamethasone is therefore indicated for the treatment of COVID-19 infection for:

- Hospitalised patients
- COVID-19 (suspected or confirmed) in patients having oxygen therapy (see guide to oxygen therapy [link](#)), non-invasive or invasive ventilation, or ECMO
- Adults, the use in children is still being studied (the RECOVERY trial included children), currently the evidence of benefit in children is unproven
- In pregnancy or breastfeeding women, prednisolone 40 mg administered by mouth (or intravenous hydrocortisone 80 mg twice daily) should be used instead of dexamethasone.

The recommended dose schedule:

- For dexamethasone 2mg tablets: dosage three tablets once a day for 10 days
- For dexamethasone 2mg/5mL oral solution: dosage 15mL once a day for 10 days

- For dexamethasone 3.3mg/mL intravenous 1ml ampoules: dosage 1.8mL (5.94mg) once a day for 10 days
- Treatment should stop if discharged from hospital within the 10 days

For patients able to swallow and in whom there are no significant concerns about enteral absorption, tablets should be prescribed. IV administration should only be used where tablets or oral solution are not appropriate, or not available.

When prescribing dexamethasone consideration needs to be given to the gastric ulcer protection effect of proton pump inhibitors according to local hospital policy.

Coadministration of dexamethasone with remdesivir has not been studied (University of Liverpool COVID-19 Drug Interactions [link](#)). Dexamethasone is a substrate of CYP3A4 and a moderate inducer of this enzyme. Due to remdesivir's rapid clearance, although remdesivir inhibits CYP3A4 it is unlikely to have a significant effect on dexamethasone. However, dexamethasone can potentially reduce remdesivir concentrations due to induction of CYP3A4. Use with caution. Remdesivir is currently available as an EAMS ([link](#)).

## Medicine supply

Hospitals should use existing supplies including any remaining stock from the RECOVERY trial. If required, hospitals should order further stock from their usual supplier but do not order more than 2 weeks expected demand at a time.

Public Health England (PHE) holds a central stock of tablets (solid and soluble), solution and ampoules of dexamethasone which can be accessed if BAU stock is not available. Hospitals can register to receive this stock using the ImmForm ordering system. Those hospitals in Great Britain (excluding Northern Ireland), not already registered with PHE's ImmForm website (<https://portal.immform.phe.gov.uk/Logon.aspx?returnurl=%2f>) should do so.

Northern Ireland stock from PHE will be handled in the same way as NI centrally supplied vaccines, full details communicated in due course.

The supply situation will be closely monitored to ensure there continues to be sufficient stock available to meet needs.

## Data collection

### Safety reporting

Any suspected adverse drug reactions (ADRs) for patients receiving dexamethasone for this indication can be reported directly to the MHRA via the new dedicated COVID-19 Yellow Card reporting site at: <https://coronavirus-yellowcard.mhra.gov.uk/>

### Clinical Outcome reporting

The Deputy Chief Medical Officer recommends that data on all patients with COVID-19 should be captured through the ISARIC 4C Clinical Characterisation Protocol (CCP) case report forms (CRFs), as coordinated by the COVID-19 Clinical Information Network (CO-CIN) ([link](#) to forms).

## Action

### Clinical Teams should:

- work with their hospital chief pharmacist to secure readiness to offer the treatment with immediate effect;
- develop and implement local policies for the use of dexamethasone;

**Pharmacy leads (Regional Pharmacy Procurement Leads in England) should:**

- manage available supplies;
- work with hospitals who have stock holding beyond projected their demand to re-distribute this stock across their region.

**Trust/Hospital Chief Pharmacists should:**

- in England work with Regional Chief Pharmacists and Regional Pharmacy Procurement leads to manage stock appropriately;
- order stock according to guidance.

**Deadlines for actions**

- Actions underway: on receipt of this alert;
- Actions complete: as soon as possible.

**Supporting Information**

More detailed information can be found at the following locations:

The ISARIC 4C (Coronavirus Clinical Characterisation Consortium) can be found at:

<https://isaric4c.net/>

## Distribution

NHS Trusts (NHS boards in Scotland and Wales)

Regional Medical Directors

Regional Chief Pharmacists

Hospital Chief Pharmacists

Trust/hospital medical directors to circulate to medical and nursing staff managing COVID-19 patients.

## Enquiries

**England**

Enquiries from NHS trusts in England should in the first instance be directed to your trust pharmacy team who will escalate issues to the Regional Pharmacist and national teams if required. Any strategic issues please contact: [england.spo-c19therapeutics@nhs.net](mailto:england.spo-c19therapeutics@nhs.net).

**Northern Ireland**

Enquiries from hospitals in Northern Ireland should in the first instance be directed to your hospital pharmacy team.

**Scotland**

Enquiries from hospitals in Scotland should in the first instance be directed to your hospital pharmacy team who should escalate queries relating to supply to [NSS.NHSSMedicineShortages@nhs.net](mailto:NSS.NHSSMedicineShortages@nhs.net) and all other issues should be escalated to the Scottish Government's Medicines Policy Team using the email address - [CPO-COVID19@gov.scot](mailto:CPO-COVID19@gov.scot).

**Wales**

Enquiries from hospitals 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](mailto:COVID-19.Pharmacy.Prescribing@gov.wales).