Department of Health & Social Care

NHS

COVID-19 Therapeutic Alert

CEM/CMO/2021/003 28 January 2021

Antimicrobials (azithromycin and doxycycline) Not Beneficial in the Management of COVID-19 (SARS-CoV-2) Positive Patients

Recommendation

It is recommended that:

Azithromycin should NOT be used in the management of confirmed or suspected COVID-19 infection either within primary care or in hospitalised patients, unless there are additional indications for which its use remains appropriate (see Product Details).

Doxycycline should NOT be used in the management of confirmed or suspected COVID-19 infection within primary care, unless there are additional indications for which its use remains appropriate (see Product Details).

Supporting Evidence

Hospitalised Patients

Results of the RECOVERY trial, a randomised, controlled, open-label, adaptive platform trial, showed no significant clinical benefit of either oral or intravenous azithromycin in patients hospitalised with COVID-19. Compared with usual standard of care alone, azithromycin (administered once daily at 500mg either orally or intravenously, for up to 10 days) did not significantly decrease length of stay or 28-day mortality. In patients not receiving invasive mechanical ventilation at baseline, there was no difference between groups in the proportion of patients progressing to the composite endpoint of invasive mechanical ventilation or death.

Primary Care

After completing an interim analysis, the conclusion from the PRINCIPLE trial, a pragmatic, randomised, controlled, open-label platform trial in primary care, is that azithromycin (500mg administered once daily, for 3 days) offers no clinically meaningful beneficial effect compared to standard of care in patients aged over 50 who are treated at home in the early stages of COVID-19. There was no evidence that azithromycin reduced hospitalisation or death, compared to standard of care, and a low probability of a meaningful benefit in terms of self-reported time to recovery.

PRINCIPLE's interim analysis also concluded that doxycycline (administered as 200mg on the first day, followed by 100mg a day for 6 days) offered no meaningful beneficial effect compared to standard of care in patient aged over 50 who are treated at home in the early stages of COVID-19. There was no evidence of a clinically meaningful benefit in terms of both time to recovery and hospital admission.

Action

NHS acute trusts / health boards / hospitals are asked to:

Ensure front line medical, nursing clinical and pharmacy teams are aware of the UK-wide recommendation that azithromycin should NOT be used in the management of COVID-19 in hospitalised patients, unless there are other licensed indications for which its use remains appropriate. Azithromycin may otherwise continue to be prescribed within the licensed indications (below), within NICE and other associated guidelines.

General practices are asked to:

Ensure that the local primary care team is aware that antimicrobials should NOT be used in the primary management of COVID-19 infection, unless there are other licensed indications for which its use remains appropriate. Azithromycin or doxycycline may otherwise continue to be prescribed within the licensed indications (below), within NICE and other associated guidelines.

Product Details

Azithromycin and doxycycline continue to be indicated in the treatment of infections when known, or likely, to be due to one or more susceptible micro-organisms, such as: acute bacterial sinusitis, acute bacterial otitis media, pharyngitis, tonsillitis, acute exacerbation of chronic bronchitis, community acquired pneumonia, skin and soft tissue infections, uncomplicated *Chlamydia trachomatis* urethritis and cervicitis.

Consideration should be given to official guidance regarding the appropriate use of antimicrobials before either azithromycin or doxycycline is prescribed.

Antimicrobial Stewardship

NICE has published guidelines on the use of antimicrobials for community-acquired pneumonia in the community and in hospitalised patients during COVID-19. These can be found at https://www.nice.org.uk/guidance/ng165 and https://www.nice.org.uk/guidance/ng173

Inappropriate antibacterial use contributes to the development of antimicrobial resistance, and opportunistic healthcare-associated infections such as Clostridium (*Clostridioides) difficile* infection.

Distribution

General Practice
Community Pharmacies
ICS /STP and Clinical Commissioning Group Pharmacy Leads
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
Enquiries from general practice and community pharmacy should in the first instance be directed to the local clinical commissioning group.

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 general practice and community pharmacy should in the first instance be directed to your local HSCB office.

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.