Department of Health & Social Care

The Scottish Government
Riaghaltas na h-Alba

Llywodraeth Cymru
Welsh Government

Department of Health
An Roinn Sláinte
Männystrie O Poustie

NHS

Rapid policy statement

Interim Clinical Commissioning Policy: Remdesivir for patients hospitalised with COVID-19 (adults and children 12 years and older)

Introduction

In response to the public health emergency posed by coronavirus disease 2019 (COVID-19), NHS England, working with the Devolved Administrations (DAs), has established a rapid policy development process to aid clinicians in offering best care and advice to patients with or at risk of COVID-19 across the UK. This document sets out the interim clinical commissioning position for the use of remdesivir for patients with COVID-19.

Commissioning position

The proposal is: remdesivir is recommended to be available as a treatment option through routine commissioning for hospitalised patients (adults and children 12 years and older) with COVID-19 according to its licence and in accordance with the criteria set out in this document.

Equality statement

Promoting equality and addressing health inequalities are at the heart of the four nations' values. Throughout the development of the policies and processes cited in this document, we have:

- Given due regard to the need to eliminate discrimination, harassment and victimisation, to advance equality of opportunity, and to foster good relations between people who share a relevant protected characteristic (as cited under the Equality Act 2010 or equivalent equality legislation) and those who do not share it; and
- Given regard to the need to reduce inequalities between patients in access to and outcomes from healthcare services and to ensure services are provided in an integrated way where this might reduce health inequalities.

Plain language summary

COVID-19 is a disease caused by a coronavirus (named SARS-CoV-2) causing many different symptoms, the most common being fever, loss of sense of taste and smell and cough. COVID-19 has spread rapidly throughout the world, with countries imposing a range of restrictions on daily life to help reduce the spread of the disease. Remdesivir (given intravenously) is an anti-viral medicine which has been shown to improve recovery time for some hospitalised patients. Remdesivir can be used to treat people with COVID-19 in hospital according to its licence and in line with this policy.

Overview

The condition

COVID-19 manifests predominantly as a respiratory illness, of widely varying clinical severity. At the most severe end of the spectrum COVID-19 results in severe pneumonia and respiratory failure with the need for mechanical ventilation. Hyperinflammatory states leading to organ dysfunction beyond the respiratory tract, have also been well described.

Intervention

Remdesivir is an adenosine nucleotide prodrug that is metabolised intracellularly to form the pharmacologically active substrate remdesivir triphosphate. Remdesivir triphosphate inhibits SARS-CoV-2 RNA polymerase which perturbs viral replication. Remdesivir is given intravenously, once daily after an initial loading dose. Reported adverse effects include transaminase elevations, infusion related reactions (hypotension, nausea, vomiting, diaphoresis) and drug hypersensitivity (www.ema.europa.eu). Additional adverse events may become more apparent with more widespread use.

Clinical problem

There is a rapidly evolving pandemic globally, with countries facing different stages of the spread of disease. Initial hospital data from UK suggest that increasing age over 50 years is a strong predictor of mortality in hospital (hazard ratio 4.02 for 50–69 years, 9.6 for 70–79 years and 13.6 for 80 years or over: Docherty et al. 2020). Children and young people appear to be less affected by the virus, with low numbers of deaths and critical care admissions in this age group (Lu et al. 2020). UK primary care record data from 17.4 million patients showed that death in hospital from COVID-19 was strongly associated with male gender, older age, Black or Asian ethnicity, deprivation, uncontrolled diabetes and hypertension (Williamson et al. 2020). As of 18th June 2020, the Intensive Care National Audit Research Centre (ICNARC) was notified of 12,573 admissions for critical care with confirmed COVID-19 in England, Wales and Northern Ireland (ICNARC 2020). Patients in hospital with COVID-19 are treated with supportive care, though there are several ongoing clinical trials assessing medical treatments. Dexamethasone has recently been shown to be effective in some circumstances.

Evidence summary

An evidence review conducted by the National Institute for Health and Care Excellence (NICE) suggested some benefit with remdesivir compared with placebo for reducing supportive measures – including mechanical ventilation – and reducing time to recovery in patients with mild, moderate or severe COVID-19 disease who are on supplemental oxygen treatment (https://www.nice.org.uk/advice/es27/evidence).

Implementation

Eligibility criteria

Patients will be eligible for treatment with remdesivir in accordance with the product licence (www.ema.europa.eu). Eligibility criteria within the Remdesivir Summary of Product Characteristics (SmPC) include:

- Hospitalised with coronavirus disease 2019 (COVID-19)[1]
- With pneumonia requiring supplemental oxygen
- Adults, and adolescents ≥ 12 years of age and ≥ 40 kg
- eGFR ≥ 30ml/min
- Alanine Aminotransferase (ALT) below 5 times the upper limit of normal at baseline

Additional criteria

In times of limited supply,[2] **additional criteria** will be necessary in order to allocate remdesivir to those with the greatest capacity to benefit (patients in the earlier stages of respiratory failure[3]). In this context the following criteria must also be met:

- At the time of decision to treat with remdesivir patients should not be receiving ongoing mechanical ventilation or ECMO. Patients who present with an initial rapid deterioration can, however, be considered for treatment with remdesivir.
- Multi-disciplinary team assessment[4] should determine if patients not suitable for escalation would benefit from initiation of treatment with remdesivir.[5]
- If patients on remdesivir require escalation, continuation of the drug should be considered by multi-disciplinary team assessment.

Pregnancy

Remdesivir should be avoided in pregnancy unless clinicians believe the benefits of treatment outweigh the risks to the individual (please see SmPC for further information).

Dose

The recommended dosage is a single loading dose of remdesivir 200mg intravenously on day 1, followed by a once daily maintenance dose of remdesivir 100 mg for the remainder of the treatment course. The total duration of treatment should be at least 5 days and not more than 10 days.

Monitoring

Renal and liver function should be monitored carefully during treatment with remdesivir as clinically appropriate.

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[1] In the absence of a confirmed virological diagnosis, remdesivir should only be used when a multidisciplinary team have a high level of confidence that the clinical and radiological features suggest that COVID-19 is the most likely diagnosis.

[2] A supply disruption alert will be issued when there is limited supply of remdesivir.

[3] Remdesivir is unlikely to improve clinical outcome in people who appear clinically to be in the recovery phase of the illness, or those who have required mechanical ventilation or ECMO for a number of days and do not have ongoing evidence of high viral burden or ongoing viral replication, nor have advanced immunosuppression that may put them at risk of reactivation (COVID-19 Therapeutics Advice & Support Group (CTAG) https://www.ctag-support.org.uk/).

[4] A multi-disciplinary team (for COVID-19) should normally include representation from a minimum of three clinicians with appropriate expertise. Recommended areas of clinical expertise include respiratory medicine, critical care, general medicine or infectious diseases.

[5] Members of the multi-disciplinary team should consult the most recent available evidence to identify individuals most likely to benefit from treatment with remdesivir.

Stopping criteria
Remdesivir should be discontinued in patients who develop **any** of the following:

- ALT ≥ 5 times the upper limit of normal during treatment with remdesivir (remdesivir may be restarted when ALT is < 5 times the upper limit of normal)
- ALT elevation accompanied by signs or symptoms of liver inflammation or increasing conjugated bilirubin, alkaline phosphatase, or international normalised ratio (INR)
- eGFR <30 mL/min

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

Remdesivir in combination with dexamethasone
Dexamethasone should be considered in the management of hospitalised adult patients with COVID-19. There is no interaction of remdesivir with dexamethasone expected. For further information please visit the University of Liverpool COVID-19 Drug Interactions website (https://www.covid19-druginteractions.org/checker) and see the SmPC for remdesivir (www.ema.europa.eu).

Governance

Data collection requirement
Provider organisations in England should register all patients using prior approval software (alternative arrangements in Scotland, Wales and Northern Ireland will be communicated) and ensure monitoring arrangements are in place to demonstrate compliance against the criteria as outlined.

Clinical outcome reporting
Hospitals managing COVID-19 patients are encouraged to submit data through the ISARIC 4C Clinical Characterisation Protocol (CCP) case report forms (CRFs), as coordinated by the COVID-19 Clinical Information Network (CO-CIN) (https://isaric4c.net/protocols/).

Effective from
This policy will be in effect from 3rd July 2020.

Policy review date
This is an interim rapid clinical policy statement, which means that the full process of policy production has been abridged: public consultation has not been undertaken. This policy may need amendment and updating if, for instance, new trial data emerges, supply of the drug changes, or a new evidence review is required. A NICE Technology Appraisal or Scottish Medicines Consortium (SMC) Health Technology Assessment or All Wales Medicines Strategy Group (AWMSG) appraisal of remdesivir for COVID-19 would supersede this policy when completed.

Definitions

COVID-19	Refers to the disease caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) virus.
Mechanical ventilation	A life support treatment which helps people breathe when they are not able to breathe enough on their own.
Extra Corporeal Membrane Oxygenation	A life support machine for people who have a severe and life-threatening illness that stops their heart or lungs from working properly.

References

Docherty, A.B., Harrison, E.M., Green, C.A., Hardwick, H.E., Pius, R., Norman, L., Holden, K.A., Read, J.M., Dondelinger, F., Carson, G., Merson, L., Lee, J., Plotkin,D., Sigfrid, L., Halpin, S., Jackson, C., Gamble, C., Horby, P.W., Nguyen-Van-Tam, J.S., Dunning, J., Openshaw, P.J.M., Baillie K., Semple, M.G. Features of 16,749 hospitalised UK patients with COVID-19 using the ISARIC WHO Clinical Characterisation Protocol. Available at https://www.medrxiv.org/content/10.1101/2020.04.23.20076042v1. Accessed online 28th April 2020.

ICNARC 2020 ICNARC report on COVID-19 in critical care 19 June 2020. https://www.icnarc.org/Our-Audit/Audits/Cmp/Reports. Date Accessed on 23rd June 2020.

Lu, X., Zhang, L., Du, H., Zhang, J., Li, Y.Y., Qu, J., Zhang, W., Wang, Y., Bao, S., Li, Y., Wu, C., Liu, D., Shao, L., Peng, X., Yang, Y., Liu, Z., Xiang, Y., Zhang, F., Silva, R.M., Pinkerton, K.E., Shen, K., Xiao, H., Xu, S., Wong, G.W.K., Chinese Pediatric Novel Coronavirus Study Team (2020) SARS-CoV-2 infection in children. New England Journal of Medicine. March 18, 2020 Online ahead of print. DOI: 10.1056/NEJMc2005073.

Williamson, E., Walker, A.J., Bhaskaran, K.J., Bacon, S., Bates, C., Morton, C.E., Curtis, H.J., Mehrkar, A., Evans, D., Inglesby, P., Cockburn, J., Mcdonald, H.I.M., MacKenna, B., Tomlinson, L., Douglas, I.J., Rentsch, C.T., Mathur, R., Wong, A., Grieve, R., Harrison, D., Forbes, H., Schultze, A., Croker, R.T., Parry, J., Hester, F., Harper, S., Perera, R., Evans, S., Smeeth, L., Goldacre, B. OpenSAFELY: factors associated with COVID-19-related hospital death in the linked electronic health records of 17 million adult NHS patients. Available online. Accessed on 26th May medRxiv 2020.05.06.20092999; https://doi.org/10.1101/2020.05.06.20092999