NIHR | Innovation Observatory

Newcastle University

Health Technology Briefing
June 2023

Dapsone for treating COVID-19

Company/Developer	Pulmonem Inc.

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 36559	NICE TSID: Not Available	UKPS ID: Not Available

Licensing and Market Availability Plans

Currently in phase III clinical trials.

Summary

Dapsone is currently in clinical development for the treatment of COVID-19. COVID-19 is an infectious respiratory disease caused by the severe acute respiratory syndrome-coronavirus 2, SARS-CoV-2. The main symptoms of COVID-19 infection are fever, a new continuous cough, and loss of taste or smell. In some patients, COVID-19 may result in severe complications such as acute respiratory distress syndrome, blood clotting, acute heart or kidney injury, and sepsis. Hospitalisation and death rates amongst COVID-19 patients remains high. There is a need to develop additional treatments to improve prognosis and reduce the burden on healthcare services.

Dapsone is a unique reformulation of a safe and affordable generic anti-inflammatory drug. Dapsone arrests the development of inflammation caused by COVID-19 infection, preventing the excessive immune reaction that is the most frequent cause of worsening symptoms and complications requiring hospitalisation. Dapsone is administered orally and efficiently absorbed in the gastrointestinal tract, and is therefore suitable for outpatient settings. If licenced, dapsone will provide an additional treatment option for COVID-19 in high-risk patients with comorbidity.

Proposed Indication

Treatment of COVID-19 in elderly adults and adults aged 40 years and older with high-risk comorbidity.[1]

Technology

Description

Dapsone (Diaminodiphenyl sulfone; PULM-001) is a sulfone class of medication that inhibits the binding of neutrophils to IgA. Since the adherence to IgA by neutrophils is a prerequisite for their activation that subsequently leads to tissue destruction, dapsone thus prevents tissue destruction by blocking the neutrophil binding to IgA on the target tissue, in addition to other anti-inflammatory effects.[2] Dapsone also inhibits cytotoxic extremely active myeloperoxidase hydrogen superoxide-halogen compound and the respiratory burst of highly toxic oxygen compounds thereby preventing further tissue damaged.[3]

Dapsone is currently in clinical development for the treatment of COVID-19 in high-risk group of elderly adults and adults over 40 years with comorbidity. In the phase III clinical trial (DAP-CORONA; NCT04935476), patients received 85mg of oral dapsone tablet twice a day for 21 days.[1]

Key Innovation

Dapsone is a reformulation of a safe and affordable generic anti-inflammatory drug that has been around for decades, used to treat inflammatory infections. Dapsone arrests the development of inflammation caused by COVID-19 infection, preventing the excessive immune reaction that is the most frequent cause of worsening symptoms and complications requiring hospitalisation. Dapsone has well-documented metabolic, pharmacokinetic and toxicological profiles; is well distributed to the fluid of the alveolar spaces in the lung; and is efficiently absorbed (70% to 80%) via the gastrointestinal tract and is therefore suitable for outpatient settings.[4] It is the only known inflammasome competitor that stops activity at the brain stem level and therefore stops brain stem initiated respiratory arrest.[5] In a recent clinical study, a significant difference was observed in the treatment of patients in the onset stage of Acute Respiratory Distress Syndrome (ARDS). The mortality rates at the ARDS onset stage were 0% with dapsone administered as a standard COVID-19 treatment and 40% without dapsone administered as a standard COVID-19 treatment.[6]

If licenced, dapsone will provide an additional option for the treatment of elderly adults and adult patients aged 40 years and over with high-risk comorbidity.

Regulatory & Development Status

Dapsone has Marketing Authorisation in the UK/EU for the following indications:[7]

- As part of a multi-drug regimen in the treatment of all forms of leprosy.
- Treatment of dermatitis herpetiformis and other dermatoses.
- Prophylaxis of malaria in combination with pyrimethamine.
- Prophylaxis of pneumocystis carinii pneumonia in immunodeficient subjects, especially AIDS patients.

Dapsone is currently in phase III/II clinical development for the following indications:[8]

- Isolated skin vasculitis
- Neoplasms
- Dementia
- Acne vulgaris

Patient Group

Disease Area and Clinical Need

Coronaviruses are a large family of related viruses that cause diseases in animals and humans. Some cause less severe disease, such as the common cold, and others cause more severe disease.[9] COVID-19 is an infectious coronavirus disease caused by the virus SARS-CoV-2.[10] COVID-19 transmission occurs when an infected person breathes out droplets and small particles that contain the virus. These droplets and particles spread to other people through the eyes, nose or mouth. Transmission can also occur by touching surfaces contaminated with the virus.[11] The main symptoms of COVID-19 include: fever; a new and continuous cough; anosmia (loss of smell); and ageusia (loss of taste). Other symptoms may include: shortness of breath; loss of appetite; myalgia (muscle ache); sore throat; headache; nasal congestion; diarrhoea, nausea and vomiting.[9] In some patients, the infection may result in severe disease with complications including acute respiratory distress syndrome, venous thromboembolism, acute myocardial or kidney injury, and sepsis.[12] The risk of severe disease and death from COVID-19 is higher in people who are older, male, from deprived areas, or from certain non-white ethnic backgrounds. Certain underlying health conditions, as well as obesity may also increase the risk of severe disease and deaths in adults.[9]

As of May 2023, there have been 20,814,517 confirmed cases of COVID-19 in England, of which, 19,260,634 are thought to be first episodes, and 1,553,937 are possible reinfection cases. In the 7-day period ending on 06/05/2023, there were 9,675 COVID-19 cases in England which resulted in case rate of 17.1 per 100,000 of the population.[13] In the week ending 19 March 2023, the overall hospital admission rate in England for patients with confirmed COVID-19 was 10.62 per 100,000.[14] In the week ending 17 March 2023 there were 512 registered deaths in England involving COVID-19, and in the same week COVID-19 accounted for 4.5% of registered deaths in the UK.[15]

Recommended Treatment Options

NICE currently recommends the following therapeutic options for COVID-19 patients:[16]

- Nirmatrelvir plus ritonavir in adults who do not need supplemental oxygen for COVID-19 and have an increased risk for progression to severe COVID-19.
- Sotrovimab in adults and young people aged 12 years and over who weigh at least 40kg, do not need supplemental oxygen, have an increased risk for progression to severe COVID-19, and nirmatrelvir plus ritonavir is contraindicated or unsuitable.
- Dexamethasone, or either hydrocortisone or prednisolone when dexamethasone cannot be used or is unavailable, to people with COVID-19 who need supplemental oxygen or have a level of hypoxia that needs supplemental oxygen but who are unable to tolerate it.
- Tocilizumab in adults who are having systemic corticosteroids and need supplemental oxygen or mechanical ventilation.

Clinical Trial Information

Trial	**DAP-CORONA,** NCT04935476; A randomised, placebo-controlled, multicentre study to assess the safety and efficacy of dapsone for the treatment of COVID-19 positive patients **Phase III** - Recruiting **Location(s):** Canada, USA **Primary completion date:** March 2022
Trial Design	Randomised, parallel assignment, triple masking, placebo-controlled

Population	N= 3000 (estimated); aged 40 years and over; symptomatic non-hospitalised adult patients with confirmed COVID-19 for at least 24 hours and no more than 7 days; with a concomitant comorbidity
Intervention(s)	Oral dapsone tablet 85mg twice daily for 21 days in addition to standard of care
Comparator(s)	Standard of care with placebo
Outcome(s)	Primary outcome measure: Composite outcome: All cause pre-hospitalization death or all-cause hospitalization [time frame: 30 days post randomisation] Number of participants requiring hospitalization or die prior to hospitalization in the first 30 days after randomisation. See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Estimated Cost

Dapsone 50mg and 100mg are already marketed in the UK.[17] However, the cost of dapsone 85mg tablet is not yet known.

Relevant Guidance

NICE Guidance

- NICE technology appraisal guidance in development GID-TA10721. Remdesivir for treating COVID-19 [ID3808]. Expected date of issue to be confirmed.
- NICE technology appraisal guidance in development GID-TA11297. Molnupiravir, remdesivir and tixagevimab plus cilgavimab for treating COVID-19 [ID6261]. Expected date of issue to be confirmed.
- NICE technology appraisal guidance in development GID-TA11227. Vilobelimab for treating COVID-19 [ID 11815]. Expected date of issue to be confirmed.
- NICE technology appraisal guidance in development GID-TA1124. Ensitrelvir for treating COVID-19 [ID 11813]. Expected date of issue to be confirmed.
- NICE technology appraisal guidance in development GID-TA1126. Sabizabulin for treating COVID-19 [ID 11814]. Expected date of issue to be confirmed.
- NICE technology appraisal guidance in development (GID-TA11324). Nirmatrelvir plus ritonavir for treating COVID-19 (Partial Rapid Review of TA878) [ID6262]. Expected date of issue to be confirmed.
- NICE technology appraisal. Casirivimab plus imdevimab, nirmatrelvir plus ritonavir, sotrovimab and tocilizumab for treating COVID-19 (TA878). March 2023. Updated April 2023.
- NICE COVID-19 rapid guideline. Managing COVID-19 (NG191). March 2023.
- NICE COVID-19 rapid guideline. Vitamin D (NG187). July 2022.

NHS England (Policy/Commissioning) Guidance

- NHS England. Interim clinical commissioning policy: Remdesivir and molnupiravir for non-hospitalised patients with COVID-19. May 2023
- NHS England. Interim Clinical Commissioning Policy: Treatments for non-hospitalised patients with COVID-19. November 2022.
- NHS England. Acute use of non-steroidal anti-inflammatory drugs (NSAIDs) in people with or at risk of COVID-19. April 2020 (last updated 2022)

Other Guidance

- World Health Organisation (WHO). Therapeutics and COVID-19: Living guideline. 2020 (Last updated January 2023).[18]
- European Respiratory Society. Management of hospitalised adults with coronavirus disease 2019 (COVID-19): A living guideline. 2021 (last updated 2022).[19]
- European Society of Clinical Microbiology and Infectious Diseases: Guidelines for coronavirus disease 2019: an update on treatment of patients with mild/moderate disease. 2022.[20]

Additional Information

Pulmonem Inc. did not enter information about this technology onto the UK PharmaScan database; the primary source of information for UK horizon scanning organisations on new medicines in development. As a result, the NIHR Innovation Observatory has had to obtain data from other sources. UK PharmaScan is an essential tool to support effective NHS forward planning; allowing more effective decision making and faster uptake of innovative new medicines for patients who could benefit. We urge pharmaceutical companies to use UK PharmaScan so that we can be assured of up-to-date, accurate and comprehensive information on new medicines.

References

1 Clinicaltrials.gov. *A Randomized, Placebo-Controlled, Multicenter Study to Assess the Safety and Efficacy of Dapsone for the Treatment of COVID-19 Positive Patients.* Available from: https://clinicaltrials.gov/ct2/show/NCT04935476 [Accessed 12 May 2023].

2 Nguyen VT, Chan L. *Dapsone: A Century-Old Medicine and a New Hope for Severe COVID-19*. 2022. Available from: https://www.scirp.org/journal/paperinformation.aspx?paperid=115135 [Accessed 12 May 2023].

3 Electronic Medicine Compendium (emc). *Dapsone 100mg Tablets: Pharmacodynamic properties.* Available from: https://www.medicines.org.uk/emc/product/11869/smpc [Accessed 16 May 2023].

4 Pulmonem. *Innovative Medical Solutions for COVID-19.* 2023. Available from: https://www.pulmonem.ca/en/ [Accessed 15 May 2023].

5 Pulmonem. *Delivering a COVID-19 Therapeutic in Record Time*. 2021. Available from: https://static1.squarespace.com/static/61d4d043bad77a1898bc81a2/t/61d8a6d499d16054

c118bb4f/1641588439144/Pulmonem_Corporate_Presentation_Dec_2021_GDS.pdf [Accessed 17 May 2023].

6 Kanwar B, Lee CJ, Lee J-H. Specific Treatment Exists for SARS-CoV-2 ARDS. *Vaccines*. 2021;9(6):635. https://www.mdpi.com/2076-393X/9/6/635.

7 Electronic Medicine Compendium (emc). *Dapsone 100mg: Therapeutic indication.* Available from: https://www.medicines.org.uk/emc/product/11736/smpc [Accessed 15 May 2023].

8 Clinicaltrials.gov. *Dapsone's current phase II/III clinical development: Indications.* Available from: https://clinicaltrials.gov/ct2/results?cond=&term=&intr=Dapsone&cntry=&state=&city=&dist=&recrs=a&recrs=b&recrs=d&recrs=f&phase=1&phase=2 [Accessed 15 May 2023].

9 UK Health Security Agency. *COVID-19: epidemiology, virology and clinical features.* 2022. Available from: https://www.gov.uk/government/publications/wuhan-novel-coronavirus-background-information/wuhan-novel-coronavirus-epidemiology-virology-and-clinical-features [Accessed 12 May 2023].

10 World Health Organisation (WHO). *Coronavirus disease (COVID-19)*. 2023. Available from: https://www.who.int/health-topics/coronavirus#tab=tab_1 [Accessed 12 May 2023].

11 Centre for Disease Control and Prevention (CDC). *How COVID-19 Spreads*. 2022. Available from: https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/how-covid-spreads.html [Accessed 12 May 2023].

12 National Institute for Health and Care Excellence (NICE). *Coronavirus-COVID-19.* Available from: https://cks.nice.org.uk/topics/coronavirus-covid-19/ [Accessed 12 May 2023].

13 GOV.UK. *Coronavirus (COVID-19) cases in the UK*. 2023. Available from: https://coronavirus.data.gov.uk/details/cases?areaType=nation&areaName=England [Accessed 12 May 2023].

14 Office for National Statistics (ONS). *Coronavirus (COVID-19) latest insights.* 2023. Available from: https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/articles/coronaviruscovid19/latestinsights.

15 Office for National Statistics (ONS). *Coronavirus (COVID-19) latest insights: Deaths*. 2023. Available from: https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/articles/coronaviruscovid19latestinsights/deaths.

16 National Institute for Health and Care Excellence (NICE). *COVID-19 rapid guideline: managing COVID-19*. Available from: https://www.nice.org.uk/guidance/ng191 [Accessed 12 May 2023].

17 British National Formulary (BNF). *Dapsone*. Available from: https://bnf.nice.org.uk/drugs/dapsone/ [Accessed 16 May 2023].

18 World Health Organisation (WHO). *Therapeutics and COVID-19: Living guideline, 13 January 2023*. 2023. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-therapeutics-2023.1 [Accessed 16 May 2023].

19 Chalmers JD, Crichton ML, Goeminne PC, Cao B, Humbert M, Shteinberg M, et al. Management of hospitalised adults with coronavirus disease 2019 (COVID-19): a European Respiratory Society living guideline. *European Respiratory Journal*. 2021;57(4):2100048. Available from: https://doi.org/10.1183/13993003.00048-2021.

20 Bartoletti M, Azap O, Barac A, Bussini L, Ergonul O, Krause R, et al. European society of clinical microbiology and infectious diseases guidelines for coronavirus disease 2019: an update on treatment of patients with mild/moderate disease. *Clinical Microbiology and Infection*. 2022;28(12):1578-90. Available from: https://doi.org/10.1016/j.cmi.2022.08.013.

NB: This briefing presents independent research funded by the National Institute for Health and Care Research (NIHR). The views expressed are those of the author and not necessarily those of the NHS, the NIHR or the Department of Health.