



<b>Early Access to Medicines Scientific Opinion-Public Assessment Report</b>	
<b>Product</b>	<b>Remdesivir 100 mg powder for concentrate for solution for infusion Remdesivir 100 mg concentrate for solution for infusion</b>
<b>Condition</b>	<b>SARS-CoV-2 infection and severe disease</b>
<b>Full indication</b>	<b>Remdesivir is indicated for the treatment of adults and adolescent patients aged <math>\geq 12</math> years and weighing at least 40 kg hospitalised with suspected or laboratory confirmed SARS-CoV-2 infection and severe disease. Patients with severe disease are those with an <math>SpO_2 \leq 94\%</math> on room air or requiring supplemental oxygen or requiring non-invasive or invasive ventilation or extracorporeal membrane oxygenation (ECMO).</b>
<b>Company</b>	<b>Gilead Sciences Ltd.</b>
<b>EAMS number</b>	<b>11972/0001 Remdesivir 100 mg powder for concentrate for solution for infusion and 11972/0002 Remdesivir 100 mg concentrate for solution for infusion</b>
<b>EAMS Scientific opinion date</b>	<b>26<sup>th</sup> May 2020</b>

The aim of the Early Access to Medicines Scheme (EAMS) is to provide earlier availability of promising new unlicensed medicines and medicines used outside their licence, to UK patients that have a high unmet clinical need. The MHRA scientific opinion provides benefit and risk information to physicians who may wish to prescribe the EAMS medicine under their own responsibility. More information about the scheme can be found here:

<http://www.mhra.gov.uk/Howweregulate/Innovation/EarlyaccesstomedicinesschemeEAMS/index.htm>

The scientific opinion is based on assessment of the information supplied to the MHRA on the benefits and risks of the medicine. As such this is a scientific opinion and should not be regarded as a medicine licensed by the MHRA or a future commitment by the MHRA to license such a medicine, nor should it be regarded as an authorisation to sell or supply such a medicine. A positive scientific opinion is not a recommendation for use of the medicine and should not be interpreted as such. Under EAMS the risk and legal responsibility for prescribing a 'special' remains with the physician, and the opinion and EAMS documentation published by the MHRA are intended only to inform physicians' decision making and not to recommend use. An EAMS scientific opinion does not affect the civil liability of the manufacturer or any physician in relation to the product. Whilst the scientific opinion is for use of the product to treat COVID-19, the opinion has been issued under EAMS and is not an exceptional authorisation or recommendation in response to the pandemic.

The General Medical Council's guidance on prescribing unlicensed medicines can be found here:

[https://www.gmc-uk.org/guidance/ethical\\_guidance/14327.asp](https://www.gmc-uk.org/guidance/ethical_guidance/14327.asp)

### **What is Remdesivir?**

Remdesivir is a medicine with broad-spectrum antiviral activity. Antiviral drugs are a group of medicines used for treating viral infections.

This medicine is available in the following pharmaceutical forms:

A powder for concentrate for solution for infusion which is reconstituted with sterile water for injection and diluted into infusion fluids prior to intravenous (IV) administration (into the patient's vein).

A concentrate for solution for infusion intended to be diluted into infusion fluids prior to intravenous (IV) administration (into the patient's vein).

### **What is Remdesivir used to treat/diagnose/prevent?**

Remdesivir is indicated for the treatment of adults and adolescent patients hospitalised with suspected or laboratory confirmed COVID-19 infection and severe disease. Remdesivir can help the patient's body to overcome the viral infection and may help them get better faster.

COVID-19 is an acute viral infection caused by a virus called SARS-CoV-2, coronavirus, and was first detected in Wuhan, China, in December 2019. The infection causes respiratory illness and spreads readily from person to person. Common signs of infection include fever, cough, shortness of breath, breathing difficulties, and other respiratory symptoms. In severe cases, COVID-19 can cause pneumonia, acute lung injury (ALI) including severe acute respiratory distress syndrome (ARDS), kidney failure, and death.

### **How is Remdesivir used?**

Remdesivir will be given to a patient with COVID-19 by a nurse or doctor in hospital, as a drip into a vein (an *intravenous infusion*) lasting 30 to 120 minutes, once a day.

### **The recommended dose for adults and adolescent patients (12 years of age and older) weighing 40 kg or more is:**

- a single starting dose of 200 mg on day 1
- then daily doses of 100 mg starting on day 2.

### **How long a course of treatment lasts depends on how unwell the patient is:**

- patients not on a ventilator (breathing machine) will be given remdesivir every day for a total 5 days but this can be extended to 10 days
- patients on a ventilator and/or on ECMO (*extracorporeal membrane oxygenation*, when blood is circulated out of the body to receive oxygen) will be given remdesivir every day for a total of 10 days.

Treatment with remdesivir does not stop people from passing the COVID-19 virus on to others, and it does not prevent infection with the virus. The patient will still need to be in isolation during their treatment.

If the patient is prescribed remdesivir, they will be given blood tests before treatment starts and will have blood tests every day during their treatment. These tests are done to check for kidney or liver problems.

### **How does Remdesivir work?**

Remdesivir acts by preventing a viral enzyme from functioning properly and thereby impairs the ability of the virus to replicate. It has a relatively broad spectrum of activity that includes several types of coronaviruses, among them SARS-CoV-2, the virus causing COVID-19.

### **How has Remdesivir been studied?**

The effects of remdesivir have been studied in several clinical studies. Pharmacokinetic (PK) data in healthy adult human subjects are available from 4 Phase 1 studies in which 138 healthy subjects have been dosed with remdesivir. The studies were designed to evaluate the safety and tolerability, PK, metabolism, and excretion of remdesivir compared with placebo.

### **What benefits and risks has Remdesivir shown during these studies?**

#### **Benefits**

In a COVID-19 clinical study remdesivir treatment reduced the time to recovery overall and in the subgroup with severe disease when given at a dose of 200mg/ on day 1 followed by a maintenance dose of 100mg/ day for a total treatment duration of 10 days. Given the high number of cases of COVID-19, and the high case fatality rate of those with severe disease, the favourable effects of remdesivir on the time of recovery in patients with severe disease are considered relevant and clinically meaningful.

### *Risks*

Like all medicines, remdesivir may cause side effects, although not everybody gets them. The main concern regarding the unfavourable effects are adverse hepatic (toxic to the liver) effects.

Commonly observed unfavourable effects included nausea and constipation, which are thought to affect tolerability.

Remdesivir has not been studied in the paediatric population with COVID-19 and there are currently limited safety data.

In summary, the MHRA considers the benefit risk balance of remdesivir in the treatment of COVID-19 to be positive for adult and adolescent patients with severe COVID-19. This evaluation takes into account the threat and risk posed by the ongoing COVID-19 pandemic to patients and public health.

### **Why has Remdesivir been given a positive Early Access to Medicine Scientific opinion?**

COVID-19 is an acute viral infection affecting primarily the respiratory tract. In most patients the disease is relatively mild, but in some patients it can become severe and even lead to death. This is particularly the case for certain groups of people such as the elderly and those with an underlying illness. No specific treatment for COVID-19 is currently available and there is an urgent unmet need for the treatment of pandemic COVID-19. Early results from clinical studies have shown that remdesivir reduced the time of recovery from 15 days to 11 days in patients with severe COVID-19 and possibly also reduced the proportion of people dying from COVID-19. The risks associated with remdesivir can be managed and do not outweigh the benefits.

Therefore, remdesivir is being made available for the treatment of hospitalized patients with severe COVID-19 disease.

### **Are there on-going clinical studies?**

There are several clinical studies ongoing where remdesivir is investigated as a treatment, some of which are sponsored by the company and others by third parties but supported by the company.

### **What measures are in place to monitor and manage risks?**

A risk management plan (RMP) has been developed to ensure that remdesivir is used as safely as possible. Based on this plan, the Company that makes remdesivir must ensure that all healthcare professionals expected to use the medicine, as well as patients, are provided with information on the medicine including possible side effects and recommendations for preventing or minimising the impact of side effects.

Information will be collected about patients before they enter the scheme and while they are being treated with the medicine to help to monitor side effects in patients being treated with remdesivir. Healthcare professionals will be asked by the Company to report side effects experienced by patients receiving remdesivir through the scheme. These safety data will be reviewed and reported to the MHRA on a regular basis by the Company.

Healthcare professionals will receive an information pack and training prior to commencement of patient treatment.

**Other information about Remdesivir – see EAMS Treatment Protocol**