Medicines & Healthcare products Regulatory Agency

MHRA

EAMS 11972/0001 Remdesivir 100 mg powder for concentrate for solution for infusion

Early Access to Medicines Scheme – Treatment protocol – Information for patients

Introduction

The aim of the Early Access to Medicines Scheme (EAMS) is to provide earlier availability of promising new unlicensed medicines (medicines that do not have a marketing authorisation or are used outside their licence) to UK patients that have a high unmet clinical need. The medicines included in the scheme are those that are intended to treat, diagnose or prevent seriously debilitating or life-threatening conditions where there are no adequate treatment options. More information about the scheme can be found here:
http://www.mhra.gov.uk/Howweregulate/Innovation/EarlyaccesstomedicinesschemeEAMS/index.htm

The information below is intended for you, the patient, and is provided by the pharmaceutical company (called scientific opinion holder) that manufactures the EAMS medicine. This medicine, which does not yet have a drug licence or is used outside its licence, may also be used in combination with other medicines. are intended only to inform physicians' decision making and not to recommend use. More information about medicines licensing can be found here:
http://www.nhs.uk/conditions/medicines-information

This medicine can be prescribed for individual patients to meet specific needs provided they are given sufficient information about the medicine to make an informed decision. The physician will be responsible for giving you all the information you need to make this decision and for obtaining informed consent from you prior to treatment. You will be asked to sign a form to confirm that you are providing informed consent to receiving the EAMS treatment. Information on consent can be found here:
https://www.nhs.uk/conditions/Consent-to-treatment

The information below is provided to help you decide with the physician on whether to use the EAMS medicine and helps explain how to use it in accordance with the pharmaceutical company's instructions for safe and proper use. 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 the medicine 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 information below may change during the time you are using the medicine if more data become available. The physician will highlight to you any changes that you need to be aware of.

Whilst you are using this medicine, data will be collected on the use and safety profile of the medicine, to ensure that the benefits of taking the medicine continue to outweigh any potential risks. The physician will answer all your questions during and after the treatment and will provide you with contact details that you should use in case of any events or problems.

Each patient enrolled in the scheme will continue to receive the EAMS product until the end of the treatment in line with prescribing and NHS guidance and as long as benefit is seen. In rare cases where the EAMS treatment may not be available anymore, your physician will discuss other options with you.

Information for the patient

Remdesivir 100 mg powder for concentrate for solution for infusion
remdesivir

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or nurse.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What remdesivir is and what it is used for

Remdesivir is an anti-virus medicine used to treat COVID-19. The active substance is remdesivir.

COVID-19 is caused by a virus called a coronavirus. Remdesivir can help your body to overcome the virus infection and may help you get better faster.

More about remdesivir
This medicine will be given in hospital to people with COVID-19. It will be given to adults and adolescent patients aged ≥ 12 years and weighing at least 40 kg. It will be given by a doctor or nurse, as a drip into a vein (an *intravenous infusion*), once a day. The treatment will last 10 days for patients who are on a ventilator, or on ECMO (*extracorporeal membrane oxygenation*, when blood is circulated out of the body to receive oxygen). The treatment will last 5 days for patients who are not being ventilated, but this can be extended to a total of 10 days.

Remdesivir is a new treatment. It has been tested in other people, but it may have effects that are not yet known. You must talk to a doctor if you do not feel better or if you feel worse during treatment.

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

It is your choice to be treated or not with remdesivir. If you decide not to have it, or to stop it at any time, it will not change your standard medical care.

Talk to your doctor if you are not sure about taking remdesivir. They will help you to understand the alternatives and decide if it is right for you.

2. What you need to know before you are given remdesivir

You will not usually be given remdesivir:

- **if you are allergic** to remdesivir, or any of the other ingredients of this medicine (listed in section 6)
- **if suffer from severe kidney problems** and have a creatinine clearance level of <30 mL/min or require renal replacement therapy (RRT)
- **if you have severe liver problems** and suffer from significantly increased liver enzymes (elevated transaminases)

➔ **Talk to a doctor or nurse as soon as possible,** if this applies to you.

Warnings and precautions
Talk to your doctor or nurse before starting on remdesivir about anything on this list:

- **if you have kidney problems**. Some people with moderate kidney problems (creatinine clearance level of <50 mL/min) may not be given this medicine. The doctor will do blood tests before starting treatment to check whether you can be given it safely.

- **if you have liver problems**. If you suffer from moderate liver problems (increased liver enzymes) you may not be given this medicine. Some people developed increased liver enzymes when given remdesivir. The doctor will do blood tests before starting treatment to check whether you can be given it safely.

- **if you are pregnant or breast-feeding**. Talk to a doctor or nurse if you are pregnant (or you might be), or if you are breast-feeding. See *Pregnancy and breast-feeding*, below.

- **if you have any serious illnesses**. People of all ages with severe chronic medical conditions like heart disease, lung disease and diabetes seem to be at higher risk from COVID-19.

- **if you are taking any other medicines.** This includes prescription, over-the-counter, vitamins or herbal products. See *Other medicines and remdesivir*, below.

Blood tests before and during treatment
If you are prescribed remdesivir, you will be given blood tests before treatment starts. Patients being treated with remdesivir will have blood tests every day during their treatment. These tests are to check for kidney or liver problems. See *Possible side effects*, below.

Paediatric patients: Children and adolescents
Remdesivir has not been tested in children, so it is not yet known exactly how safe or effective it will be for them. This medicine is only to be given to adolescents from the age of 12 years and older who weigh 40 kg or more, in the same dosage as adults.

Other medicines and remdesivir
Tell your doctor or nurse about any other medicines you are taking, or have recently taken. This includes prescription, over-the-counter, vitamins or herbal products. It is not yet known exactly how remdesivir affects every other medicine, or is affected by them.

The remdesivir infusion will not be given in the same drip as any other medicines.

Pregnancy and breast-feeding
Tell your doctor or nurse if you are pregnant, or if you might be. There is not enough information to be sure that remdesivir is safe for use in pregnancy. Remdesivir will only be given if the potential benefit justifies the potential risk to the mother and the unborn child.

Tell your doctor or nurse if you are breast-feeding. It is not yet known whether remdesivir passes into human breast milk. Breast-feeding is not recommended while receiving remdesivir.

Remdesivir contains a cyclodextrin
This medicine contains 3 g Betadex (E459) in each 100 mg dose of remdesivir (6 g in the starting dose). Betadex is a *cyclodextrin emulsifier* that helps the medicine to disperse in the body.

3. How remdesivir is given

Remdesivir will be given to you in hospital, by a nurse or doctor, 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 aged ≥ 12 years and 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 you are:

- Patients **not on a ventilator** 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**.

If you are given more or less remdesivir than you should be
As remdesivir is only used in hospital, it is unlikely that you will be given too much or too little. If you have been given an extra dose, or missed one, **tell your nurse or doctor straight away**.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. Because this is a new medicine, there may be other side effects that are not yet known.

Very common side effects
(these may affect more than 1 in 10 patients)
- Blood tests may show an increase in liver enzymes, called *transaminases.*

Other side effects are possible
(not known how many people are affected)
- The side effects of getting any medicine by vein are brief pain, bleeding, bruising, soreness, swelling and infection where the needle enters.

Reporting of side effects
- If you notice any side effects, **talk to your doctor or nurse**. This includes any possible side effects not listed in this leaflet. You can also report side effects via the dedicated COVID-19 Yellow Card reporting site at coronavirus-yellowcard.mhra.gov.uk. By reporting side effects, you can help provide more information on the safety of the medicine.

5. How to store remdesivir

This medicine will usually be stored in the hospital pharmacy.

- **Before use,** store vials of remdesivir powder below 30°C until the day they are needed.

- **Once prepared,** the medicine should be used immediately. If necessary, vials of reconstituted remdesivir or bags of infusion solution can be stored for up to 4 hours at room temperature (20°C to 25°C), or up to 24 hours in a fridge (2°C to 8°C). Do not leave more than 24 hours between reconstitution and administration.

Keep this medicine out of the sight and reach of children.

See *Instructions for healthcare professionals*, below.

6. Contents of the pack and other information

What remdesivir contains
- The active substance is remdesivir. Each vial contains 100 mg remdesivir for reconstitution and dilution for infusion.
- **The other ingredient** is Betadex sulfobutyl ether sodium (E459).

What remdesivir looks like and contents of the pack
Remdesivir 100 mg powder for concentrate for solution for infusion is a sterile, preservative-free powder that is to be reconstituted with 19 mL of Sterile Water for Injection and diluted into 0.9% saline prior to administration by intravenous infusion. It is supplied in a single-dose clear glass vial.

The appearance of the powder is white to off-white to yellow.
Remdesivir is available in cartons containing 1 vial.

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The following information is intended for healthcare professionals only.

Instructions for healthcare professionals

REMDESIVIR
100 mg powder for concentrate for solution for infusion

Each single-dose vial contains 100 mg of remdesivir as a white to off-white to yellow powder for reconstitution and dilution.

Summary of treatment

Remdesivir should be administered by intravenous infusion in 0.9% saline over 30 to 120 minutes.

The recommended dose for adults and adolescent patients aged ≥ 12 years and 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.

The recommended treatment duration:

- Patients **not on a ventilator** will be given remdesivir **every day for a total of 5 days but this can be extended to 10 days**.

- Patients **on a ventilator** and/or on **ECMO** will be given remdesivir **every day for a total of 10 days**.

The powder must be reconstituted and then diluted with saline under aseptic conditions. Administer the infusion immediately or as soon as possible after preparation.

All patients must have their liver function and creatinine clearance checked before starting treatment and then daily. Serum chemistries, haematology, ALT, AST, bilirubin and alkaline phosphatase must also be checked daily.

Monitor the patient for side effects during and after the infusion. See below for details on reporting of side effects.

Adults and adolescent patients weighing 40 kg or more
Reconstitute the powder - adults and adolescent patients (12 years of age and older) weighing 40 kg or more:
Remove the required number of single-use vial(s) from storage. For each vial:
- Aseptically reconstitute remdesivir powder for concentrate for solution for infusion by addition of 19 mL of Sterile Water for Injection using a suitably sized syringe and needle per vial.
    - Discard the vial if a vacuum does not pull the Sterile Water for Injection into the vial.
- Immediately shake the vial for 30 seconds.
- Allow the contents of the vial to settle for 2 to 3 minutes. A clear solution should result.
- If the contents of the vial are not completely dissolved, shake the vial again for 30 seconds and allow the contents to settle for 2 to 3 minutes. Repeat this procedure as necessary until the contents of the vial are completely dissolved.
- Following reconstitution, each vial contains 100 mg/20 mL (5 mg/mL) of remdesivir concentrate for solution for infusion.
- Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.
- After reconstitution, the total storage time before administration (including any time before or after dilution into intravenous infusion fluids) should not exceed 4 hours at room temperature (20°C to 25°C) or 24 hours at refrigerated temperature (2°C to 8°C).

Dilute the concentrate for solution for infusion - adults and adolescent patients (12 years of age and older) weighing 40 kg or more:
Care should be taken to prevent inadvertent microbial contamination. As there is no preservative or bacteriostatic agent present in this product, aseptic technique must be used in preparation of the final parenteral solution. It is always recommended to administer IV medication immediately after preparation when possible
- Using Table 1, determine the volume of 0.9% saline to withdraw from the infusion bag.

Table 1: Recommended dilution instructions - remdesivir powder for concentrate for solution for infusion in adults and adolescent patients (12 years of age and older) ≥ 40 kg

Remdesivir dose	0.9% saline infusion bag volume to be used	Volume of saline to be withdrawn and discarded from 0.9% saline infusion bag	Required volume of reconstituted remdesivir concentrate for solution for infusion
200 mg (2 vials)	250 mL	40 mL	2 × 20 mL
	100 mL	40 mL	2 × 20 mL
100 mg (1 vial)	250 mL	20 mL	20 mL
	100 mL	20 mL	20 mL

- Withdraw the required volume of saline from the bag using an appropriately sized syringe and needle. Discard the saline that was withdrawn from the bag.
- Withdraw the required volume of reconstituted remdesivir concentrate for solution for infusion from the remdesivir vial using an appropriately sized syringe per Table 1.
- Discard any unused portion remaining in the remdesivir vial.
- Transfer the required volume of reconstituted remdesivir concentrate for solution for infusion to the selected infusion bag.
- Gently invert the bag 20 times to mix the solution in the bag. Do not shake.
- The prepared solution is stable for 4 hours at room temperature (20°C to 25°C) or 24 hours in the refrigerator (2°C to 8°C) (including any time before dilution into intravenous infusion fluids).

Administer the infusion - adults and adolescent patients (12 years of age and older) weighing 40 kg or more:

Remdesivir should be infused over 30 to 120 minutes as described in Table 2. After infusion is complete, flush with at least 30 mL of 0.9% saline. Discard any unused remdesivir powder for concentrate for solution for infusion, and diluted solution for infusion. Do not administer as an intramuscular (IM) injection.

The prepared diluted solution should not be administered simultaneously with any other medication. The compatibility of remdesivir solution for infusion with IV solutions and medications other than 0.9% saline is not known.

Table 2: Recommended rate of infusion— for reconstituted and diluted remdesivir powder for concentrate for solution for infusion in adults and adolescent patients (12 years of age and older) ≥ 40 kg

Infusion bag volume	Infusion time	Rate of infusion
250 mL	30 min	8.33 mL/min
	60 min	4.17 mL/min
	120 min	2.08 mL/min
100 mL	30 min	3.33 mL/min
	60 min	1.67 mL/min
	120 min	0.83 mL/min

Monitor and report side effects

Monitor the patient for side effects during and after the infusion.

Report side effects via the national reporting system.

Store remdesivir safely

- **Before use,** store remdesivir vials below 30°C until they are required.
- Remdesivir powder appears white to off-white to yellow.
- **Once prepared,** the medicine should be used immediately. If necessary, vials of reconstituted remdesivir or bags of infusion solution can be stored for up to 4 hours at room temperature (20°C to 25°C), or up to 24 hours in a fridge (2°C to 8°C). Do not leave more than 24 hours between reconstitution and administration.

Do not reuse or save remdesivir infusion solution for future use. Partially used reconstituted remdesivir or diluted solution for infusion should be discarded. This product contains no preservative.

Scientific Opinion Holder

Gilead Sciences Limited
280 High Holborn
London
WCIV 7EE

Manufacturer

Gilead Sciences Ireland UC
Carrigtohill
County Cork, T45 DP77
Ireland

This protocol was revised in May 2020

Additional Information

Patient data to be collected
Patient data collected during the scheme are mostly used for safety surveillance and cannot replace a proper clinical trial to support a marketing authorisation. These data are required by the MHRA to help verify that the patient's condition complies with the EAMS indication and help interpret the side effects and other events occurring during and after the EAMS treatment.

Contact information

Details for reporting safety data:

- Email: Safety_FC@gilead.com
- Tel: +44 1223 897 500
- Fax: +1 650 522 5477

General Medical Information enquiries:

- Email: UKMed.Info@gilead.com
- Tel: 08000 113 700