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MINISTRY OF HEALTH
Palackého náměstí 375/4, 128 01 Prague 2

Prague, 24 April

2020

Ref. No. MZDR 17280/2020-

3/OLZP

MZDRX01A1HLU

DECISION

The Ministry of Health, as the competent administrative authority pursuant to Section 11(a) of Act No. 378/2007 Coll., on Pharmaceuticals and on the amendment of certain related laws (hereinafter referred to as the “Act on Pharmaceuticals”), as amended, has decided on the following measure:

In the interest of protecting public health in relation to the current spread of the originator of the disease, the SARS-CoV-2 coronavirus which causes the COVID-19 disease, and in order to ensure the availability of medicinal products important to providing medical care, the Ministry of Health in accordance with Section 8(6) of the Act on Pharmaceuticals

temporarily permits

the distribution, dispensing and use of the unregistered human medicinal product **REMDESIVIR (GS-5734) 100 mg, concentrate for infusion solution, lagena 20 ml and REMDESIVIR (GS- 5734) 100 mg, powder for concentrate for infusion solution, lagena 30 ml, manufacturer: Gilead Sciences, Ireland UC, IDA Business & Technology Park, Carrigtohill, Co. Cork, Ireland**, whose exterior and interior packaging is in the English language in the version for clinical evaluation (hereinafter referred to as

the “medicinal product REMDESIVIR:).

The following conditions must be fulfilled for the distribution, dispensing and use of the said medicinal product REMDESIVIR:

1. The medicinal product REMDESIVIR is designated for the treatment of adult patients and children over 12 years of age with a body weight of over 40 kg, who require artificial lung ventilation. These are patients with an already confirmed COVID-19 infection (PCR method) or patients who have been in contact with a confirmed case of COVID-19 disease and are awaiting the results of testing (PCR method). Treatment using the medicinal product REMDESIVIR may only be commenced upon hospitalisation.
2. Distribution of the medicinal product REMDESIVIR in the Czech Republic is ensured by Gilead Sciences Limited, 280 High Holborn, London, Great Britain.
3. The medicinal product REMDESIVIR will only be supplied to pharmacies which supply the following workplaces:
 - *Nemocnice Na Bulovce, Budínova 67/2, 180 81 Prague 8 - Libeň,*
 - *Fakultní nemocnice v Motole, V Úvalu 84, 150 06 Prague 5,*
 -- *Všeobecná fakultní nemocnice v Praze, U Nemocnice 499/2, 128 08 Prague 2, . .*
 -- *Fakultní nemocnice u sv. Anny v Brně, Pekařská 53, 656 91 Brno..... ..*
4. Gilead Sciences s.r.o. will provide the healthcare service providers listed in paragraph 3 with information about the procedure for ordering the medicinal product REMDESIVIR and will ensure that the attending physicians have the current version of the document • *Instructions for preparing and administering Remdesivir* and specialised information in the scope of the *Investigator's Brochure*.
5. The distributor is obliged to inform the Institute about performed deliveries of the medicinal product REMDESIVIR to the healthcare facilities at latest within 48 hours from delivery of the product, via marketreport@sukl.cz. The report includes information about the date of the performed delivery, form of medication, number of packages of the product, batch, and name of the healthcare facility to which the product was delivered.
- 6. The dispensing of the medicinal product REMDESIVIR requires a doctor's prescription.**
7. The attending physicians are obliged to become familiar with the *Instructions for preparing and administering Remdesivir* and the specialised information in the scope of the *Investigator's Brochure*, and to proceed accordingly during

treatment.

8. Healthcare service providers are ordered to ensure the patient's informed consent (or that of the legal guardian) to the use of the non-registered medicinal product REMDESIVIR.
9. The attending physician is ordered to report any negative side effects in accordance with Section 93b(1) of the Act on Pharmaceuticals, and any other negative side effects which occur in connection to the administration of the non-registered medicinal product, in the same manner as per Section 93b(1) of the Act on Pharmaceuticals.

• **This measure is effective for 8 months from the date of its posting on the official bulletin of the Ministry of Health.**

Rationale:

On 21 April 2020, the Ministry received a request from Gilead Sciences s.r.o., registered office at Na strži 1702/65, Nusle, 140 00 Prague 4, Company ID No. 24268551 (hereinafter "Gilead Sciences"), concerning the further decision of the Ministry of Health, under which the Ministry of Health in accordance with Section 8(6) of the Act on Pharmaceuticals may temporarily permit the distribution, dispensing and use of the unregistered human medicinal product REMDESIVIR.

On 23 April 2020, the Ministry received a submission from Gilead Sciences, by which the original request of 21 April 2020 was amended in terms of the patients for whom the product is intended and the change of one workplace where the product should be administered to patients to treat the COVID-19 disease.

In order to accelerate access to the unregistered human medicinal product REMDESIVIR for patients suffering from severe COVID-19 disease, Gilead Sciences has shifted from individual compassionate use, which was approved by decision of the Ministry of Health on 17 March 2020, Ref. No. MZDR 12059/2020-3/OLZP, to an extended access program (EAP).

On 24 April 2020, the Ministry called on the State Drug Control Institute (hereinafter the "Institute") to submit an expert opinion on the relevant request from Gilead Sciences, in the meaning of Section 8(6) of the Act on Pharmaceuticals.

• On 24 April 2020, the Ministry received the Institute's expert opinion Ref. No. sukII02742/2020 on the requested matter. In terms of the decisive facts, the Institute stated in the part of its opinion titled 1. Subject of the request, that it agrees with the

conclusions of the *Assessment Report on compassionate use* of the Committee for Medicinal Products for Human Use of the European Medicines Agency, in that the benefits of using the medicinal product REMDESIVIR outweigh the risks within compassionate use. The known risks of the product are similar to the risks of using other antivirals. The safety of administration to humans was tested in clinical studies, albeit for a different indication (ebola). In the absence of other effective treatment of COVID-19 disease, the effectiveness and safety for the purposes of this program may be deemed adequately proven.

In the conclusion of its expert opinion, the Institute stated that considering the fact that the medicinal product REMDESIVIR does not have any alternative on the Czech market, it is a matter of procuring a medicinal product to treat a serious health condition, and therefore the Institute recommended permitting the use of the medicinal product REMDESIVIR whilst observing the aforementioned conditions.

Upon assessment of the expert references and given the expert opinion of the Institute, the Ministry states the following:

In connection with the adverse development of the epidemiological situation in terms of the occurrence of the COVID-19 disease caused by the new coronavirus designated as SARS-CoV-2 in Europe, it is necessary to ensure the availability of the medicinal product REMDESIVIR in the Czech Republic.

The Ministry has already permitted the distribution, dispensing and use of the unregistered medicinal product REMDESIVIR under the decision dated 17 March 2020, Ref. No. MZDR 12059/2020-3/OLZP. Because Gilead Sciences, in order to accelerate access to the unregistered human medicinal product REMDESIVIR for patients suffering from severe COVID-19 disease, has shifted from individual compassionate use, which was approved within the above-mentioned decision, to an extended access program (EAP), the issuing of another decision by the Ministry is required.

The extended access program was approved by the Committee for Medicinal Products for Human Use of the European Medicines Agency (EMA) - *Assessment Report on compassionate use of the Remdesivir dated 3 April 2020* (Procedure No. EMEA/H/K/5622/CU <https://www.ema.europa.eu/en/news/ema-provides-recommendations-compassionate-use-remdesivir-covid-19>), and should enable the collection of data from all treated patients.

The Assessment Report of the Committee for Medicinal Products for the Human Use of the European Medicines Agency (EMA) states that *Remdesivir* is a nucleotide prodrug, which is intercellularly metabolized on the adenosine triphosphate analog, which inhibits viral RNA polymerase and has a broad spectrum of effect against filoviruses (e.g. ebola

virus, Marburg virus), coronaviruses (e.g. SARS coronavirus, MERS coronavirus) and paramyxoviruses (e.g. RSV, Nipah virus, Hendra virus). Remdesivir has proven antiviral activity against the SARS-CoV and MERS-CoV disease in animal models.

The manufacturer of the medicinal product REMDESIVIR responsible for releasing the batches of both medicinal forms to EEA countries is Gilead Sciences Ireland UC, IDA Business & Technology Park, Carrigtohill, Co. Cork, Ireland. The product is not registered in any country, and at present six clinical trials of the product are underway in several countries around the world, including Germany, Italy, Spain, Denmark, France, the Netherlands, Sweden and Great Britain.

The conditions stated in the decision were stipulated by the Ministry of Health in order to ensure the safety of the used medicinal product REMDESIVIR, in particular because this medicinal product is not registered in any country and only limited data exists about its safety and the efficacy of its use.

Given the fact that this is a medicinal product which has no alternative on the market in the Czech Republic, and the matter concerns the procurement of a medicinal product to treat serious health conditions, the Ministry of Health temporarily permits the distribution, dispensing and use of the medicinal product REMDESIVIR, while fulfilling the conditions specified above, for a period of 8 months from the posting of this measure on the official bulletin of the Ministry of Health. This period is stipulated based on the unforeseeable development of the COVID-19 epidemiological situation. When handling



this medicinal product, it is necessary to observe the provisions of the Act on Pharmaceuticals, with the exception of the foregoing particularities. <

prof. MUDr. Roman Prymula, CSc., Ph. D.
Healthcare Deputy

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