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

Prague, 29 April 2020

Ref. No. MZDR 18092/2020-2/OLZP

MZDRX01A3EW6

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 Medicinal Products

temporarily permits

the distribution, dispensing and use of the non-registered human medicinal product

HYDROXYCHLOROQUINE SULFATE TABLETS, USP 200 MG

(hydroxychloroquine sulfate) coated tablets, 100X200 MG

Producer: Sandoz Inc., Princeton, NJ 08540, New Jersey, USA,

the packaging of which is in the English language (hereinafter the "medicinal product HYDROXYCHLOROQUINE-SULFATE SANDOZ").

The following conditions are stipulated for the distribution, dispensing and use of the medicinal product HYDROXYCHLOROQUINE-SULFATE SANDOZ:

1. **The medicinal product HYDROXYCHLOROQUINE-SULFATE SANDOZ is designated for treating patients in the Czech Republic with proven COVID-19 infection, exclusively within the framework of hospitalisation.** Use in this case applies also to the provisioning of the patient with the necessary quantity of the medicinal product HYDROXYCHLOROQUINE-SULFATE SANDOZ upon concluding hospitalisation or when transferring the patient to another healthcare service provider pursuant to Section 5(8)(a)(2) of the Act on Pharmaceuticals.
2. Sandoz s.r.o., registered office at Na Pankráci 1724/129, 140 00 Prague 4 - Nusle, Company ID No. 41692861 (hereinafter "Sandoz") is obliged to submit to the State

Electronic signature - 30 April 2020
Signature author's certificate:
Name: Eva Sadílková
Issued by: PostSignum Qualified
29.10.2020 12:06:26-000 +01

Institute for Drug Control the certificates for other batches of the medicinal product HYDROXYCHLOROQUINE SULFATE SANDOZ, if they are distributed to the Czech Republic, and are not the batches: JM2447, JM2448, JM2449, JN2545, even before they are marketed, to the address marketreport@sukl.cz .

3. The distribution of the medicinal product HYDROXYCHLOROQUINE-SULFATE SANDOZ in the Czech Republic is ensured by:
   - **Movianto Česká republika s.r.o.,** registered office at Podolí 78e, 664 03 Podolí, Company ID No. 63479010.
4. Sandoz will provide the information leaflet for the medicinal product HYDROXYCHLOROQUINE SULFATE SANDOZ in the Czech language to the distributor, who will submit the information leaflet to the pharmacy with the delivery.
5. The medicinal product HYDROXYCHLOROQUINE-SULFATE SANDOZ will only be supplied by the distributor to pharmacies which supply providers of inpatient bed care.
6. The distributor is obliged to inform the Institute about performed deliveries of the medicinal product HYDROXYCHLOROQUINE-SULFATE SANDOZ to healthcare facilities at latest within 48 hours from delivery of the product, via marketreport@sukl.cz. The report will include information about the date of delivery, number of product packages, batch and name of the healthcare facility to which the product was delivered.
7. **The dispensing of the medicinal product HYDROXYCHLOROQUINE-SULFATE SANDOZ requires a doctor's prescription (request).** The product can be dispensed only at the workplace of the inpatient bed care provider ensuring the treatment of patients hospitalised and proven to have the COVID-19 disease.
8. Healthcare services providers are ordered to ensure the **patient's informed consent** (or that of the legal guardian) with the use of the non-registered medicinal product HYDROXYCHLOROQUINE-SULFATE SANDOZ.
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 HYDROXYCHLOROQUINE SULFATE SANDOZ, 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 26 March 2020, the Ministry of Health called on the State Drug Control Institute (hereinafter referred to as the "Institute") to submit an expert opinion pursuant to Section 8(6) of the Act on Pharmaceuticals, concerning non-registered medicinal products which contain the active substances *hydroxychloroquine.*

On 28 April 2020, the Ministry of Health received the expert opinion from the Institute, dated 27

April 2020, Ref. No. sukll04892/2020, for the medicinal product HYDROXYCHLOROQUINE SULFATE SANDOZ. In the introduction to its opinion, the Institute observed that in its decision of 7 April 2020, Ref. No. MZDR 13360/2020-3/OLZP, the Ministry of Health had already permitted the distribution, dispensing and use of the non-registered medicinal product HYDROXYCHLOROQUINE-SULFAAT TEVA. However, the number of packages of the medicinal product HYDROXYCHLOROQUINE-SULFAAT TEVA is limited (approximately 330 packages of 30 coated tablets each) and given the unpredictable development of the number of patients with COVID-19 disease, it is not presently possible to estimate the sufficient number of packages required for their treatment. In its opinion on ensuring another medicinal product with the active substance *hydroxychloroquine*, the Institute stated that the quality and safety of the non-registered medicinal product HYDROXYCHLOROQUINE SULFATE SANDOZ is substantiated by its registration in the USA, and constitutes the securing of a medicinal product to treat a serious health condition. With regard to the foregoing, the Institute recommended permitting the use of the non-registered medicinal product HYDROXYCHLOROQUINE SULFATE SANDOZ while observing the conditions stipulated by it.

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

In connection to the global spread of the SARS-CoV-2 coronavirus, which causes the COVID-19 disease, there is currently a high demand for certain medicinal products, which either reduce the symptoms of the given disease or may be expected to be beneficial in treating the COVID-19 disease, although these medicinal products are registered for the treatment of other diseases. These medicinal products include medicinal products which contain the active substance *hydroxychloroquine.* The effectiveness of the *hydroxychloroquine* in treating COVID-19 disease has not yet been sufficiently proven, and its used is based on the document *Recommended procedure for treating COVID-19*.

The active substance *hydroxychloroquine* suppresses the overproduction of cytokine within the “cytokine storm”, which causes the very serious course of the disease with damage to a number of vital organs. Furthermore, the active substance *hydroxychloroquine* raises the pH in endosomes, lysosomes and the Golgi apparatus, whereas endosomes are important in the process of the virus’ penetration into the cell. It also disrupts the glycosylation of angiotensin which converts type 2 enzyme (ACE2), a membrane protein through which the virus binds itself to the target cells; hence, it blocks the penetration of the virus into the cells on two levels.

V In the Czech Republic, the medicinal product PLAQUENIL, which contains the active substance *hydroxychloroquine sulfate,* is registered and marketed. Based on the summary of product characteristics, this medicinal product is indicated to treat adults suffering from systemic lupus erythematosus, discoid lupus erythematosus, rheumatoid arthritis and photodermatosis. In the pediatric population, the medicinal product PLAQUENIL is indicated in treating juvenile idiopathic arthritis (in combination with other treatment), discoid and systemic lupus erythematosus. Other indications for the medicinal product PLAQUENIL are the prevention and treatment of acute attacks of malaria caused by *Plasmodium vivax*, *P. ovale and P. malariae* and sensitive strains of *P. falciparum*, and the radical treatment of malaria caused by sensitive strains of *P. falciparum*. Based on available information, the medicinal product PLAQUENIL is also applied in indications which are not listed in the summary of product characteristics (sarcoidosis, interstitial lung disease in children, Sjogren’s syndrome with

extraglanduar manifestations, undifferentiated or mixed connective tissue diseases, overlapping syndromes between connective tissue diseases, dermatomyositis). On 7 April 2020, the Ministry of Health had already permitted the distribution, dispensing and use of the non-registered medicinal product HYDROXYCHLOROQUINE-SULFAAT TEVA, but the number of packages of the this product is limited (approximately 330 packages of 30 coated tablets each). It is not presently possible to estimate the number of patients with COVID-19 disease for whom the medicinal product with the active substance *hydroxychloroquine* may be needed for treatment. For this reason, it is desirable to allow the distribution, dispensing and use of another medicinal product containing the active substance *hydroxychloroquine.*

The aim of this measure of the Ministry of Health is to ensure both the availability of the medicinal product PLAQUENIL to treat patients already undergoing therapy (in the approved indications or unregistered indications, for which the medicinal products PLAQUENIL has been used for some years), and to ensure the availability of a medicinal product with the active substance *hydroxychloroquine* to treat patients with the COVID-19 disease.

The Ministry of Health permits the distribution, dispensing and use of another non-registered human medicinal product HYDROXYCHLOROQUINE SULFATE SANDOZ. The non-registered medicinal product HYDROXYCHLOROQUINE-SULFATE SANDOZ will be designated for treating patients in the Czech Republic with a proven COVID-19 infection; treatment may be commenced exclusively within the framework of hospitalisation.

Dispensing of the medicinal product HYDROXYCHLOROQUINE-SULFATE SANDOZ requires a doctor's prescription, as does the registered medicinal product PLAQUENIL, which contains the same active substance.

In order to ensure information for the attending physician, Sandoz is obliged to provide the information leaflet for the medicinal product HYDROXYCHLOROQUINE SULFATE SANDOZ in the Czech language to the distributor, who will submit it to the pharmacy with the delivery. The product information leaflet will also be published at the Institute's website (www.sukl.cz).

Given that the medicinal product HYDROXYCHLOROQUINE-SULFATE SANDOZ is not registered in the Czech Republic, the condition for its use when providing healthcare services is the informed consent of the patient (or their legal guardian).

The Ministry of Health has stipulated an effective term for this decision of 8 months from the date of its posting on the official bulletin. This period is stipulated based on the currently expected 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 aforementioned particularities.

Prof. MUDr. Roman Prymula, CSc., Ph.D.

Deputy for Healthcare

Clause documenting authorised conversion of the document contained in this data message

This document, which was created by converting a paper input into electronic form under the order number 128436306-25785200430160000, consisting of 4 sheets, is literally identical to the content of the input.

Authorised document conversion does not confirm the correctness and accuracy of the information contained in the documents and their compliance with legislation.

Security element:
no security element

Entity performing authorised document conversion:
Ministry of Health of the Czech Republic

Date clause issued:
30 April 2020

Name, surname, and signature of the person who has performed the authorised conversion:
Eva Sadílková

128436306-25785-200430160000

Note:
This clause can be checked in the central clause records accessible via means enabling remote access at the address https://www.czechpoint.cz/overovacidolozky.