REPUBLIC OF BULGARIA

Ministry of Health

Minister of Health

DRAFT

O R D E R

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Pursuant to Article 36 of the Treaty on the Functioning of the European Union, Article 10 of Regulation (EU) 2015/479 of the European Parliament and of the Council of 11 March 2015 on common rules for exports, Article 73 of the Code of Administrative Procedure and in relation to the shortage of medicinal products for certain life-threatening diseases,

I H E R E B Y O R D E R:

I. Within the meaning of Article 217a(3) of the Law on Medicinal Products for Human Use, I prohibit the export of the following medicinal products, which have received marketing authorisation pursuant to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency and medicinal products, and which were granted with an authorisation for use pursuant to Article 26(1) of the Law on Medicinal Products for Human Use, classified according to an anatomical therapeutic chemical (ATC) classification in accordance with the requirements of the World Health Organisation (WHO) into pharmacological groups as follows:

1. A10A "Insulins and analogues" - medicinal products of the group with the following trade names:

- Actrapid Penfill, Solution for injection, 100 IU/ml - 3 ml, Pack: 5;
- Levemir Penfill, Solution for injection, 100 U/ml - 3 ml, Pack: 10;
- Insulatard Penfill, Suspension for injection, 100 IU/ml - 3 ml, Pack: 5;

- Tresiba Solution for injection 100 IU/ml –3 ml -5 Pre-filled pen (FlexTouch);

- Fiasp, Solution for injection, 100 U/ml – 3 ml, Pack: 10 (2x5) pre-filled pens (multipack);

- Fiasp, Solution for injection, 100 U/ml-3 ml, Pack: 10 Cartridges;

- NovoMix 30 Penfill, Suspension for injection, 100 U/ml - 3 ml, Pack: 10;

- Humalog, Solution for injection, 100 IU/ml - 3 ml (3.5 mg/ml, Pack: 10;

- Lyumjev, Solution for injection, 200 U/ml – 3 ml, Pack: 10;

- Xultophy, Solution for injection in pre-filled pen, 100 U/ml/3.6 mg/ml - 3 ml, Pack: 3.

2. A10BK "Sodium-glucose co-transporter 2 (SGLT-2) inhibitors" – medicinal products with trade names:

- Forxiga Film-coated tablet 10 mg x30;

- Jardiance Film-coated tablet 10 mg x30.

3. J01 "Antibacterial medicinal products for systemic use" – medicinal products from the INN group: ‘Amoxicillin, clavulanic acid’ and INN: ‘Azithromycin’ in pharmaceutical forms “powder for oral suspension” and “granules for oral suspension”.

4. J06BD "Antiviral monoclonal antibodies" - medicinal product with trade name - Synagis Solution for injection 100 mg/ml - 0.5 ml - x1.

II. Reasons:

Diabetes is a chronic disease that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces. Insulin is a hormone that regulates blood sugar. Increased blood sugar, hyperglycemia, is the result of uncontrolled diabetes and over time leads to serious damage to many of the body’s systems, especially nerves and blood vessels.

Type 1 diabetes (known as insulin dependent) is characterised by insufficient insulin production and requires daily parenteral insulin administration.

Type 2 diabetes affects the way glucose in the body is absorbed and transformed into energy. This is a pathological condition in which cells either fail to respond normally to the hormone insulin or reduce the number of insulin receptors in response to hyperinsulinaemia.

The main danger in diabetes is its chronic complications. Diabetes leads to the development of damage to the eyes, kidneys, nervous system, cardiovascular diseases, brain strokes, pain in the lower extremities, etc.

In order to analyse the situation regarding the availability of medicinal products for the treatment of diabetes, anti-infectious medicinal products and the medicinal product with International Nonproprietary Names (INN) Palivizumab on the pharmaceutical market and patients’ access to them, information was requested from the Bulgarian Drug Agency (BDA) on the available quantities of medicinal products from pharmacological groups subject to the export ban for the wholesalers and marketing authorisation holders, and from the Regional Health

Inspectorates on the checks carried out in community pharmacies on the availability of medicinal products, by covering large and smaller settlements. Information from the marketing authorisation holders was requested on the currently available quantities of medicinal products of group A10A "Insulins and analogues", group A10BK "Sodium-glucose co-transporter 2 (SGLT-2) inhibitors" and the medicinal product with International Nonproprietary Names (INN) Palivizumab by batch number and expiry date, as well as information was required on the delivered relevant quantities since the beginning of the year of the afore-mentioned medicinal products of the same groups and the planned follow-up deliveries in the 6 upcoming months. From the website of the National Health Insurance Fund (NHIF), an inquiry was made on the consumption of medicinal products and the number of persons who pay social security contributions.

Following a summary and review of the information received from the specified institutions and from the marketing authorisation holders, it is clearly observed that the following insulins with a commercial name: Actrapid Penfil (Insulin – human), Levemir Penfill (Insulin detemir), Insulatard Penfil (Insulin – human), and Tresiba 100 IU/ml - 3 ml are subject to irregular delivery, reduced quantity delivery, or delivery delays in 11-12 of all districts in the country, or approximately 40%.

For medicinal products: Fiasp Flex touch 100 IU/ml - 3 ml, NovoMix 30 Penfill 300 IU and Humalog 300 IU issues have been observed in approximately or more than 30 % of all districts, while for medicinal products with a trade name Fiasp cartriges 100 IU/ml - 3 ml cartriges, Lyumjev 200U/ml - 3ml and Xultophy 100U/ml/3.6 mg/ml - 3 ml, shortages have been reported in approximately 18 % of all districts in the country. For the rest of the reported insulins, issues problems have been observed in individual districts and pharmacies.

Following an analysis on the information received, it was found that there was a difficulty in supplying both pharmacies and patients with the medicinal products of the pharmacological group A10A “Insulins and analogues” with the above-mentioned trade names. In view of the above, it is necessary to prohibit the export of the medicinal products in question.

With regard to medicinal products belonging to the pharmacological group "Sodium-glucose co-transporter 2 (SGLT-2) inhibitors":

On the territory of our country, the following medicinal products have a valid marketing authorisation and an established price: Forxiga film-coated tablet 10 mg (INN Dapagliflozin), Jardiance film-coated tablet 10 mg (Empagliflozin) and Invokana film-coated tablet 100 mg (INN Canagliflozin). Medicinal products, according to the approved Summary of Product Characteristics, are indicated for the treatment of adults with inadequate control of type 2 diabetes mellitus as an adjunct to diet and exercise: as monotherapy in cases where the use of metformin is inappropriate due to intolerability or in addition to other medicinal products for the treatment of diabetes. Alerts of shortage, difficulty, or refusal of delivery are observed in about 36% of the

districts in the country for the medicinal product Jardiance and 32% for the medicinal product Forxiga, respectively. For the medicinal products Jardiance 10 mg and Forxiga 10 mg, the number of patients (the number of persons insured with sickness insurance) treated with these products has increased significantly. Between January and November 2024, the increase of the patients' number treated (reimbursed by the NHIF) with Jardiance 10 mg was approximately 1.8 times. The increase in patients receiving therapy (reimbursed by the NHIF) with the medicinal product Forxiga 10 mg was about 1.6-fold. Due to the increased number of patients undergoing therapy with the aforementioned medicinal products, a noticeable increase in consumption is observed.

Due to these data, the need for an export ban shall be justified only for the medicinal products Forxiga film-coated tablet 10 mg (INN Dapagliflozin) and Jardiance film-coated tablet 10 mg (Empagliflozin).

As regards medicinal products of the following pharmacological group: J01 "Anti-infectious medicinal products for systemic use" – all medicinal products in the group in pharmaceutical forms "powder for oral suspension" and "granules for oral suspension":

From the data provided by the Regional Health Inspectorate, it can be noted that delays and irregularities in deliveries, including refusals from wholesalers' warehouses, have been mainly observed for medicinal products belonging to the INN: Amoxicilline, clavulanic acid; and INN: Azithromycin

Currently, there is an increase in respiratory diseases in the country; consequently, the use of the above-mentioned medicinal products has increased. This necessitates an export ban on those medicinal products.

For the medicinal product with the trade name Synagis Solution for injection 100 mg/ml - 0.5 ml - x1:

Synagis, solution for injection, 100 mg/ml - 0.5 ml - x1 (INN Palivizumab) is authorised in the country under the EU centralised procedure. The product is indicated for the prevention of serious lower respiratory tract diseases requiring hospitalisation caused by respiratory syncytial virus (RSV) in children at high risk of RSV disease.

The medicinal product is included in Annexes 1 and 4 of the Positive Drug List and is the only medicinal product in the PDL corresponding to INN Palivizumab.

During the current winter period, there has been an increase in demand for Palivizumab due to the increased risk of respiratory syncytial virus (RSV) disease among newborns and young children, which warrants a ban on its export.

Although the mechanisms laid down in the legislation to restrict the export of medicinal products laid down in Chapter Nine "b" "Export of Medicinal Products". Specialised electronic system for follow-up and analysis of medicinal products" in the Law on Medicinal Products for Human Use, as it could be noted from the analysis of the data received from the above-mentioned

institutions, a shortage of medicinal products continues to be observed. This is also evidenced by the lack of these medicinal products in pharmacies, found by the RHI, while one of the possible reasons for this shortage is that these products may be exported from the territory of the Republic of Bulgaria to other countries in quantities, creating prerequisites for a potential shortage of these medicinal products on the Bulgarian market.

Regardless of the legal nature of the activity carried out, the export of medicinal products referred to in point I, as well as the observed delays in the deliveries, disrupts the balance between the medicinal products supplied on the territory of the country and the increased demand for them to meet the health needs of the population.

Following an in-depth analysis of the current situation with regard to the availability of the above-mentioned groups of medicinal products and the information provided above, it was found necessary to introduce an export prohibition on the groups of medicinal products identified in point I.

In addition, by setting the time limit, referred to in paragraph III of the Order, for the ban on the export of the medicinal products, referred to in paragraph I, a balance will be struck between, on the one hand, the objective of the measure applied – i.e. to ensure a sufficient quantity of these medicinal products necessary for the treatment of Bulgarian patients, to protect their health and to guarantee the continuity of their drug therapy – and, on the other hand, to not infringe for a long period of time the right of economic operators to carry out the free movement of the goods in which they trade, in the case at hand: medicinal products.

The objective sought – to provide the Bulgarian pharmaceutical market with sufficient medicinal products to meet the needs of the population – should be proportionate to the potential economic benefits that would accrue to the holders of marketing authorisations for medicinal products if they were able to export the described products during the period in question. The prohibition period introduced does not violate the principle of proportionality laid down in the Administrative Procedure Code (APC), the main purpose of which is that the administrative act and its implementation may not affect rights and legitimate interests to a greater extent than necessary for the purpose for which the act is issued (Article 6(2) of the APC).

The duration of the prohibition, as well as the specific medicinal products, have been determined in strict compliance with the principle of proportionality, in order to protect the health of the population and in compliance with the prohibition of arbitrary discrimination or disguised restriction on trade between Member States referred to in Article 36 of the Treaty on the Functioning of the European Union.

III. The ban under point I shall apply from 21/02/2025 to 24/03/2025.

IV. The order shall be published on the website of the Ministry of Health and shall be sent to the Customs Agency for information and implementation.

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Министър на здравеопазването