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**Objections to the initiation of the procedure for the revocation of marketing authorizations granted to STADA Arzneimittel AG for Dimethylfumarat STADA 120 mg and 240 mg gastroresistant hard capsules**

**File-No.: ML-7/1091**

Dear Mrs. Mäe,

In response to your letter dated 28.03.2024, we object to the revocation of the marketing authorizations for the following reasons.

1. **It cannot be concluded from the ECJ judgement of 16.03.2023 that Tecfidera has received the benefit of data protection**

Contrary to your argumentation, the European Court of Justice (ECJ) has not confirmed in the joined cases C-438/21 P, C-439/21 P and C-440/21 P that Tecfidera has been granted the benefit of data protection for eight years under Article 14(11) of Regulation (EC) No 726/2004.

The ECJ only stated in its judgment of 16.03.2023, as can be seen from paragraphs 106 and 107, that the European Commission (EC) did not commit a manifest error of assessment in concluding in its decision of 30.01.2014, based on the assessment of the Committee for Medicinal Products for Human Use (CHMP) given at that time, that Tecfidera did not belong to the same global marketing authorisation with Fumaderm.

However, as you might be aware, there is new scientific knowledge based on the CHMP's opinion of 11.11.2021[1], which found that Fumaderm already contains only dimethyl fumarate (DMF) as an active substance and that monoethyl fumarate (MEF) does not have active substance quality. This new scientific evaluation has not been judged by the ECJ.

Therefore, even if the ECJ judgement of 16.03.2023 is interpreted in a way that Tecfidera should have received the benefit of data protection for eight years starting from 03.02.2014, the circumstances have significantly changed on 11.11.2021. In light of the above, it cannot be concluded with certainty from the ECJ judgement of 16.03.2023 that Tecfidera has validly received a data exclusivity.

2. **The alleged benefit of data protection expired on 03.02.2022 and can no longer be asserted**

Even if it is accepted that Tecfidera had received the benefit of data protection for eight years starting from 03.02.2014, a possible violation of the data exclusivity period cannot be, in any case, asserted beyond the end of the corresponding protection period on 03.02.2022. The exclusive right of exploitation of the marketing authorization holder ended on this date. There is no subsequent protection, i.e., protection by data exclusivity that extends beyond 03.02.2022.

We note that, in the 8 + 2 + 1 regulation, the Community legislator refrained from linking any sanction to premature processing of an application or granting of an authorization. Similarly, there are no specific sanctions established in the Estonian Medicinal Products Act. Consequently, since the data exclusivity period of eight years has expired, the pre-applicant (Biogen Netherlands B.V.) no longer has the right to assert a violation of this right.

3. **Marketing authorizations were lawful administrative acts at the time of granting**

[1] Please see minutes for the meeting on 08-11.11.2021 of the Committee for Medicinal Products for Human Use, available here: https://www.ema.europa.eu/en/documents/minutes/minutes-chmp-meeting-8-11-november-2021_en.pdf.

Marketing authorizations are administrative acts. The lawfulness of an administrative act is determined at the time of issuing the administrative act (§ 158(2) of the Code of Administrative Court Procedure). At the time of issuing the marketing authorizations (03.03.2023), more than eight years had passed from 03.02.2014. This means that the preconditions to applying § 76(6)1) of the Medicinal Products Act are not fulfilled.

According to § 76(6)1) of the Medicinal Products Act, the Republic of Estonia Agency of Medicines (Agency) may revoke a marketing authorisation if the conditions serving as the basis for granting the marketing authorisation have changed or have not been fulfilled. At the time of issuing the marketing authorisations (03.03.2023), STADA Arzneimittel AG and the Agency had the full right to rely on the 03.02.2014 marketing authorisation granted to Biogen Netherlands B.V. as more than eight years had passed. This means that, compared to 03.03.2023, the conditions serving as the basis for granting the marketing authorisation have not changed.

The reference to the 30.02.2014 marketing authorisation was needed only to release STADA Arzneimittel AG from the obligation to provide data in proof of the efficacy and safety of the medicinal product (§ 65(4)2) of the Medicinal Products Act). Therefore, even if the initial application had deficiencies because STADA Arzneimittel AG could arguably not be released from its obligation to provide data in proof of the efficacy and safety of the relevantmedicinal products before the expiry of eight years from 03.02.2014, these deficiencies no longer existed starting from 03.02.2022. The Agency lawfully accepted that the efficacy and safety of Dimethylfumarat STADA 120 mg and 240 mg gastroresistant hard capsules was proven because they were bioequivalent to Tecfidera in respect of which a marketing authorisation was granted more than eight years ago (30.01.2014).

We emphasize that the Agency granted the marketing authorizations in question on 03.03.2023, i.e. more than a year after the expiry of the alleged protection period. This means that, at the time of granting, the marketing authorizations were not unlawful because the alleged data exclusivity period had already expired and both STADA Arzneimittel AG and the Agency had the full right to rely on the 03.02.2014 marketing authorisation.

Furthermore, we would like to point out that Estonia was not the Reference Member State in the decentralized approval procedure, but only a Concerned Member State. The relevant day 0 on which

Sweden, as the Reference Member State, started the decentralized procedure was 14.02.2022, in other words, after 03.02.2022, when the alleged data exclusivity expired. Therefore, the granting of these marketing authorisations cannot be considered unlawful also due to the proceedings being initiated before the expiry of the alleged data exclusivity.

In any case, the fact that the applications for the marketing authorisations were filed with the Agency on 01.12.2021, i.e., just two months before the expiry of the alleged data exclusivity, cannot be considered a deficiency which would justify such detrimental measure as revocation of the marketing authorizations.

4. **Revocation of the marketing authorizations is not justified under the principle of right of discretion**

Even if the preconditions to applying § 76(6)1) of the Medicinal Products Act were fulfilled, § 76(6)1) of the Medicinal Products Act does not obligate the Agency to revoke the marketing authorizations but gives the Agency the right of discretion. Pursuant to § 64(2) of the Administrative Procedure Act, an administrative authority shall resolve the repeal of an administrative act according to the right of discretion, unless repeal of the administrative act is prohibited by law or repeal of the administrative act is required by law. In this case, the repeal of the administrative act is not required by the law, i.e., the Agency is required to resolve the repeal according to the right of discretion.

Pursuant to § 64(1) of the Administrative Procedure Act, upon exercise of the right of discretion, the consequences of the issue of an administrative act and repeal of an administrative act for a person, the completeness of the proceedings for the issue of the administrative act, significance of the reasons for the repeal of the administrative act and the relation thereof with the participation of a person in proceedings for the issue of the administrative act and with the other activities of the person, the time which has passed after issue of the administrative act and other relevant facts shall be taken into account. Therefore, the Agency is required to take into account all relevant facts and exercise the right of discretion diligently.

The ECJ judgement to which the Agency refers as the basis for revoking the marketing authorisations was made already on 16.03.2023, i.e., less than two weeks after the marketing

authorizations were issued. However, the Agency did not notify STADA Arzneimittel AG of its opinion that the marketing authorisations may need to be revoked before more than a year had passed both from the issuing of the marketing authorisations as well as from the ECJ judgment. The more time has passed from the date of issuing an administrative act the stronger is its addressee's certainty that the act remains in force. If the Agency had considered revoking the marketing authorisations in March 2023, STADA Arzneimittel AG could have reapplied and received new marketing authorisations before the expiry of ten years from 03.02.2014. The Agency's delay in considering the effects of the 16.03.2023 ECJ judgment and revoking the marketing authorisations only in the middle of 2024 would inevitably delay the entry of Dimethylfumarat STADA 120 mg and 240 mg gastroresistant hard capsules and restrict competition with Tecfidera in Estonia.

Pursuant to § 66(2)2) of the Administrative Procedure Act, an administrative act which was lawful at the moment of issue may be proactively repealed to the detriment of a person if the administrative authority had the right not to issue the administrative act due to factual circumstances which changed later or on the basis of a rule of law which is amended afterwards, and public interest that the administrative act be repealed outweighs the person's certainty that the administrative act remains in force. This means that, if the Agency considers that the factual circumstances have changed, the Agency is required to evaluate whether the public interest that the marketing authorisations are revoked outweighs the interests of STADA Arzneimittel AG.

The revocation of the marketing authorizations in question is not in the public interest. On the contrary, the revocation of the marketing authorisations would be detrimental to the public interests, specifically to the use of the Estonian Health Insurance Fund budget and to public health in general. If the marketing authorizations are revoked, STADA Arzneimittel AG cannot market in Estonia its pharmaceutical products **Dimethylfumarat STADA 120 mg and 240 mg, which are generic versions of Tecfidera. As a result, the Estonian Health Insurance Fund would not be able to establish a reference price for medicinal products consisting of DMF and would be forced to continue compensating for the use of the relevant medicinal products with higher prices. This in turn would result in the Estonian Health Insurance Fund not being able to use the Health Insurance Fund budget effectively and purposefully. Since the budget is limited, compensating for one medicinal product with a higher price means inevitably that some other medicinal product is left without compensation or, even worse, some patients are left without necessary treatment.**

**At the same time, t**he revocation of the marketing authorizations would not serve any other purpose than to overcome an alleged formal deficiency. As already explained, even if it would be accepted that Tecfidera benefited from the eight-year period of data protection, the period of data protection expired on 03.02.2022. This means that the marketing authorizations that are intended to be revoked would have to be granted again immediately upon a new application. Thus, the revocation of the marketing authorizations would result only in a postponement of the right of STADA Arzneimittel AG to market its products in Estonia and inefficient use of the resources by the Agency in reconducting the proceedings for issuing the marketing authorizations.

5. **The revocation procedure cannot be conducted by the Agency**

Additionally, we would like to point out that in the present decentralized approval procedure, the Reference Member State was Sweden (SE/H/02212), and Estonia was just a Concerned Member State. According to the case law of the ECJ in the Astellas case (see ECJ - Astellas, judgment of 14.03.2018, C-557/16), only the Reference Member State is authorized to propose appropriate measures in such constellations. In this case, Reference Member State has not initiated a procedure for the revocation of the marketing authorizations.

Once the decentralized approval procedure has been completed, the Estonian Agency of Medicines as the national authority is bound by the outcome of the procedure, i.e. the granting of approval, and can no longer question the outcome on its own initiative (see ECJ - Astellas, judgment of 14.03.2018, C-557/16, in particular paragraphs 26, 30, 31).

6. **There are less burdensome measures available than revocation of the marketing authorizations**

Finally, we emphasize that there is also no justification for the revocation of the marketing authorizations since the alleged deficiency can be eliminated with less burdensome measures. Pursuant to § 76(6)1) of the Medicinal Products Act, the Agency may amend, suspend or revoke the marketing authorisation if the conditions serving as the basis for granting the marketing authorisation have changed. You have explained that the Agency considered the implementation of less burdensome measures (suspending or amending the marketing authorisation), but found it to be

impossible. However, you have not provided any explanation on why the marketing authorizations cannot be amended in a situation where, in case of revocation, the marketing authorisations would need to be granted again immediately.

We assume that you are aware that there are currently 6 actions pending before the General Court of the European Union alleging, in the first or second plea, a manifest error of assessment in the interpretation of the judgment of the ECJ of 16.03.2023, in particular on the part of our sister company Aliud (Ref. T-309/23). We expect a decision from the court shortly.

In any case, only a suspension of the marketing authorizations until the end of the marketing protection or a decision of the General Court of the European Union to annul the extension of the marketing protection by 1 year would be appropriate as a less burdensome administrative measure.

**Conclusion**

STADA Arzneimittel AG asks the Estonian Agency of Medicines to terminate the administrative proceedings with a resolution not to revoke the marketing authorizations.

Best regards,

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