Reports of Cases

JUDGMENT OF THE COURT (Fourth Chamber)

16 March 2023 *

(Appeal – Public health – Medicinal products for human use – Directive 2001/83/EC – Regulation (EC) No 726/2004 – Application for marketing authorisation for a generic version of the medicinal product Tecfidera – Decision of the European Medicines Agency (EMA) not to validate the application for marketing authorisation – Earlier European Commission decision taking the view that Tecfidera was not covered by the same global marketing authorisation as Fumaderm – Previously authorised combination medicinal product – Subsequent marketing authorisation for a component of the combination medicinal product – Assessment of the existence of a global marketing authorisation)

In Joined Cases C-438/21 P to C-440/21 P,

THREE APPEALS under Article 56 of the Statute of the Court of Justice of the European Union, brought on 14 July 2021 (C-438/21 P and C-439/21 P) and 15 July 2021 (C-440/21 P),

European Commission, represented initially by S. Bourgois, L. Haasbeek and A. Sipos, and subsequently by L. Haasbeek and A. Sipos, acting as Agents,

appellant,

the other parties to the proceedings being:

Pharmaceutical Works Polpharma S.A., established in Starogard Gdański (Poland), represented by N. Carbonnelle, avocat, S. Faircliffe, Solicitor, and M. Martens, advocaat,

applicant at first instance,

European Medicines Agency (EMA), represented by S. Drosos, H. Kerr and S. Marino, acting as Agents,

defendant at first instance,

Biogen Netherlands BV, established in Badhoevedorp (Netherlands), represented by C. Schoonderbeek, advocaat,

intervener at first instance (C-438/21 P),

and

* Language of the cases: English.

Biogen Netherlands BV, established in Badhoevedorp, represented by C. Schoonderbeek, advocaat,

appellant,

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applicant at first instance,

European Commission, represented initially by S. Bourgois, L. Haasbeek and A. Sipos, and subsequently by L. Haasbeek and A. Sipos, acting as Agents,

Biogen Netherlands BV, established in Badhoevedorp, represented by C. Schoonderbeek, advocaat,

interveners at first instance (C-440/21 P),

THE COURT (Fourth Chamber),

composed of C. Lycourgos, President of the Chamber, L.S. Rossi, J.-C. Bonichot, S. Rodin and O. Spineanu-Matei (Rapporteur), Judges,

Advocate General: L. Medina,

Registrar: R. Stefanova-Kamisheva, Administrator,

having regard to the written procedure and further to the hearing on 30 June 2022,

after hearing the Opinion of the Advocate General at the sitting on 6 October 2022,

gives the following

Judgment

1 By their respective appeals, the European Commission (C-438/21 P), Biogen Netherlands BV ('Biogen') (C-439/21 P) and the European Medicines Agency (EMA) (C-440/21 P) seek to have set aside the judgment of the General Court of the European Union of 5 May 2021, *Pharmaceutical Works Polpharma* v *EMA* (T-611/18, EU:T:2021:241; 'the judgment under appeal'), by which the General Court annulled the EMA's decision of 30 July 2018 not to validate the application submitted by Pharmaceutical Works Polpharma S.A. ('Polpharma') with a view to obtaining a marketing authorisation for a generic version of the medicinal product Tecfidera ('the decision at issue').

Legal context

Directive 2001/83/EC

2 Recitals 9 and 12 of Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use (OJ 2001 L 311, p. 67), as amended by Directive 2012/26/EU of the European Parliament and of the Council of 25 October 2012 (OJ 2012 L 299, p. 1) ('Directive 2001/83'), state:

'(9) Experience has shown that it is advisable to stipulate more precisely the cases in which the results of toxicological and pharmacological tests or clinical trials do not have to be provided with a view to obtaining authorisation for a medicinal product which is essentially similar to an authorised product, while ensuring that innovative firms are not placed at a disadvantage.

…

(12) With the exception of those medicinal products which are subject to the centralised Community authorisation procedure established by Council Regulation (EEC) No 2309/93 of 22 July 1993 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Agency for the Evaluation of Medicinal Products [(OJ 1993 L 214, p. 1)] a marketing authorisation for a medicinal product granted by a competent authority in one Member State ought to be recognised by the competent authorities of the other Member States unless there are serious grounds for supposing that the authorisation of the medicinal product concerned may present a risk to public health. In the event of a disagreement between Member States about the quality, the safety or the efficacy of a medicinal product, a scientific evaluation of the matter should be undertaken according to a Community standard, leading to a single

decision on the area of disagreement binding on the Member States concerned. [That] decision should be adopted by a rapid procedure ensuring close cooperation between the Commission and the Member States.'

3 Article 1 of Directive 2001/83 provides:

'For the purposes of this Directive, the following terms shall bear the following meanings:

…

2. *Medicinal product:*
   (a) Any substance or combination of substances presented as having properties for treating or preventing disease in human beings; or
   (b) Any substance or combination of substances which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis.

…

3a *Active substance*:

Any substance or mixture of substances intended to be used in the manufacture of a medicinal product and that, when used in its production, becomes an active ingredient of that product intended to exert a pharmacological, immunological or metabolic action with a view to restoring, correcting or modifying physiological functions or to make a medical diagnosis.

…'

4 Article 6(1) of Directive 2001/83 provides as follows:

'No medicinal product may be placed on the market of a Member State unless a marketing authorisation has been issued by the competent authorities of that Member State in accordance with this Directive or an authorisation has been granted in accordance with 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 (OJ 2004 L 136, p. 1)] …

When a medicinal product has been granted an initial marketing authorisation in accordance with the first subparagraph, any additional strengths, pharmaceutical forms, administration routes, presentations, as well as any variations and extensions shall also be granted an authorisation in accordance with the first subparagraph or be included in the initial marketing authorisation. All these marketing authorisations shall be considered as belonging to the same global marketing authorisation, in particular for the purpose of the application of Article 10(1).'

5 Article 10(1) and (2) of that directive provides:

'1. By way of derogation from Article 8(3)(i), and without prejudice to the law relating to the protection of industrial and commercial property, the applicant shall not be required to provide the results of pre-clinical tests and of clinical trials if he can demonstrate that the medicinal

product is a generic of a reference medicinal product which is or has been authorised under Article 6 for not less than eight years in a Member State or in the [European Union].

A generic medicinal product authorised pursuant to this provision shall not be placed on the market until ten years have elapsed from the initial authorisation of the reference product.

…

The ten-year period referred to in the second subparagraph shall be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorisation holder obtains an authorisation for one or more new therapeutic indications which, during the scientific evaluation prior to their authorisation, are held to bring a significant clinical benefit in comparison with existing therapies.

2. For the purposes of this Article:

(a) "reference medicinal product" shall mean a medicinal product authorised under Article 6, in accordance with the provisions of Article 8;

(b) "generic medicinal product" shall mean a medicinal product which has the same qualitative and quantitative composition in active substances and the same pharmaceutical form as the reference medicinal product, and whose bioequivalence with the reference medicinal product has been demonstrated by appropriate bioavailability studies. The different salts, esters, ethers, isomers, mixtures of isomers, complexes or derivatives of an active substance shall be considered to be the same active substance, unless they differ significantly in properties with regard to safety and/or efficacy. In such cases, additional information providing proof of the safety and/or efficacy of the various salts, esters or derivatives of an authorised active substance must be supplied by the applicant. The various immediate-release oral pharmaceutical forms shall be considered to be one and the same pharmaceutical form. Bioavailability studies need not be required of the applicant if he can demonstrate that the generic medicinal product meets the relevant criteria as defined in the appropriate detailed guidelines.'

6 Article 30(1) of Directive 2001/83 provides:

'If two or more applications submitted in accordance with Articles 8, 10, 10a, 10b, 10c and 11 have been made for marketing authorisation for a particular medicinal product, and if Member States have adopted divergent decisions concerning the authorisation of the medicinal product or its suspension or revocation, a Member State, the Commission or the applicant or the marketing authorisation holder may refer the matter to the Committee for Medicinal Products for Human Use, hereinafter referred to as "the Committee", for the application of the procedure laid down in Articles 32, 33 and 34.'

7 Under Article 31(1) of that directive:

'The Member States, the [European] Commission, the applicant or the marketing authorisation holder shall, in specific cases where the interests of the [European] Union are involved, refer the matter to the Committee for application of the procedure laid down in Articles 32, 33 and 34 before any decision is reached on an application for a marketing authorisation or on the suspension or revocation of a marketing authorisation, or on any other variation of the marketing authorisation which appears necessary.

…’

Regulation No 726/2004

8 Recitals 17 and 19 of Regulation No 726/2004 state:

‘(17) [The European Union] should have the means to carry out a scientific evaluation of the medicinal products presented in accordance with the decentralised … authorisation procedures. Moreover, with a view to ensuring the effective harmonisation of administrative decisions taken by Member States with regard to medicinal products presented in accordance with decentralised authorisation procedures, it is necessary to endow the [European Union] with the means to resolve disagreements between Member States concerning the quality, safety and efficacy of medicinal products.

…

(19) The chief task of the [EMA] should be to provide [EU] institutions and Member States with the best possible scientific opinions so as to enable them to exercise the powers regarding the authorisation and supervision of medicinal products conferred on them by [EU] legislation in the field of medicinal products. Only after a single scientific evaluation procedure addressing the quality, safety and efficacy of high-technology medicinal products has been conducted by the [EMA], applying the highest possible standards, should marketing authorisation be granted by the [European Union], and this should be done by means of a rapid procedure ensuring close cooperation between the Commission and Member States.’

9 Under Article 3(3) of that regulation:

‘A generic medicinal product of a reference medicinal product authorised by the [European Union] may be authorised by the competent authorities of the Member States in accordance with Directive 2001/83/EC and Directive 2001/82/EC [of the European Parliament and of the Council of 6 November 2001 on the Community code relating to veterinary medicinal products (OJ 2001 L 311, p. 1)] under the following conditions:

(a) the application for authorisation is submitted in accordance with Article 10 of Directive 2001/83/EC or Article 13 of Directive 2001/82/EC;

(b) the summary of the product characteristics is in all relevant respects consistent with that of the medicinal product authorised by the [European Union] except for those parts of the summary of product characteristics referring to indications or dosage forms which were still covered by patent law at the time when the generic medicine was marketed; and

(c) the generic medicinal product is authorised under the same name in all the Member States where the application has been made. For the purposes of this provision, all the linguistic versions of the INN (international non-proprietary name) shall be considered to be the same name.’

10 Article 4(1) of that regulation provides:

‘Applications for the marketing authorisations referred to in Article 3 shall be submitted to the [EMA].’

11 Article 5(1) of that regulation states:

‘A Committee for Medicinal Products for Human Use is hereby established. The Committee shall be part of the [EMA].’

12 The first subparagraph of Article 57(1) of Regulation No 726/2004 provides:

‘The [EMA] shall provide the Member States and the institutions of the [European Union] with the best possible scientific advice on any question relating to the evaluation of the quality, safety and efficacy of medicinal products for human or veterinary use which is referred to it in accordance with the provisions of [EU] legislation relating to medicinal products.’

13 Under Article 60 of that regulation:

‘At the request of the Commission, the [EMA] shall, in respect of authorised medicinal products, collect any available information on methods that Member States’ competent authorities use to determine the added therapeutic value that any new medicinal product provides.’

Regulation (EC) No 1234/2008

14 Article 2 of Commission Regulation (EC) No 1234/2008 of 24 November 2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products (OJ 2008 L 334, p. 7), as amended by Commission Regulation (EU) No 712/2012 of 3 August 2012 (OJ 2012 L 209, p. 4) (‘Regulation No 1234/2008’), provides:

‘For the purposes of this Regulation, the following definitions shall apply:

…

4. “Extension of a marketing authorisation” or “extension” means a variation which is listed in Annex I and fulfils the conditions laid down therein;

…’

15 Annex I to that regulation, entitled ‘Extensions of marketing authorisations’, contains the following passage:

‘1. Changes to the active substance(s):

(a) replacement of a chemical active substance by a different salt/ester complex/derivative, with the same therapeutic moiety, where the efficacy/safety characteristics are not significantly different;

…’

16 That regulation repealed Commission Regulation (EC) No 1085/2003 of 3 June 2003 concerning the examination of variations to the terms of a marketing authorisation for medicinal products for human use and veterinary medicinal products falling within the scope of Regulation No 2309/93 (OJ 2003 L 159, p. 24).

Background to the dispute

17 The background to the dispute is set out in paragraphs 1 to 51 of the judgment under appeal and, for the purposes of the present proceedings, may be summarised as follows.

18 On 9 August 1994, the Bundesinstitut für Arzneimittel und Medizinprodukte (Federal Institute for Drugs and Medical Devices, Germany; 'the BfArM') granted Fumapharm AG two marketing authorisations concerning two strengths of a medicinal product called Fumaderm, indicated for the treatment of psoriasis. Fumaderm was authorised as a fixed combination medicinal product of dimethyl fumarate ('DMF') and various monoethyl fumarate ('MEF') salts. In accordance with Article 10(1) of Directive 2001/83, the regulatory data protection period ('RDP') of Fumaderm expired in 2004. Those marketing authorisations were ultimately transferred to Biogen Idec Ltd.

19 On 28 February 2012, Biogen Idec submitted to the EMA, pursuant to Article 4(1) of Regulation No 726/2004, an application for marketing authorisation for Tecfidera – Dimethyl fumarate ('Tecfidera'), a medicinal product for human use.

20 On 30 January 2014, the Commission adopted Implementing Decision C(2014) 601 final granting marketing authorisation under Regulation No 726/2004 for Tecfidera ('the implementing decision of 30 January 2014'). A summary of that implementing decision was published in the *Official Journal of the European Union* on 28 February 2014 (OJ 2014 C 59, p. 1).

21 By that decision, Tecfidera was authorised as a mono-substance medicinal product, composed of DMF, and indicated for the treatment of multiple sclerosis. The Commission also held that Tecfidera did not belong to the same global marketing authorisation as Fumaderm, within the meaning of the second subparagraph of Article 6(1) of Directive 2001/83. In that regard, recital 3 of the implementing decision of 30 January 2014 stated:

'[DMF], the active substance of "[Tecfidera]", is part of the composition of the authorised medicinal product Fumaderm which [consists] of DMF and calcium salt of ethyl fumarate, magnesium salt of ethyl hydrogen fumarate and zinc salt of ethyl hydrogen fumarate ([MEF]), belonging to the same marketing authorisation holder. The Committee for Medicinal Products for Human Use concluded that MEF and DMF are both active and are not the same active substance since they do not share the same therapeutic moiety. Therefore, it is considered that Tecfidera containing DMF is different from Fumaderm the other already authorised medicinal product composed of DMF and [MEF]. Therefore "[Tecfidera]", the application of which was based on Article 8(3) of [Directive 2001/83], and the already authorised medicinal product Fumaderm do not belong to the same global marketing authorisation as described in Article 6(1) of [that directive].'

22 On 27 November 2017, Polpharma submitted a request to the EMA for confirmation that it was eligible to submit a marketing authorisation application under the centralised procedure in accordance with Article 3(3) of Regulation No 726/2004 for a generic medicinal product known as Dimethyl Fumarate Pharmaceutical Works Polpharma, derived from the reference medicinal product Tecfidera.

23 By the decision at issue, adopted on 30 July 2018, the EMA informed Polpharma that it was unable to validate its application. The EMA stated that, according to recital 3 of the implementing decision of 30 January 2014, Tecfidera and the already authorised medicinal product Fumaderm did not belong to the same global marketing authorisation within the meaning of the second subparagraph of Article 6(1) of Directive 2001/83, on the ground that MEF and DMF were both active and did not correspond to the same active substance since the therapeutic moiety was not the same in each of those medicinal products. The EMA considered that Tecfidera benefited from its own eight-year RDP and that that period of protection had not yet expired. In view of those findings, the EMA stated that the reference to data relating to the pre-clinical tests and clinical trials set out in the Tecfidera file was not authorised for the purpose of submitting an application for marketing authorisation under Article 10(1) of Directive 2001/83.

The procedure before the General Court and the judgment under appeal

24 By application lodged at the Registry of the General Court on 9 October 2018, Polpharma brought an action for annulment of the decision at issue.

25 By orders of the General Court of 19 March 2019, Biogen, that is to say the company to which the marketing authorisation for Tecfidera had been transferred, and the Commission were granted leave to intervene in support of the form of order sought by the EMA.

26 In support of its action, Polpharma relied on a single plea in law, alleging that the implementing decision of 30 January 2014 was unlawful. In essence, it submitted that that decision, which constituted the legal basis of the decision at issue, should, in accordance with Article 277 TFEU, be declared inapplicable, it being unlawful inasmuch as the Commission had found that Tecfidera and Fumaderm were different and that, consequently, they were not covered by the same global marketing authorisation. In that regard, Polpharma submitted that, when faced with an application for marketing authorisation for an active substance which forms part of a previously authorised fixed combination medicinal product, the assessment of whether there is a difference between that combination and that isolated active substance depends on whether the individual active substances of the combination provide a documented and relevant therapeutic contribution within that combination. Polpharma deduced from this that the decision at issue, which refused to validate the application for marketing authorisation for a generic medicinal product derived from Tecfidera, had no legal basis and had to be annulled, inter alia on the grounds of a failure to state reasons pursuant to Article 296 TFEU.

27 In the first place, in paragraphs 85 to 149 of the judgment under appeal, the General Court found that the plea of illegality invoked by Polpharma against the implementing decision of 30 January 2014 was admissible. First of all, it classified that decision as an ‘act of general application’, inasmuch as it found that Tecfidera did not belong to the same global marketing authorisation as Fumaderm, which had previously been authorised. Next, it noted that the Commission had expressly relied on the assessments of the Committee for Medicinal Products for Human Use, established by Article 5(1) of Regulation No 726/2004 and forming part of the EMA (‘the CHMP’), in order to deduce that Tecfidera and Fumaderm did not belong to the same global marketing authorisation. It considered that Polpharma was therefore entitled, in order to demonstrate the unlawfulness of the implementing decision of 30 January 2014, to challenge the assessments that appear in the CHMP documents relating to Tecfidera, on which that implementing decision was based and which formed an integral part of its statement of reasons. Lastly, after analysing the information in the file, the General Court concluded that Polpharma

would not have been entitled to bring a direct action for annulment of that implementing decision. It noted that, in particular, Polpharma's interest in seeking the annulment of the latter was not current and vested, but future and uncertain at the time when it would have been entitled to bring an action for annulment against that implementing decision.

28 In the second place, the General Court upheld the plea of illegality and held that the decision at issue, which was based on the implementing decision of 30 January 2014, was unfounded and had to be annulled.

29 In order to reach that conclusion, the General Court, first, in paragraphs 173 to 180 of the judgment under appeal, examined the concept of a 'global marketing authorisation' and its objectives. It stated in this regard that that concept, which is referred to in the second subparagraph of Article 6(1) of Directive 2001/83, follows the line of well-established case-law of the Court of Justice, which developed that concept in particular to take account of the objective of the 'abridged' procedure, which is to save the time and expense needed to gather the results of the pharmacological and toxicological tests and clinical trials, and to avoid the repetition of tests on humans or animals. It also mentioned, having regard to Article 10 of Directive 2001/83, the objective of '[promoting] research on new therapeutic indications with a significant clinical benefit and bringing an improvement to the quality of life and welfare of the patient' while ensuring 'an appropriate balance between such innovations and the need to favour the production of generic medicines'.

30 Second, in paragraphs 181 to 218 of the judgment under appeal, the General Court examined the applicable EU law and developments in scientific knowledge in the years from 1994 to 2014. In that regard, it found that, in adopting the implementing decision of 30 January 2014, the Commission had been faced, for the first time at EU level, with the question whether or not an authorised fixed combination medicinal product and a component of that combination belonged to the same global marketing authorisation. It also took the view that, in answering the question whether or not the marketing authorisation for Tecfidera – the only active substance of which was a component of Fumaderm – belonged to the same global marketing authorisation, the Commission had been required to take account of the fact that the EU law relating to combination medicinal products as well as scientific knowledge differed significantly from that which existed in 1994 when the national authority had granted the marketing authorisation for Fumaderm. The General Court took the view that, in that particular context, the Commission had acted correctly in asking the CHMP to assess whether DMF, which Tecfidera contains, differed from Fumaderm, which contained DMF and MEF.

31 Third, and without ruling on the applicability of Article 31 of Directive 2001/83 in that case, in paragraphs 219 to 238 of the judgment under appeal, the General Court found that, in the context of the marketing authorisation procedures implemented at EU level or in the Member States, the EMA and the Commission perform a particular function, which is not comparable to the function of the national authorities. It took the view that the principle of mutual recognition cannot therefore prevent the CHMP, following the submission of an application for marketing authorisation under the centralised procedure, from examining the assessments previously carried out by a national authority or from carrying out an independent assessment itself.

32 Fourth, in paragraphs 239 to 273 of the judgment under appeal, the General Court held that, when the implementing decision of 30 January 2014 was adopted, the EMA and the Commission had, or could have had, data capable of rendering implausible the theory that MEF played a role within Fumaderm.

33 Fifth, after having set out all those considerations, the General Court stated, in paragraph 281 of the judgment under appeal, that it was clear from recital 3 of the implementing decision of 30 January 2014 that the assessment that Tecfidera differs from Fumaderm and is not covered by the same global marketing authorisation as Fumaderm was based on the CHMP's finding that MEF and DMF are both active and are not the same active substance, and on the finding that a marketing authorisation had already been granted for Fumaderm as a combination medicinal product composed of DMF and MEF.

34 However, according to the General Court, those findings were not sufficient to conclude that Tecfidera was covered by a different global marketing authorisation from that of Fumaderm. In paragraph 282 of the judgment under appeal, it held in this regard that, in view of the objectives of such a global marketing authorisation, the EU law applicable to combination medicinal products in 1994 and the development of scientific knowledge between 1994 and 2014, the particular function performed by the EMA and the Commission, and the data available – or which could have been available – to them which rendered implausible the theory that MEF played a role within Fumaderm, the Commission was not entitled to conclude that Tecfidera was covered by a different global marketing authorisation from that of Fumaderm, which had previously been authorised, without verifying or requesting the CHMP to verify whether and, if necessary, how, the BfArM had assessed the role of MEF within Fumaderm, or without requesting the CHMP to verify that role.

35 In paragraphs 289 and 293 of the judgment under appeal, the General Court deduced from this that, since the Commission had not analysed all the relevant data that had to be taken into consideration in order to conclude that Tecfidera and Fumaderm were not covered by the same global marketing authorisation, the implementing decision of 30 January 2014 was vitiated by a manifest error of assessment. In paragraphs 295 and 296 of the judgment under appeal, it upheld the plea of illegality raised by Polpharma and, consequently, held that the decision at issue, which was based on the implementing decision of 30 January 2014, was unfounded and had to be annulled.

Procedure before the Court of Justice and forms of order sought

36 By document lodged at the Court Registry on 4 May 2022, Biogen requested that Case C-439/21 P be given priority treatment under Article 53(3) of the Rules of Procedure of the Court of Justice. On 6 May 2022, the President of the Court decided that there was no need to give the case priority over others.

37 By decision of 10 May 2022, Cases C-438/21 P to C-440/21 P were joined for the purposes of the oral procedure and the judgment.

38 By its appeal in Case C-438/21 P, the Commission, supported by Biogen, claims that the Court should:

– set aside the judgment under appeal;

– reject the application at first instance; and

– order Polpharma to pay the costs.

39 By its appeal in Case C-439/21 P, Biogen, supported by the Commission, claims, in essence, that the Court should:

– set aside the judgment under appeal;

– dismiss the action at first instance or refer the case back to the General Court, if necessary; and

– order Polpharma to pay the costs.

40 By its appeal in Case C-440/21 P, the EMA, supported by the Commission and Biogen, claims that the Court should:

– set aside the judgment under appeal;

– reject the application at first instance; and

– order Polpharma to pay the costs of the proceedings at first instance and on appeal.

41 In Cases C-438/21 P to C-440/21 P, Polpharma claims that the Court should:

– dismiss the appeals;

– uphold the judgment under appeal; and

– order the Commission, Biogen and EMA to pay the costs incurred in their respective appeals.

The requests that the oral part of the procedure be reopened

42 Following the delivery of the Advocate General's Opinion, Polpharma, by documents lodged at the Court Registry on 24 November 2022 and 20 January 2023, requested that the oral part of the procedure be reopened, pursuant to Article 83 of the Rules of Procedure.

43 In accordance with that provision, the Court may at any time, after hearing the Advocate General, order the reopening of the oral part of the procedure, in particular if it considers that it lacks sufficient information, or where a party has, after the close of that part of the procedure, submitted a new fact which is of such a nature as to be a decisive factor for the decision of the Court, or where the case must be decided on the basis of an argument which has not been debated.

44 In support of its requests, Polpharma submits that, as regards the procedure for the renewal of the marketing authorisation for Fumaderm in 2013, the Advocate General's Opinion is based on the incorrect assumption that a therapeutic contribution of MEF was confirmed by the BfArM.

45 However, it must be noted that, under the second paragraph of Article 252 TFEU, the Advocate General, acting with complete impartiality and independence, is to make, in open court, reasoned submissions on cases which, in accordance with the Statute of the Court of Justice of the European Union, require his or her involvement. It is not therefore an opinion addressed to the judges or to the parties which stems from an authority outside the Court, but rather, it is the individual reasoned opinion, expressed in open court, of a Member of the Court of Justice itself. In those circumstances, the Advocate General's Opinion cannot be debated by the parties. Moreover,

the Court is not bound either by the Advocate General's submissions or by the reasoning which led to those submissions. Consequently, a party's disagreement with the Opinion of the Advocate General, irrespective of the questions that the Advocate General examines in his or her Opinion, cannot in itself constitute grounds justifying the reopening of the oral procedure (judgment of 9 June 2022, *Préfet du Gers and Institut national de la statistique et des études économiques*, C-673/20, EU:C:2022:449, paragraph 41 and the case-law cited).

46 In the present case, it is apparent from the requests to reopen the oral part of the procedure that, by those requests, Polpharma is in fact seeking to respond to the interpretation made by the Advocate General of the factual and legal circumstances underlying the first ground of appeal in Case C-438/21 P, the third ground of appeal in Case C-439/21 P and the first ground of appeal in Case C-440/21 P. However, as is apparent from Article 83 of the Rules of Procedure and from the case-law cited in the preceding paragraph of the present judgment, such a ground is not one which is capable of justifying the reopening of the oral part of a procedure. Furthermore, since those circumstances were the subject of extensive discussion between the parties to the appeals during the written part of the procedure and also at the hearing, the Court considers, after hearing the Advocate General, that it has all the information necessary to rule on the appeals and that the case does not have to be decided in the light of a new fact which is of such a nature as to be a decisive factor for its decision or an argument which has not been debated before it.

47 In those circumstances, there is no need to order the reopening of the oral part of the procedure.

The appeals

48 In support of their respective appeals in Cases C-438/21 P, C-439/21 P and C-440/21 P, the Commission, Biogen and the EMA ('the appellants') put forward four similar grounds of appeal.

49 By the first ground of appeal in Case C-438/21 P, the third ground of appeal in Case C-439/21 P and the first ground of appeal in Case C-440/21 P, the Commission, Biogen and the EMA, respectively, rely, in essence, on the failure to take into consideration the BfArM's assessment of Fumaderm when renewing Fumaderm's marketing authorisation in 2013, and on distortion of the facts.

50 By the second ground of appeal in Case C-438/21 P, the second ground of appeal in Case C-439/21 P and the third ground of appeal in Case C-440/21 P, the Commission, Biogen and the EMA, respectively, allege, in essence, infringement of the second subparagraph of Article 6(1) of Directive 2001/83 and misinterpretation of the concept of a 'global marketing authorisation'.

51 By the third ground of appeal in Case C-438/21 P, the fourth ground of appeal in Case C-439/21 P and the second ground of appeal in Case C-440/21 P, the Commission, Biogen and the EMA, respectively, allege, in essence, a failure to have regard for the system of decentralised application of EU legislation on pharmaceutical products, established by Regulation No 726/2004 and Directive 2001/83, and failure to observe the principles of conferral of powers and subsidiarity as laid down in Article 5 TEU and the principle of mutual trust.

52 By the fourth ground of appeal in Case C-438/21 P, the fifth ground of appeal in Case C-439/21 P and the fourth ground of appeal in Case C-440/21 P, the Commission, Biogen and the EMA, respectively, allege, in essence, disregard of the scope of judicial review, in that the General Court substituted its own scientific assessment for that of the competent regulatory authorities.

53 Lastly, in addition to those four similar grounds of appeal, Biogen, by its first ground of appeal in Case C-439/21 P, alleges misapplication of Article 277 TFEU by the General Court, inasmuch as the latter found that the plea of illegality raised by Polpharma against the implementing decision of 30 January 2014 was admissible.

The first ground of appeal in Case C-439/21 P

Arguments of the parties

54 By its first ground of appeal in Case C-439/21 P, Biogen claims that the General Court erred in law in finding that the plea of illegality raised against the implementing decision of 30 January 2014 was admissible, even though that decision could have been challenged directly by Polpharma in 2014.

55 In that regard, more specifically, it claims that, first, the General Court wrongly held, in paragraph 137 of the judgment under appeal, that the implementing decision of 30 January 2014 entailed implementing measures and that the decision at issue constituted one of those measures. Second, the General Court erred in relying on the finding, made in paragraph 136 of the judgment under appeal, that, since Polpharma had been able to demonstrate that the implementing decision of 30 January 2014 was capable of having a direct effect on its legal situation only by submitting a generic application, the decision at issue was a necessary implementing measure.

56 Polpharma submits that this ground of appeal should be rejected.

Findings of the Court

57 It should be noted that, by its first ground of appeal in Case C-439/21 P, Biogen seeks to challenge paragraphs 136 and 137 of the judgment under appeal, in so far as the General Court there held, in essence, that the implementing decision of 30 January 2014 entailed implementing measures and that the decision at issue constituted one of those measures.

58 However, it is apparent from the assessment made by the General Court in paragraphs 138 to 147 of the judgment under appeal that its conclusion, in paragraph 148 of the judgment under appeal, that Polpharma would not have been entitled to bring an action on the basis of Article 263 TFEU for the annulment of the implementing decision of 30 January 2014, was founded, in any event, on the finding that Polpharma did not have a current and vested interest in bringing proceedings against that decision.

59 It follows that the first ground of appeal in Case C-439/21 P must be rejected as ineffective.

The second ground of appeal in Case C-438/21 P, the second ground of appeal in Case C-439/21 P and the third ground of appeal in Case C-440/21 P

Arguments of the parties

60 By their respective grounds of appeal, directed against paragraphs 173 to 180, 236 to 238, 274, 275, 280 to 282, 288, 289 and 292 of the judgment under appeal, the Commission, Biogen and the EMA allege, in essence, infringement of the second subparagraph of Article 6(1) of Directive 2001/83. In particular, they complain that the General Court misinterpreted the concept of 'global marketing authorisation' referred to in that provision.

61 In that regard, the appellants claim that the General Court infringed that provision, as interpreted by the case-law of the Court of Justice, by holding that the EMA and the Commission should, in the context of the assessment of whether Fumaderm and Tecfidera belong to the same global marketing authorisation, have carried out a reassessment of the qualitative composition in terms of active substances of the initial medicinal product, namely Fumaderm, which is a combination medicinal product, in order to ascertain whether MEF and DMF each make a therapeutic contribution within that combination.

62 In their view, the test which the General Court thereby applied is not justified either by the second subparagraph of Article 6(1) of Directive 2001/83 or by the legislative objectives underlying the concept of 'global marketing authorisation'.

63 First, according to the appellants, the clear wording of the second subparagraph of Article 6(1) of Directive 2001/83 lists exhaustively all possible subsequent developments of a medicinal product coming within the scope of an existing global marketing authorisation. Those changes include other strengths, pharmaceutical forms, administration routes and presentations of an initial medicinal product, as well as variations and extensions of the marketing authorisation for that medicinal product. The concepts of 'variation' and 'extension' are expressly defined in Regulation No 1234/2008 and there is no doubt that the elimination of the active substance of a product initially authorised, or its replacement by a different active substance, cannot be regarded as a development covered by the global marketing authorisation of the initially authorised product.

64 It follows from the very wording of the second subparagraph of Article 6(1) of Directive 2001/83 that two medicinal products containing active substances which do not share the same therapeutic moiety, and which are therefore different, cannot be regarded as belonging to the same global marketing authorisation. The importance of the therapeutic moiety for considering substances or goods to be different was also recognised in the judgment of 20 January 2005, *SmithKline Beecham* (C-74/03, EU:C:2005:39). It is therefore necessary to compare the qualitative composition in terms of active substances of the initial medicinal product, as established in its marketing authorisation, with the qualitative composition in terms of active substances of the second medicinal product.

65 According to the appellants, the General Court wrongly imported, into the assessment of the existence of a global marketing authorisation, an assessment concerning the risk-benefit balance of the initial medicinal product, which was part of the procedure for granting marketing authorisation for that medicinal product. In that regard, the appellants claim that establishing the qualitative composition, in terms of active substances, of a medicinal product comes within the remit of the competent authority, at national or EU level, which grants the marketing authorisation for the initial medicinal product and includes, in the case of a fixed combination

medicinal product, the assessment of whether the two active substances make a documented therapeutic contribution within that combination. If this is not the case, a product should be authorised as a medicinal product containing only one active substance. By contrast, the assessment of the qualitative composition in terms of active substances of the initial medicinal product does not form part of the assessment of the global marketing authorisation. The General Court's approach would encourage a systematic reassessment of decisions previously adopted.

66 Second, according to the appellants, the aims and context of the concept of 'global marketing authorisation' support the literal interpretation of the second subparagraph of Article 6(1) of Directive 2001/83. According to settled case-law, that concept and the RDP linked to it seek to ensure a fair balance between the protection of innovative companies and the interests of competition which are served by the marketing of generic medicinal products. The aim of the concept of a 'global marketing authorisation' is to achieve that balance, while providing a practical criterion for determining whether two medicinal products belong to the same global marketing authorisation, as stated in recital 9 of Directive 2001/83. Therefore, in the present case, since Fumaderm was authorised as a fixed combination medicinal product containing two active substances, that medicinal product and Tecfidera could belong to the same global marketing authorisation only if those two substances are not different. However, the CHMP concluded that that was not the case, since they do not have the same therapeutic moiety.

67 In addition, the EMA is of the view that the test established by the General Court is also contrary to Article 10(2)(b) of Directive 2001/83, inasmuch as it could lead to the situation of a generic product using de facto as its reference medicinal product, for the purpose of calculating the expiry of the RDP, a product with a different qualitative composition in terms of active substances.

68 Lastly, Biogen adds that, if, under Article 10(2)(b) of Directive 2001/83, the active substances of two medicinal products under comparison are different, they cannot be considered to be mere variants of the same product and cannot form part of the same global marketing authorisation. Moreover, in doubting whether the therapeutic contribution of the MEF had been correctly assessed in the context of the marketing authorisation for Fumaderm, the General Court actually doubted whether that marketing authorisation had been validly granted in accordance with the legal and regulatory requirements of the European Union. However, only medicinal products which have been granted marketing authorisation in accordance with those requirements are capable of being a reference medicinal product and of starting a global marketing authorisation.

69 Polpharma disputes the appellants' arguments.

70 It submits that the publicly available scientific evidence supports the conclusion that the component MEF, removed from the fixed combination medicinal product in order to obtain the monotherapy, does not make a significant or relevant therapeutic contribution within that combination. The second subparagraph of Article 6(1) of Directive 2001/83 does not specifically address that situation since its wording does not provide a clear answer to the determination of the scope of the global marketing authorisation for Fumaderm.

71 In its view, it is essential for the protection offered by the RDP to be balanced against the need to provide an effective system allowing cheaper generic versions of innovative medicinal products to gain access to the market once an appropriate period of market protection for innovators has expired.

72 In that regard, in the first place, Polpharma acknowledges that the changes referred to in Article 6(1) of Directive 2001/83 do not cover a change in active substance profile. However, Fumaderm and Tecfidera have the same active substance profile, with the result that the issue of a 'change' of active substance(s) does not arise and the analysis of Regulation No 1085/2003 is irrelevant in the present case.

73 According to Polpharma, where two products contain the same (or deemed to be the same, for RDP purposes) active substance(s) and belong to the same marketing authorisation holder, they are, quite simply, the 'same' medical product for global marketing authorisation purposes. The presence or absence of an inactive 'excipient' component in a product (or of a component with insignificant or clinically irrelevant activity) has no relevance in this regard. It is only once it has been concluded that Tecfidera and Fumaderm are the same product for the purposes of the global marketing authorisation that the wording of the second subparagraph of Article 6(1) of Directive 2001/83 then becomes relevant in order to confirm that the differences, such as a different indication, do not in any way alter the conclusion that they belong to the same global marketing authorisation.

74 Consequently, in Polpharma's view, the verification of MEF's therapeutic contribution within Fumaderm is the correct and proportionate method for confirming whether there is a difference between Fumaderm and Tecfidera for the purposes of the RDP.

75 By contrast, the test whereby it is sufficient to compare the authorised qualitative compositions in terms of active substances of Tecfidera and Fumaderm in order to determine a RDP-relevant difference is too simplistic to ensure that it will result in a correct RDP determination. Polpharma submits that the General Court was right to state, in paragraph 292 of the judgment under appeal, that such an approach presented the risk, in the case in hand, of an RDP being granted contrary to the objectives pursued by the concept of a 'global marketing authorisation'.

76 In that regard, Polpharma also agrees with the General Court's view that the situation which gave rise to the judgment of 28 June 2017, *Novartis Europharm* v *Commission* (C-629/15 P and C-630/15 P, EU:C:2017:498, paragraph 72), was different from that of the present case.

77 Similarly, the judgment of 20 January 2005, *SmithKline Beecham* (C-74/03, EU:C:2005:39), referred to by the Commission, was based on a very different factual background. However, that judgment establishes a fundamental principle that the 'sameness' of active substances for RDP purposes must be interpreted in the light of the purpose of the RDP provisions, in order to give proper effect to the wording of the legislation.

78 In the second place, Polpharma contends that, in the case of a fixed combination medicinal product, the risk-benefit balance does not necessarily say anything about the specific therapeutic activity or risks of the substances if they were to be administered individually. Accordingly, it is misleading to argue that the General Court's approach consists of importing into the concept of a global marketing authorisation an assessment that pertains to the assessment of the risk-benefit balance of the initial medicinal product, because the assessment of the relevant therapeutic contribution of MEF within Fumaderm, for RDP purposes, was not a necessary component of the assessment of the marketing authorisation application for that medicinal product. Polpharma states that it is not in dispute that the BfArM validly granted a marketing authorisation for Fumaderm; the General Court focused on the need to verify whether, for the purposes of the global marketing authorisation, the components of Fumaderm make a relevant and significant therapeutic contribution.

79 In the third place, Polpharma is of the view that the test adopted by the General Court is not contrary to Article 10(2)(b) of Directive 2001/83, given that it could be necessary to identify more than one version of the reference product. In the present case, Tecfidera would be the reference medicinal product mentioned in the application for marketing authorisation for a generic medicinal product, whereas Fumaderm would be the reference medicinal product used to demonstrate that the RDP had expired. Alternatively, if those two medicinal products belong to the same global marketing authorisation, then the qualitative composition of Fumaderm in terms of active substances for the purposes of that global marketing authorisation and of the RDP would be deemed to be the same as that of Tecfidera.

Findings of the Court

80 By their respective grounds of appeal, the appellants complain, in essence, that the General Court erred in law in holding that, in the context of the assessment as to whether two medicinal products belong to the same global marketing authorisation within the meaning of the second subparagraph of Article 6(1) of Directive 2001/83, the Commission was obliged to verify the assessment of the qualitative composition in terms of active substances of the first medicinal product authorised by a competent national authority as a fixed combination medicinal product, in order to establish that those substances each make a therapeutic contribution within that combination.

81 As a preliminary point, it must be recalled that the first subparagraph of Article 6(1) of Directive 2001/83 establishes, as a prerequisite for the placing of any medicinal product on the market of a Member State, the issuing of a marketing authorisation. That authorisation may be granted either by the competent national authorities, in accordance with Directive 2001/83, or by the Commission, under Regulation No 726/2004.

82 Furthermore, the second subparagraph of Article 6(1) of Directive 2001/83, read in conjunction with recital 9 of Directive 2001/83, sets out exhaustively the subsequent developments to which a medicinal product which has been granted a first marketing authorisation may be subject, the corresponding authorisations of which are considered to belong to the same global marketing authorisation, as the Court of Justice stated in the judgment of 28 June 2017, *Novartis Europharm* v *Commission* (C-629/15 P and C-630/15 P, EU:C:2017:498, paragraph 72), irrespective of the authorisation procedures specific to each of those subsequent developments, whether it be the variation of the initial marketing authorisation for that medicinal product or the grant of a separate marketing authorisation. Those developments are any additional strengths, pharmaceutical forms, administration routes, presentations, as well as any variations and extensions of the medicinal product that was granted an initial marketing authorisation.

83 In the present cases, in the light of the substance of the appellants' criticism of the General Court, it is necessary to examine whether a difference in the qualitative composition of an authorised medicinal product, in terms of active substances, within the meaning of Article 1(3a) of Directive 2001/83, is among the subsequent developments provided for in the second subparagraph of Article 6(1) of that directive.

84 In the first place, it is not disputed that such a difference in the qualitative composition of an authorised medicinal product does not constitute an additional strength, pharmaceutical form, administration route or even presentation.

85 In the second place, as regards the words 'any variations and extensions' in the second subparagraph of Article 6(1) of Directive 2001/83, the Court has already held that these refer to a variation to the terms of a marketing authorisation or an extension thereof, within the meaning of Regulation No 1085/2003 (judgment of 28 June 2017, *Novartis Europharm* v *Commission*, C-629/15 P and C-630/15 P, EU:C:2017:498, paragraph 66).

86 Regulation No 1085/2003 was replaced by Regulation No 1234/2008, which refers, first, to 'variations' or 'variations to the terms of a marketing authorisation' and, second, to 'extensions', which correspond, with the exception of urgent safety restrictions, to the most significant variations. In accordance with Article 2 of that regulation, the extension of a marketing authorisation refers to any variation which is listed in Annex I to that regulation and which fulfils the conditions laid down therein. In particular, point 1(a) of that Annex I provides that the extension of a marketing authorisation results from the 'replacement of a chemical active substance by a different salt/ester complex/derivative, with the same therapeutic moiety, where the efficacy/safety characteristics are not significantly different'.

87 It follows, as the Advocate General observed, in essence, in points 55 and 56 of her Opinion, that the difference in the qualitative composition of a medicinal product due to the replacement of the active substance(s) of that medicinal product by another substance or substances with a different therapeutic moiety cannot be classified as a 'variation and extension' within the meaning of the second subparagraph of Article 6(1) of Directive 2001/83.

88 In the present case, as is stated in paragraphs 16 to 38 of the judgment under appeal, the adoption of the implementing decision of 30 January 2014 was preceded by an assessment, by the CHMP, of the issue of whether DMF differed from Fumaderm, which contains DMF and MEF. The CHMP concluded that Fumaderm, which contains DMF and MEF, and Tecfidera, which contains DMF as a mono-substance, were different, since DMF and MEF do not have the same therapeutic moiety and therefore do not correspond to the same active substance.

89 In the light of the relevant provisions set out above, such an assessment by the CHMP was sufficient, contrary to what the General Court ruled, for the purpose of determining whether the medicinal products in question do or do not belong to 'the same global marketing authorisation' within the meaning of the second subparagraph of Article 6(1) of Directive 2001/83. Accordingly, by holding, in paragraphs 280 to 289 and 293 of the judgment under appeal, that the Commission was also required to verify that the active substance in the first medicinal product authorised had a 'therapeutic contribution' that the composition of the second medicinal product authorised did not, and that it was for the Commission to verify the 'role' played by that substance in the first medicinal product by examining whether and how that role had been analysed by the national authority that had issued a marketing authorisation for that medicinal product or by asking the CHMP to verify the role played by MEF within Fumaderm, the General Court had failed to have regard for those relevant provisions.

90 Moreover, the taking into consideration of the objectives of the second subparagraph of Article 6(1) of Directive 2001/83 did not impose on the Commission the obligation to carry out the verification referred to in paragraph 89 of the present judgment.

91 In that regard, it must be noted that, in accordance with the second subparagraph of Article 6(1) of Directive 2001/83, the first marketing authorisation and the marketing authorisations relating to the development of the initial medicinal product are considered to belong to the same global marketing authorisation, in particular for the purpose of using the abridged procedure on expiry

of the applicable RDP, as stated in Article 10(1) of that directive. Thus, in the light of the link which the second subparagraph of Article 6(1) establishes between the RDP and the global marketing authorisation, that latter concept is essential for determining the conditions under which applicants may refer, in the abridged procedure, to the data contained in the file of the reference medicinal product.

92 The existence of a global marketing authorisation within the meaning of the second subparagraph of Article 6(1) of Directive 2001/83 means, in essence, that a single RDP, as provided for in Article 10(1) of that directive, applies to the developments of a medicinal product already authorised provided for in that Article 6 from the date of authorisation of that medicinal product. Therefore, by preventing the prolongation of the RDP of an existing product on the basis of mere variants undeserving of its benefit, the second subparagraph of Article 6(1) of Directive 2001/83 seeks to ensure a fair balance between the protection of innovative companies and general interests that are served by the marketing of generic medicinal products.

93 However, inasmuch as the wording of the second subparagraph of Article 6(1) of Directive 2001/83 and the context in which that provision occurs do not mean that the concept of a 'global marketing authorisation' applies to medicinal products with different qualitative compositions, within the meaning set out in paragraph 86 above, the objectives of that provision cannot in themselves justify the need to verify, beyond a qualitative comparison of those products in order to assess whether they belong to the same global marketing authorisation, the therapeutic contribution of the active substance or substances of the first medicinal product authorised.

94 In the light of all of the foregoing considerations, it must be held that the General Court erred in law in holding that, in the context of the assessment as to whether two medicinal products belong to the same global marketing authorisation within the meaning of Article 6(1) of Directive 2001/83, as interpreted by the case-law of the Court of Justice, the Commission is required to verify that the active substance in the first medicinal product authorised at national level had a therapeutic contribution that the composition of the medicinal product subsequently authorised by the Commission itself did not.

95 In those circumstances, the second ground of appeal in Case C-438/21 P, the second ground of appeal in Case C-439/21 P and the third ground of appeal in Case C-440/21 P must be upheld.

96 Since the error of law established above is such as to lead to the judgment under appeal being set aside, the appeals must be upheld without there being any need to rule on the other grounds of appeal.

The action before the General Court

97 In accordance with the second sentence of the first paragraph of Article 61 of the Statute of the Court of Justice of the European Union, if the decision of the General Court is set aside, the Court of Justice may itself give final judgment in the matter, where the state of the proceedings so permits.

98 That is the position in the present cases, since the single plea in law in the action at first instance seeking annulment of the decision at issue was the subject of an exchange of arguments before the General Court and its examination does not require any further measure of organisation of

procedure or inquiry to be taken in the cases (see, to that effect, judgment of 8 September 2020, *Commission and Council* v *Carreras Sequeros and Others*, C-119/19 P and C-126/19 P, EU:C:2020:676, paragraph 130).

99 In support of its application for annulment, Polpharma raises a single plea in law, alleging that the implementing decision of 30 January 2014 is unlawful in so far as the Commission considered in that decision that Tecfidera did not belong to the same global marketing authorisation as Fumaderm. In essence, Polpharma submits that that decision, which is the sole legal basis for the decision at issue, is unlawful and must, in accordance with Article 277 TFEU, be declared inapplicable. Consequently, it submits, the decision at issue, which refuses to validate the application for marketing authorisation for a generic medicinal product derived from Tecfidera, has no legal basis and must be annulled, inter alia on the grounds of a failure to state reasons pursuant to Article 296 TFEU.

100 Polpharma submits that, in the implementing decision of 30 January 2014, the Commission applied an incorrect test and committed a manifest error of assessment when it concluded that Tecfidera and Fumaderm were different and that Tecfidera was therefore not covered by the global marketing authorisation for Fumaderm. In the first place, the test applied did not take into account all the relevant factors. In the second place, if the CHMP and the Commission had applied the appropriate test and had taken into account all the relevant factors, they could not have decided that Tecfidera did not come within the scope of the global marketing authorisation for Fumaderm.

101 Thus, both of those complaints seek to claim that the implementing decision of 30 January 2014 is vitiated by a manifest error of assessment on the ground that, when adopting that decision, the Commission relied only on certain factors, and not on all the available and relevant data which should have been taken into consideration. More specifically, Polpharma claims that, when faced with an application for marketing authorisation for an active substance which is part of a previously authorised combination medicinal product, the assessment as to whether there is a difference between that combination and that isolated active substance depends on whether the individual active substances in the combination provide a documented and relevant therapeutic contribution within that combination. Thus, according to Polpharma, the comparison for the purpose of establishing whether Fumaderm and Tecfidera are ‘different’ for the purposes of the global marketing authorisation is not a mere comparison of two active substances with each other.

102 The EMA, supported by the Commission and Biogen, disputes those arguments.

103 In that regard, it should be noted that, by the decision at issue, the EMA informed Polpharma that it was not in a position to validate its application for a marketing authorisation for a generic medicinal product derived from the reference medicinal product Tecfidera. It stated that, according to recital 3 of the implementing decision of 30 January 2014, Tecfidera and the already authorised medicinal product Fumaderm did not belong to the same global marketing authorisation within the meaning of Article 6(1) of Directive 2001/83, on the ground that MEF and DMF, which make up Fumaderm, were both active and did not correspond to the same active substance, since their therapeutic moiety was not the same. It stated that it followed that Tecfidera, which contains DMF, differed from Fumaderm, the other medicinal product already authorised.

104 It is thus apparent from the implementing decision of 30 January 2014 that the CHMP compared the two medicinal products concerned, in terms of active substances, in order to conclude that, because the therapeutic moiety of the active substances comprising the first medicinal product was not the same, that medicinal product was different from the second medicinal product, which was composed of one of its substances, with the result that the two medicinal products were not covered by the same global marketing authorisation, in accordance with the second subparagraph of Article 6(1) of Directive 2001/83.

105 While Polpharma disputes the merits of the test applied by the Commission in the present case, it is apparent from paragraphs 86 to 89 of the present judgment that, for the purpose of deciding whether or not two products belong to the same global marketing authorisation within the meaning of the second subparagraph of Article 6(1) of Directive 2001/83, that institution was entitled to rely on such a comparison of Fumaderm and Tecfidera and was not required to verify the therapeutic contribution of MEF within Fumaderm or, a fortiori, the relevance of that contribution.

106 Therefore, by relying, in the implementing decision of 30 January 2014, on the finding that MEF and DMF, of which Fumaderm is composed, were two active substances with different therapeutic moiety and that the composition of Tecfidera and Fumaderm was different in terms of active substances, the Commission did not make a manifest error of assessment in concluding that Tecfidera did not belong to the same global marketing authorisation, within the meaning of the second subparagraph of Article 6(1) of Directive 2001/83, as Fumaderm.

107 In the light of the foregoing considerations, the single plea in law alleging that the implementing decision of 30 January 2014 is unlawful must be rejected and, accordingly, the action must be dismissed.

Costs

108 Pursuant to Article 184(2) of the Rules of Procedure of the Court of Justice, the Court is to make a decision as to costs where the appeal is well founded and the Court itself gives final judgment in the case.

109 Article 138(1) of those rules, which is applicable to appeal proceedings by virtue of Article 184(1) of the same rules, provides that the unsuccessful party is to be ordered to pay the costs if they have been applied for in the successful party's pleadings.

110 Since Polpharma has been unsuccessful after the appeals have been allowed, and since the Commission, Biogen and the EMA have applied for costs, Polpharma must be ordered to bear its own costs and to pay those incurred by the Commission, Biogen and the EMA both at first instance in Case T-611/18 and in the present appeals in Cases C-438/21 P to C-440/21 P.

On those grounds, the Court (Fourth Chamber) hereby:

1. **Sets aside the judgment of the General Court of the European Union of 5 May 2021, *Pharmaceutical Works Polpharma* v *EMA* (T-611/18, EU:T:2021:241);**

2. **Dismisses the action brought by Pharmaceutical Works Polpharma S.A. in Case T-611/18;**

3. Orders Pharmaceutical Works Polpharma S.A. to bear its own costs and to pay those incurred by the European Commission, Biogen Netherlands BV and the European Medicines Agency (EMA).

Lycourgos Rossi Bonichot

Rodin Spineanu-Matei

Delivered in open court in Luxembourg on 16 March 2023.

A. Calot Escobar C. Lycourgos
Registrar President of the Chamber