Reports of Cases

JUDGMENT OF THE GENERAL COURT (Tenth Chamber, Extended Composition)

13 November 2024*

(Medicinal products for human use – Generic medicinal products – Decision granting marketing authorisation for the medicinal product for human use Dexmedetomidine Accord – dexmedetomidine – Eligibility of a medicinal product as a reference medicinal product – Article 10(1) and (2) of Directive 2001/83/EC)

In Case T-223/20,

Orion Oyj, established in Espoo (Finland), represented by C. Schoonderbeek, lawyer, J. Mulryne and E. Amos, Solicitors, and J. Stratford, Barrister-at-Law,

applicant,

v

European Commission, represented by L. Haasbeek, E. Mathieu and R. Lindenthal, acting as Agents,

defendant,

supported by

Accord Healthcare, SL, represented by C. Drew, Solicitor, D. Piccinin, Barrister, and T. Johnston, Barrister-at-Law,

intervener,

THE GENERAL COURT (Tenth Chamber, Extended Composition),

composed of S. Papasavvas, President, O. Porchia, L. Madise, P. Nihoul and S. Verschuur (Rapporteur), Judges,

Registrar: A. Marghelis, Administrator,

having regard to the written part of the procedure,

further to the hearing on 27 February 2024,

gives the following

* Language of the case: English.

Judgment

1 By its action under Article 263 TFEU, the applicant, Orion Oyj, seeks the annulment of Commission Implementing Decision C(2020) 942 (final) of 13 February 2020 granting marketing authorisation under Regulation (EC) No 726/2004 of the European Parliament and of the Council [of 31 March 2004 laying down Union 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)] for 'Dexmedetomidine Accord – dexmedetomidine' ('Dexmedetomidine Accord'), a medicinal product for human use ('the contested decision').

Background to the dispute

2 The applicant is a pharmaceutical company which has its registered office in Finland and which develops, manufactures and markets, for human and veterinary use, pharmaceuticals, active pharmaceutical ingredients and diagnostic tests.

The Czech marketing authorisation for Precedex

3 At the start of the 1990s, the applicant developed the active substance called 'dexmedetomidine hydrochloride'.

4 On 9 September 1994, the applicant entered into a licensing and supply agreement with Abbott Laboratories Inc. ('Abbott'), under which it granted Abbott an exclusive licence to manufacture and market dexmedetomidine hydrochloride in 'all countries and territories of the world except Finland, Sweden, Norway, Denmark and Iceland'. In addition, that contract provided that Fermion, a subsidiary of the applicant, was to supply that active substance to Abbott.

5 In that context, on 18 December 1998, Abbott submitted to the European Medicines Agency (EMA), which, at the time of the facts, was called the European Agency for the Evaluation of Medicinal Products (EMEA), by means of the centralised procedure under Article 3 of Council Regulation (EEC) No 2309/93 of 22 July 1993 laying down Community procedures for the authorization 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), an application for marketing authorisation for dexmedetomidine hydrochloride, under the trade name Primadex, subsequently called Precedex ('Precedex'). The indication for Precedex was as follows: 'alpha 2 sedative with analgesic properties for use in an intensive care setting'.

6 In the context of that application for marketing authorisation, Abbott submitted, inter alia, three clinical studies in order to demonstrate the safety and efficacy of Precedex and support its assessment of Precedex's benefit/risk balance.

7 During the examination of the application for marketing authorisation for Precedex, the rapporteur and the co-rapporteur within the EMA's Committee for Medicinal Products for Human Use ('the CHMP'), which, at the time of the facts, was called the Committee for Proprietary Medicinal Products (CPMP), raised serious concerns about the adequacy of the three clinical studies. More specifically, their assessment report set out 16 questions and 4 major objections, which were endorsed by the CHMP at its meeting held on 18 to 20 May 1999. Those objections related to (i) the fact that the clinical data was not representative of the patient

population concerned by the proposed indication, (ii) the lack of evidence of the safety and efficacy of Precedex without additional sedation, (iii) the lack of comparison with existing sedatives, and (iv) the insufficiency of data on its cardiovascular effects.

8 In those circumstances, given the scale and cost of the additional clinical studies which the CHMP considered necessary, Abbott, on 16 March 2000, withdrew the original application and subsequently ceased its attempts to obtain a marketing authorisation from the European Commission through the centralised procedure.

9 Thereafter, Abbott decided to request various marketing authorisations for Precedex from several European countries which were not yet members of the European Union, including the Czech Republic.

10 Accordingly, on 29 August 2000, Abbott made an application for marketing authorisation to the Státní ústav pro kontrolu léčiv (SUKL, State Institute for Drug Control, Czech Republic).

11 According to the applicant, the clinical data submitted in support of that application for marketing authorisation were identical to the data enclosed with the original application made to the EMA (see paragraph 5 above), since Abbott had not carried out any additional study.

12 On 23 October 2002, Abbott obtained a marketing authorisation for Precedex in the Czech Republic from the SUKL, in accordance with Czech law as in force at that time ('the Czech marketing authorisation for Precedex'). Precedex was indicated for 'sedation of intubated patients during mechanical ventilation therapy in intensive care units' and was to 'be administered as a continuous infusion for up to 24 hours'.

13 At the request of the SUKL, two external experts examined certain documents submitted by Abbott in support of the application for the Czech marketing authorisation for Precedex, namely the package leaflet of the medicinal product at issue and a summary of its characteristics in Czech and other documents in English. The assessment report of those experts, the creation of which required 20 hours of work between 25 September and 15 November 2000, contained approximately four pages of text and did not make any reference to the clinical studies submitted by Abbott.

14 On 25 March 2002, the applicant and Abbott agreed an amendment to the exclusive licence to manufacture and market dexmedetomidine hydrochloride, whereby 'Europe' and 'the former states of the Soviet Union' were withdrawn from the territory of that licence. Thus, Abbott returned to the applicant the exclusive licence to manufacture and market Precedex in states which, on that date, were Members of the European Union.

15 On 1 May 2004, the Czech Republic joined the European Union.

16 Under Articles 2, 10, 24 and 54 of the Act concerning the conditions of accession of the Czech Republic, the Republic of Estonia, the Republic of Cyprus, the Republic of Latvia, the Republic of Lithuania, the Republic of Hungary, the Republic of Malta, the Republic of Poland, the Republic of Slovenia and the Slovak Republic and the adjustments to the Treaties on which the European Union is founded (OJ 2003 L 236, p. 33), the Czech Republic was required to apply EU law from the date of its accession.

17 On 3 May 2004, with the applicant's agreement, Abbott assigned the exclusive licence to manufacture and market Precedex in several European countries, such as the Czech Republic, to Hospira Inc.

18 The sales of Precedex made in the Czech Republic by Abbott and Hospira between November 2002 and December 2006 were limited and completely ceased from 2007.

19 On 30 September 2008, Hospira returned to the applicant the exclusive licence to manufacture and market Precedex in certain countries, including the Czech Republic.

20 On 10 June 2010, the applicant requested the withdrawal of the Czech marketing authorisation for Precedex, shortly after acquiring it from Hospira, and that withdrawal became effective as from 30 July 2010.

The marketing authorisation for Dexdor

21 On 18 December 2005, the CHMP, following an application for marketing authorisation submitted by the applicant, confirmed that such an application in respect of a medicinal product with dexmedetomidine hydrochloride as its active substance, called Dexdor, could follow the centralised procedure, on the ground that that latter, under Article 3(2)(b) of Regulation No 726/2004, constituted a 'significant therapeutic … innovation', even though the placement of Precedex, which contains the same active substance, on the market had already been approved in the Czech Republic (see paragraph 12 above).

22 Subsequently, the applicant launched a clinical programme designed to respond to the serious concerns expressed by the CHMP in the analysis of the original application made to the EMA in respect of Precedex (see paragraph 7 above).

23 In 2008, while the clinical programme for Dexdor was ongoing, the applicant submitted an application for a paediatric investigation plan in accordance with Article 7 of Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004 (OJ 2006 L 378, p. 1). In those circumstances, the applicant reminded the EMA of the existence of the Czech marketing authorisation for Precedex, while disputing its compliance with EU law. By letter of 5 February 2009, the EMA contacted the SUKL to request from it details regarding the date on which the Czech marketing authorisation for Precedex was granted and the compliance of that authorisation with EU law. In its reply of 20 February 2009, the SUKL stated that all the national marketing authorisations granted since 1998, such as the Czech marketing authorisation for Precedex, complied with EU law. On the basis of that reply, the EMA informed the applicant that it was not required to submit a paediatric investigation plan.

24 On 14 January 2010, a pre-submission meeting took place between the EMA and the applicant concerning the application for marketing authorisation for Dexdor. At that meeting, the applicant reiterated that, in its view, the Czech marketing authorisation for Precedex did not comply with EU law, with the result that Precedex was not eligible as a reference medicinal product, within the meaning of Article 10(1) and (2)(a) 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 2004/27/EC of the European Parliament and of the Council of 31 March 2004 (OJ 2004 L 136, p. 34), for a generic

medicinal product within the meaning of Article 10(2)(b) of that directive. The applicant also stated that it intended to surrender the Czech marketing authorisation for Precedex as soon as it received it. The EMA replied that, if a party wished to dispute an existing marketing authorisation, it had to do so in court when the application for marketing authorisation for a generic medicinal product was submitted.

25 In September 2010, after completing the clinical programme, the applicant submitted to the EMA, by means of the centralised procedure, an application for marketing authorisation for Dexdor.

26 On 21 July 2011, Dexdor obtained a positive opinion from the CHMP.

27 On 16 September 2011, the Commission granted the applicant, under Article 3 of Regulation No 726/2004, a marketing authorisation for Dexdor. The indication was as follows: 'for sedation of adult intensive care unit ["ICU"] patients requiring a sedation level not deeper than arousal in response to verbal stimulation (corresponding to Richmond Agitation-Sedation Scale (RASS) 0 to -3)'. That indication was narrower than that granted to Precedex.

28 On 22 September 2011, the EMA published the European Public Assessment Report ('the EPAR') on Dexdor. That report contains 79 pages, of which 70 are dedicated to the scientific assessment carried out by the CHMP between 20 October 2010 and 21 July 2011, which addresses, in particular, quality aspects, clinical and non-clinical aspects and clinical efficacy and safety, before assessing the benefit/risk balance of the medicinal product. In addition, the EPAR indicates that marketing authorisations for the active substance dexmedetomidine had already been granted both in Poland in 2001 and in several countries outside of the European Economic Area (EEA) since 1999.

29 Lastly, on 5 January 2018, the applicant submitted to the EMA an application to extend the marketing authorisation for Dexdor in order to include the following indication: 'for sedation of non-intubated adult patients prior to and/or during diagnostic or surgical procedures requiring sedation, i.e. procedural/awake sedation'.

30 On 28 June 2018, the EMA published the EPAR on the additional indication referred to in paragraph 29 above. That report contains 142 pages, of which 125 are dedicated to the scientific assessment carried out by the CHMP between 27 January and 28 June 2018, which addresses, in particular, clinical aspects and clinical efficacy and safety, before assessing the benefit/risk balance of the medicinal product for the additional indication proposed.

31 On 6 August 2018, the Commission approved that additional indication.

The exchanges between the applicant and the Commission concerning the Czech marketing authorisation for Precedex in 2015 and 2016

32 In the course of 2015, the applicant became aware that applications for marketing authorisation for generic medicinal products had been submitted in several Member States.

33 By letter of 14 July 2015, the applicant stated that the applications relating to the national marketing authorisations previously granted for Precedex (see paragraph 28 above) were based on a dossier which had previously been considered insufficient by the EMA, with the result that those marketing authorisations for Precedex had not been granted in accordance with EU law.

Moreover, the applicant requested that the Commission adopt measures to establish that Dexdor was entitled to the whole of the regulatory data protection period provided for by Article 10(1) of Directive 2001/83 and Article 14(11) of Regulation No 726/2004 ('the RDP period').

34 In its reply of 24 July 2015, the Commission stated that the EMA would examine compliance with the RDP period at the time of the submission of an application for marketing authorisation for a generic medicinal product in the centralised procedure.

35 By letter of 30 March 2016, the applicant reiterated that, in its view, the Czech marketing authorisation for Precedex did not comply with EU law, with the result that it could not be taken into account for the calculation of the RDP period. In that context, the applicant claimed, in particular, that the assessment report prepared by the Czech experts following the application for that marketing authorisation did not meet the requirements of EU law. Furthermore, it again requested that the Commission intervene in the procedures at national level.

36 By letter of 17 May 2016, the Commission stated that it had been informed that the applicant's specific questions had been discussed several times, and for the last time in April 2016 at a meeting of the Coordination Group for Mutual Recognition and Decentralised Procedures – Human, and that, at that meeting, the Member State concerned had explained the reasons for which Precedex could be regarded as a reference medicinal product. The Commission concluded that, accordingly, it was no longer in a position to intervene in that case.

37 By letter of 20 May 2016, the applicant requested that the Commission confirm its position.

38 In its reply of 3 June 2016, the Commission explained that it was not participating in the ongoing application procedures for marketing authorisation at issue at national level; that it was not an appellate body, with the result that it was not in a position to intervene; and that, in the event that the holder of a marketing authorisation disagreed with the decision of the competent authority at national level, the Court of Justice of the European Union had recognised that holder's right, under certain conditions, to seek judicial review.

The marketing authorisation for Dexmedetomidine Accord

39 On 23 November 2018, the intervener submitted to the EMA an application for marketing authorisation for Dexmedetomidine Accord, a generic medicinal product, within the meaning of Article 10(2) of Directive 2001/83, of the reference medicinal products Precedex and Dexdor.

40 That application relied on pharmaceutical, preclinical and clinical data submitted in support of the application for marketing authorisation for Dexdor and referred to Precedex only in respect of the concept of global marketing authorisation and, accordingly, the starting point for the RDP period.

41 More specifically, the intervener was of the opinion that the RDP period for Dexdor had expired on 1 May 2010 on the ground that it was covered, pursuant to the second subparagraph of Article 6(1) of Directive 2001/83, by the same global marketing authorisation as Precedex. Therefore, in its view, Dexdor was not entitled to its own independent RDP period.

42 In the course of examining the application for marketing authorisation for Dexmedetomidine Accord, the EMA sent, on 30 November 2018, an email to the SUKL requesting from it certain information concerning the Czech marketing authorisation for Precedex: (i) the date on which

the application for marketing authorisation had been submitted; (ii) the date on which the marketing authorisation had been granted in accordance with EU law; (iii) information relating to a potential suspension, withdrawal or revocation of the marketing authorisation for public health reasons; (iv) the legal basis on which the marketing authorisation had been granted; and (v) the legal status of the marketing authorisation, under Article 70 of Directive 2001/83.

43 In response, the SUKL stated, in an email of 4 December 2018, (i) that the application for marketing authorisation for Precedex had been submitted on 31 August 2000; (ii) that Precedex had been approved on 21 November 2002, but that, because of the Czech Republic's accession to the European Union on 1 May 2004, that medicinal product had to be regarded as having been approved in accordance with EU law only from the latter date; (iii) that the marketing authorisation had not been revoked for public health reasons, but had been withdrawn following a request of 10 June 2010 from its holder, which was, at the time, the applicant, with effect from 30 July 2010; (iv) that Precedex had been approved in accordance with Article 8(3) of Directive 2001/83; and (v) that that medical product was subject to medical prescription.

44 On 5 August 2019, the applicant's representatives sent a letter to the EMA, in which it was once again stated, in particular, that the application for marketing authorisation for Precedex had relied on the same clinical studies as those which had been submitted to and rejected by the EMA; that the assessment report on that application prepared by the Czech experts (enclosed in Annexes 5 and 6 to that letter) did not comply with EU law; that Abbott, and subsequently Hospira, were the holders of the Czech marketing authorisation for Precedex; and that, shortly after the transfer of that marketing authorisation to the applicant in 2010, the latter had surrendered that authorisation. A copy of that letter was sent to the Commission.

45 By letter of 19 September 2019, the EMA stated that the applicant's comments had been carefully examined, while noting that it only validated applications which complied with EU law. A copy of that letter was sent to the Commission.

46 On 12 December 2019, the CHMP adopted a positive opinion, recommending the grant of a marketing authorisation for Dexmedetomidine Accord.

47 On the same day, the EMA published the EPAR on Dexmedetomidine Accord, which summarised the scientific assessment which it had carried out between 28 December 2018 and 12 December 2019. That report contains 18 pages, of which ten are dedicated to the scientific assessment carried out by the CHMP, which addresses, in particular, quality aspects, clinical and non-clinical aspects, before assessing the benefit/risk balance of the medicinal product.

48 As regards the eligibility of Precedex as a reference medicinal product, it is stated in the EPAR referred to in paragraph 47 above that the application for marketing authorisation for Dexmedetomidine Accord, 'concerns a generic medicinal product as defined in Article 10(2)(b) of [Directive 2001/83] and refers to a reference product, as defined in Article 10(2)(a) of [Directive 2001/83], for which, taking into account the accession of [the] Czech Republic to the [European Union] on 1st May 2004, it is considered that a marketing authorisation has been granted in a Member State in accordance with [EU law] and on the basis of a complete dossier in accordance with Article 8(3) of [Directive 2001/83]'.

49 On 13 February 2020, by the contested decision, the Commission authorised the marketing of Dexmedetomidine Accord. The indication was identical to that granted to Dexdor and was, therefore, narrower than that granted to Precedex.

Forms of order sought

50 The applicant claims that the Court should:

– annul the contested decision;

– order the Commission to pay the costs.

51 The Commission and the intervener contend that the Court should:

– dismiss the action;

– order the applicant to pay the costs.

Law

52 In support of its action, the appellant puts forward three pleas in law.

53 The first plea alleges infringement of Article 10(1) and (2)(a) of Directive 2001/83, in so far as Precedex was accepted as a reference medicinal product even though the Czech marketing authorisation for that medicinal product had not been granted in accordance with EU law, in particular Article 12(2) of Regulation No 726/2004 and Article 8(3) of Directive 2001/83.

54 The second plea alleges infringement of Article 14(11) of Regulation No 726/2004, read in conjunction with Article 10(1) and Article 6(1) of Directive 2001/83, in so far as the Commission concluded that the RDP period for Dexdor had expired on the ground that the two reference medicinal products, Precedex and Dexdor, were covered by the same global marketing authorisation, despite the non-compliance of the Czech marketing authorisation for Precedex with EU law.

55 The third plea alleges infringement of the duty to state reasons and breach of the principle of sound administration, in so far as the contested decision does not provide reasons in support of either the conclusion that the Czech marketing authorisation for Precedex had been granted in accordance with EU law or the conclusion that either the Commission or the EMA had impartially examined the information which the applicant had provided in that respect on several occasions.

56 Accordingly, the main question is whether, in the light of the circumstances specific to the present case, the Commission examined, to the requisite legal standard, the eligibility of Precedex as a reference medicinal product within the meaning of Article 10(1) and (2)(a) of Directive 2001/83.

57 That question must be examined in the light of the essential objective pursued by the applicable regulation, namely to safeguard public health by employing means which will not hinder the development of the pharmaceutical industry or trade in medicinal products within the European Union, as is apparent from recitals 2 and 3 of Directive 2001/83.

58 However, since the Commission relies, in essence, on its lack of competence in that respect, it is appropriate to begin by examining the arguments put forward by the latter before responding to the substantive arguments put forward by the applicant to show that Precedex was not eligible as a reference medicinal product.

The examination carried out by the EMA and the Commission

59 As a preliminary point, it should be observed that, in the present case, the examination of the eligibility of Precedex as a reference medicinal product was confined to an exchange of emails between the EMA and the SUKL, during which the EMA asked five questions (see paragraph 42 above), to which the SUKL replied (see paragraph 43 above).

60 In that regard, it must be noted that, in response to the EMA's second question, concerning the date on which the Czech marketing authorisation for Precedex was granted in accordance with EU law, the SUKL stated that that marketing authorisation had been granted on 21 November 2002, but that, because of the Czech Republic's accession to the European Union on 1 May 2004, that authorisation was regarded as complying with EU law from the latter date.

61 In order to provide proof of the eligibility of Precedex as a reference medicinal product, the EMA reproduced that reply from the SUKL in the EPAR on Dexmedetomidine Accord (see paragraph 48 above).

62 However, the parties agree on the fact that a marketing authorisation cannot be regarded as complying with EU law merely because the issuing country joined the European Union after the grant of that marketing authorisation unless that country provided for transitional measures to make it compliant with EU law. In the absence of such transitional measures, the Czech Republic had to ensure that the Czech marketing authorisation for Precedex was, from 1 May 2004, compliant with Directive 2001/83, but the lack of such measures could not give rise to any presumption that that marketing authorisation did, in fact, comply with EU law.

63 Moreover, the SUKL replied to the third and fourth questions put by the EMA that the Czech marketing authorisation for Precedex had been granted in accordance with Article 8(3) of Directive 2001/83 and that it had not been withdrawn for public health reasons (see paragraph 43 above).

64 In those circumstances, it may be considered that, by accepting Precedex as a reference medicinal product, the Commission relied solely on the SUKL's statement that the Czech marketing authorisation for that medicinal product complied with EU law on 1 May 2004, the date on which the Czech Republic joined the European Union, without carrying out any additional examination.

The Commission's competence to examine the eligibility of Precedex as a reference medicinal product and its obligation in that regard

65 As stated in paragraph 58 above, in response to the first plea in law put forward by the applicant, the Commission, supported by the intervener, submits that the applicant's argument concerning the ineligibility of Precedex as a reference medicinal product is irrelevant in so far as both the Commission and the EMA were bound by the SUKL's statement that the Czech marketing authorisation for Precedex complied with EU law from 1 May 2004. Accordingly, in the

Commission's view, they were not competent, in the course of examining the application for marketing authorisation for Dexmedetomidine Accord, to carry out an examination of the eligibility of Precedex as a reference medicinal product.

66 It argues that it is apparent from the judgment of 14 March 2018, *Astellas Pharma* (C-557/16, EU:C:2018:181), that it is not for the Commission to review the lawfulness of decisions adopted by the SUKL, or their compliance with EU law. Therefore, the competence of the Commission and of the EMA is confined to obtaining confirmation from the competent authority which granted the marketing authorisation for the reference medicinal product that that authorisation complies with EU law.

67 In addition, the judgment of 16 October 2008, *Synthon* (C-452/06, EU:C:2008:565, paragraph 32), establishes that it is not for the Commission or the EMA to carry out a new scientific assessment of a reference medicinal product previously approved by a competent authority of a Member State.

68 Furthermore, the Commission and the intervener rely on the judgment of 16 March 2023, *Commission and Others* v *Pharmaceutical Works Polpharma* (C-438/21 P to C-440/21 P, EU:C:2023:213), to claim that neither the EMA nor the Commission were permitted to carry out an assessment of the Czech marketing authorisation for Precedex, since, first, such an assessment was not part of the examination consisting in ascertaining whether or not the two medical products were covered by the same global marketing authorisation, and, secondly, while it was not necessary to re-examine the questions of fact concerning the active substances of the original marketing authorisations, it was also unnecessary to re-examine the questions concerning the compliance of those authorisations with EU law.

69 In other words, the Commission, supported by the intervener, submits that it cannot call into question the eligibility of Precedex as a reference medicinal product.

70 In that regard, it should, as a preliminary point, be recalled that, under Article 3(1) of Regulation No 726/2004, Article 6(1) of the same regulation and Article 6(1) of Directive 2001/83, no medicinal product may be placed on the market unless a marketing authorisation has been granted by the competent authority in accordance with the substantive requirements laid down by that directive.

71 In particular, Article 8(3) of Directive 2001/83 provides that each application is to be accompanied by a full dossier containing the results of pharmaceutical and pre-clinical tests and of clinical trials, and Article 21(4) of that directive provides that the national competent authority is to draw up an assessment report in which it makes its comments on, inter alia, those results.

72 Article 10 of Directive 2001/83, which applies to the centralised procedure on the basis of Article 6(1) of Regulation No 726/2004, however, provides for an abridged procedure for the purpose of granting authorisation for a generic medicinal product of a reference medicinal product, which is defined, in Article 10(2)(a), as 'a medicinal product authorised under Article 6, in accordance with the provisions of Article 8 [of the same regulation]'. That abridged procedure exempts the party applying for marketing authorisation for the generic medicinal product from the obligation to provide the results of pharmaceutical and pre-clinical tests or of clinical trials. That exemption is intended to allow producers of generic medical products to save the time and expense needed to gather that data and to avoid the repetition of tests on humans or animals

where not absolutely necessary (judgments of 16 October 2003, *AstraZeneca*, C-223/01, EU:C:2003:546, paragraph 42, and of 18 June 2009, *Generics (UK)*, C-527/07, EU:C:2009:379, paragraph 23).

73 However, the abridged procedure does not provide for any relaxation of the requirements of safety and efficacy which must be met by medicinal products approved in the European Union. Accordingly, that procedure is only available where all the particulars and documents demonstrating the safety and efficacy of the reference medicinal product are and remain available to the competent authority before which the application for marketing authorisation for a generic medicinal product is brought (judgments of 5 October 1995, *Scotia Pharmaceuticals*, C-440/93, EU:C:1995:307, paragraph 17; of 16 October 2003, *AstraZeneca*, C-223/01, EU:C:2003:546, paragraph 27; and of 23 October 2014, *Olainfarm*, C-104/13, EU:C:2014:2316, paragraphs 25, 28 and 29). Indeed, access to those particulars and documents allows the latter to ascertain, if necessary, the safety and efficacy of the reference medicinal product and, accordingly, of the generic medicinal product which is the subject of the application for marketing authorisation.

74 Similarly, where the marketing authorisation for a reference medicinal product has been withdrawn for reasons of safety or efficacy, or where the competent authority before which the application for marketing authorisation for a generic medicinal product is brought has evidence which casts doubt on the safety or efficacy of the reference medicinal product, that product may be refused as a reference medicinal product (see, to that effect, judgment of 16 October 2003, *AstraZeneca*, C-223/01, EU:C:2003:546, paragraph 45).

75 Therefore, the eligibility of a medicinal product as a reference medicinal product, within the meaning of Article 10(2)(a) of Directive 2001/83, depends on its compliance with the substantive requirements laid down in that directive in order to ensure the safeguarding of public health. The legislature has not laid down a rule obliging a competent authority before which the application for marketing authorisation for a generic medicinal product is brought to recognise the marketing authorisation for a reference medicinal product previously granted by another competent authority.

76 That being the case, it must be observed that Directive 2001/83 and Regulation No 726/2004 form a uniform and harmonised legal framework applicable to the authorisation of medicinal products, within which those products must satisfy the same substantive requirements and may claim the same protection, irrespective of the authorisation procedure (judgment of 15 September 2015, *Novartis Europharm* v *Commission*, T-472/12, EU:T:2015:637, paragraphs 74 and 76).

77 Since the Commission and the competent authorities of the Member States are subject to the same harmonised rules, they may consider that a marketing authorisation granted by one of them was preceded by a careful examination of the results of pharmaceutical and pre-clinical tests and of clinical trials, thus ensuring a reliable assessment of the benefit/risk balance of the medicinal product, in accordance with the substantive requirements stemming from EU law. That follows directly from the purpose of the abridged procedure provided for in Article 10(1) of Directive 2001/83 (see paragraph 72 above).

78 Therefore, the Commission was correct to claim that it was able, in principle, to rely on the confirmation which it had requested from the SUKL, under the third subparagraph of Article 10(1) of Directive 2001/83, that the Czech marketing authorisation for Precedex had indeed been granted.

79 However, it should be noted that the third subparagraph of Article 10(1) of Directive 2001/83 authorises the authority before which the application for marketing authorisation for a generic medicinal product is brought – the Commission in the present case – to request that the authority which authorised the reference medicinal product transmit to it not only a confirmation that the reference medicinal product is or has been authorised, but also all other relevant documentation. As is apparent from the case-law (see paragraph 73 above), that documentation may include the results of pharmaceutical and pre-clinical tests and of clinical trials submitted in support of the application for marketing authorisation for the reference medicinal product and also the assessment of those results carried out by the competent authority.

80 Accordingly, as the Commission acknowledged in its oral arguments and in response to the Court's questions at the hearing, it is permitted to request more information from the competent authority which authorised the marketing authorisation for the reference medicinal product, and even request that that authority give it access to the dossier relating to that marketing authorisation, where it possesses evidence which calls into question the fact that that marketing authorisation is based on a dossier demonstrating the safety and efficacy of that medicinal product in accordance with the substantive requirements laid down by Directive 2001/83.

81 Furthermore, it should also be borne in mind that the principle of sound administration, provided for in Article 41(1) of the Charter of Fundamental Rights of the European Union, to which the applicant refers in its third plea in law and which entails the duty of diligence, requires that the competent institution examine carefully and impartially all the relevant aspects of the individual case (see, to that effect, judgments of 27 September 2012, *Applied Microengineering* v *Commission*, T-387/09, EU:T:2012:501, paragraph 76 and the case-law cited, and of 16 September 2013, *ATC and Others* v *Commission*, T-333/10, EU:T:2013:451, paragraph 84 and the case-law cited).

82 In the light of the foregoing, it is appropriate to conclude, both on the basis of Article 10(1) and (2) of Directive 2001/83, applied to the centralised procedure on the basis of Article 6(1) of Regulation No 726/2004, and of the principle of sound administration, that, contrary to what the Commission claims, it was competent to examine the eligibility of Precedex as a reference medicinal product and was required to do so where the information provided by the applicant before the contested decision was adopted may have called into question the eligibility of that product as a reference medicinal product.

83 That conclusion cannot be called into question by the references made by the Commission and the intervener to the judgments of 16 October 2008, *Synthon* (C-452/06, EU:C:2008:565, paragraph 32), of 14 March 2018, *Astellas Pharma* (C-557/16, EU:C:2018:181), and of 16 March 2023, *Commission and Others* v *Pharmaceutical Works Polpharma* (C-438/21 P to C-440/21 P, EU:C:2023:213).

84 Contrary to what the Commission and the intervener claim, in its judgment of 16 March 2023, *Commission and Others* v *Pharmaceutical Works Polpharma* (C-438/21 P to C-440/21 P, EU:C:2023:213), the Court of Justice merely determined the existence of a global marketing authorisation.

85 Similarly, it is appropriate to reject the application by analogy, sought by the Commission and the intervener, of the principle set out in the judgment of 14 March 2018, *Astellas Pharma* (C-557/16, EU:C:2018:181), that the courts of a Member State, hearing an action brought by the holder of the marketing authorisation for a reference medicinal product against the marketing authorisation for

a generic medicinal product granted by the competent authority of that Member State, have no jurisdiction to ascertain whether the marketing authorisation for the reference medicinal product granted in another Member State complied with EU law. It is clear that that principle, which addresses the jurisdiction of national courts, is not directly applicable in the present case.

86 Indeed, the case which gave rise to the judgment of 14 March 2018, *Astellas Pharma* (C-557/16, EU:C:2018:181), concerns the specific framework of the decentralised procedure, within the meaning of Article 28 of Directive 2001/83, in which the Member States concerned by the application for marketing authorisation at issue each, in principle, exercise their jurisdiction on an equal footing, whereas the present case concerns the centralised procedure, in which the Commission is competent to adopt a decision for the European Union. Accordingly, that judgment concerns, in a general manner, the jurisdiction of the national courts of the Member States, and not that of the Commission as the competent authority in a centralised procedure.

87 In addition, it is appropriate to reject the Commission's argument that the application by analogy of the mutual recognition procedure, provided for in Article 28(1) and (2) of Directive 2001/83, and of judgment of 16 October 2008, *Synthon* (C-452/06, EU:C:2008:565), confirms the Commission's lack of competence to examine the eligibility of Precedex as a reference medicinal product. Without it being necessary to rule on the applicability of that analogy, that procedure and that judgment confirm that, even though the competent authority before which an application for marketing authorisation for a generic medicinal product is brought must, in principle, recognise a marketing authorisation for a reference medicinal product already granted by another competent authority, the former authority is exempt from that obligation if it has information which calls into question the fact that that marketing authorisation was granted on the basis of a dossier containing all the necessary particulars and documents and that a rigorous assessment of that dossier, in particular the results of pharmaceutical and pre-clinical tests and of clinical trials, has taken place.

88 Indeed, it is apparent from the judgment of 16 October 2008, *Synthon* (C-452/06, EU:C:2008:565), that, even if the competent authority of a Member State before which an application for mutual recognition is brought must, in principle, recognise the marketing authorisation already granted by the competent authority of another Member State, that obligation is subject to the availability of the dossier containing all the particulars and documents required by Article 8(3) of Directive 2001/83, such as the results of pharmaceutical and pre-clinical tests and of clinical trials, and of an evaluation report containing the comments of the competent authority relating, in particular, to those results (Article 21(4) of that directive).

89 Furthermore, the conclusion in paragraph 82 above likewise cannot be called into question by the argument raised by the Commission, supported by the intervener, that the applicant had other opportunities to dispute the compliance of the Czech marketing authorisation for Precedex and, in that context, to invoke the deficiencies of the dossier enclosed with the application for that marketing authorisation, which call into question the eligibility of Precedex as a reference medicinal product, such as withdrawing the Czech marketing authorisation for Precedex, challenging that authorisation before the Czech courts or bringing a complaint before the Commission under Article 258 TFEU.

90 In fact, the Commission's competence to examine the eligibility of a reference medicinal product and its obligation to do so do not depend on the opportunities which the holder of the marketing authorisation for that medicinal product may have had to dispute that marketing authorisation previously (see paragraphs 70 to 82 above).

91 In any event, it must be stated that the argument of the Commission and the intervener is incorrect.

92 In that regard, first, it should be observed that the applicant did not become the holder of the Czech marketing authorisation for Precedex until 2010, (see paragraph 20 above), therefore it may be concluded that it requested withdrawal of that marketing authorisation as soon as possible after having acquired it, it being understood that it could not make such a request before becoming holder of that marketing authorisation.

93 As regards, secondly, the claim that the applicant could have contested the Czech marketing authorisation for Precedex before the Czech courts, it must be observed that the Commission and the intervener have not provided any evidence capable of calling into question the applicant's claim that it did not have standing to bring proceedings against that marketing authorisation before the Czech courts.

94 In respect of, thirdly, the possibility for the applicant to bring a complaint before the Commission in respect of Article 258 TFEU, it is sufficient to note that it is apparent from the documents before the Court that the applicant actually, on several occasions, informed the Commission of its concerns regarding the eligibility of Precedex as a reference medicinal product (see paragraphs 23, 24, 33, 35 and 44, above), without the Commission having responded in any way to the concerns thus expressed.

95 It follows from the foregoing, as indicated in paragraph 82 above, that the Commission was required to examine the alleged deficiencies of the dossier enclosed with the application for the Czech marketing authorisation for Precedex where those deficiencies may have called into question the eligibility of Precedex as a reference medicinal product.

The evidence calling into question the eligibility of Precedex as a reference medicinal product

96 In the context of the first plea in law, the applicant submits that Precedex was not eligible as a reference medicinal product since the Czech marketing authorisation for that medicinal product did not comply with EU law, in particular Article 8(3) of Directive 2001/83 and Article 12(2) of Regulation No 726/2004. In that regard, it claims mainly that the dossier on which the Czech marketing authorisation for Precedex was based contains the same clinical studies as those submitted by Abbott to the EMA in 1999 and that no new clinical study was submitted to the SUKL when the Czech Republic joined the European Union. The applicant made that claim to the Commission well before the contested decision was adopted, in particular by sending a letter to the Commission on 14 July 2015 (see paragraph 33 above) and by sending a letter to the EMA, a copy of which was sent to the Commission, on 5 August 2019 (see paragraph 44 above).

97 At first sight, that claim, which the applicant based on information allegedly received from Abbott and the SUKL, seems likely given, first, the short period of approximately five months which elapsed between the withdrawal by Abbott of the application for marketing authorisation for Precedex from the EMA (on 16 March 2000) and the submission of the application for marketing authorisation for the same medicinal product to the SUKL (on 31 August 2000), and, secondly, the fact that Abbott has not shown any intention to invest in additional clinical studies concerning Precedex (see paragraphs 8 to 10 above).

98 In addition, as is noted in paragraphs 79 and 82 above, the Commission could have easily ascertained whether Abbott had, in fact, submitted the same clinical studies to the EMA and the SUKL, by requesting that the latter furnish it with a copy of the dossier or, more specifically, the clinical studies.

99 It is therefore necessary to examine whether that claim by the applicant, assuming it is established, may call into question the eligibility of Precedex.

100 In that regard, it should be observed that Article 8(3) of Directive 2001/83, read in conjunction with Annex I to that directive, specifies the particulars and documents which must be present in the dossier accompanying an application for marketing authorisation. They include, inter alia, the results of pharmaceutical and pre-clinical tests and of clinical trials which must, in particular, be relevant for the intended indication and enable a sufficiently well-founded and scientifically valid opinion to be formed on the benefit/risk balance of the medicinal product. In the absence of those particulars and documents, the application for marketing authorisation must be rejected without the competent authority having any discretion on that point (judgment of 12 November 1996, *Smith & Nephew* and *Primecrown*, C-201/94, EU:C:1996:432, paragraph 30).

101 It is also necessary to note the specific nature of the present case in the light of the situation which usually arises when the abridged procedure is applied. While it is common practice that the authority before which the application for marketing authorisation for the reference medicinal product is brought is the first to assess the clinical studies and the competent authority before which the application for marketing authorisation for the generic medicinal product is brought then reproduces that assessment, in the present case, the order of events is reversed. The EMA, tasked in 2018 with examining the application for marketing authorisation for the generic medicinal product, Dexmedetomidine Accord, had already examined the clinical studies relating to the application for marketing authorisation for the reference medicinal product, Precedex, before those studies were submitted to the SUKL (see paragraphs 5 to 7 and 39 to 49 above).

102 In that context, the applicant refers to the following facts, which are not disputed by the Commission.

103 Following the marketing authorisation application submitted by Abbott to the EMA in 1998, the rapporteur and the co-rapporteur within the CHMP raised serious concerns about the adequacy of the three clinical studies submitted by Abbott (see paragraph 7 above). In particular, according to the CHMP, those studies did not suffice to demonstrate the benefit/risk balance of Precedex.

104 Despite several attempts by Abbott to respond to the concerns of the CHMP, all the members of that committee took the view that it was appropriate to adopt a negative opinion and to recommend that the Commission reject Abbott's application. Abbott subsequently withdrew its application in March 2000 instead of waiting for its formal rejection (see paragraph 8 above).

105 In that context, the applicant has stated, without being challenged by the Commission, that it was common practice at the time for the competent authorities to encourage the party applying for a market authorisation to withdraw its application and seek scientific advice if they were of the opinion that that application was likely to be rejected for fundamental reasons.

106 Without it being necessary to examine whether the application for marketing authorisation for Precedex must be regarded as having been rejected by the Commission, within the meaning of Article 12(2) of Regulations No 2309/93 and No 726/2004, which require the competent

authorities of the Member States to recognise fully the rejection of an application for marketing authorisation in a centralised procedure, it should be observed that it is apparent from the Commission's recommendations in the document entitled 'Notice to Applicants – Volume 2A: Procedures for marketing authorisation – Chapter 2: Mutual Recognition' that a dossier subject to a negative opinion from the CHMP, such as the one relating to the aforementioned application, should, in principle, be supplemented, under Article 8(3) of Directive 2001/83, with new pre-clinical tests and clinical trials in order to be accepted.

107 The version of the recommendations referred to in paragraph 106 above, published in February 2004 and in force on the date on which the Czech Republic joined the European Union, and the version published in February 2007, which was in force when the contested decision was adopted, each provide, in paragraph 2.3 thereof, that the mutual recognition procedure at national level cannot be used in respect of dossiers which have already been submitted in the centralised procedure, but which have been withdrawn after an assessment by the EMA of the clinical data submitted. In addition, it is apparent from paragraph 2.3 of the version of those recommendations published in February 2007 that such a dossier must have been supplemented with new clinical studies before it may be submitted as a new application. That interpretation of those recommendations, as supported by the applicant, had not been disputed by the Commission.

108 Even though the recommendations referred to in paragraphs 106 to 107 above cannot alter the scope of provisions of EU law, it is necessary to attribute a certain significance to them in so far as they represent the harmonised views of the Commission and the competent authorities of the Member States on the application of Directive 2001/83 (see, to that effect, judgments of 16 October 2003, *AstraZeneca*, C-223/01, EU:C:2003:546, paragraph 28, and of 20 January 2005, *SmithKline Beecham*, C-74/03, EU:C:2005:39, paragraph 42). Moreover, it is apparent from settled case-law that, by adopting and publishing recommendations, an EU institution, such as the Commission, imposes a limit on the exercise of its discretion and cannot, in principle, depart from those recommendations (see, to that effect, judgments of 11 September 2008, *Germany and Others* v *Kronofrance*, C-75/05 P and C-80/05 P, EU:C:2008:482, paragraph 60, and of 10 November 2022, *Commission* v *Valencia Club de Fútbol*, C-211/20 P, EU:C:2022:862, paragraph 35).

109 Accordingly, the possible lack of additional clinical studies in the dossier relating to the Czech marketing authorisation for Precedex was evidence which the Commission possessed and which called into question the fact that that marketing authorisation was based on clinical data enabling a well-founded and scientifically valid opinion to be formed on the benefit/risk balance of that medicinal product, as required by Article 8(3) of Directive 2001/83, read in conjunction with Annex I to that directive.

110 In that context, the Commission, supported by the intervener, claims that if the applicant genuinely took the view that the clinical dossier submitted by Abbott to the SUKL was inadequate, it could have easily prevented that medicinal product from being designated as a reference medicinal product by simply requesting that the Czech marketing authorisation for Precedex be withdrawn on the basis of public health concerns. It is apparent from the judgment of 16 October 2003, *AstraZeneca* (C-223/01, EU:C:2003:546, paragraph 45) that a medicinal product, for which the marketing authorisation has been withdrawn for such a reason, cannot be regarded as a reference medicinal product within the meaning of Article 10(2)(a) of Directive 2001/83.

111 In that regard, it should be noted, as regards the circumstances of the withdrawal of the Czech marketing authorisation for Precedex in 2010, that the nature of the concerns raised by the CHMP in 1999 (see paragraph 7 above) implied the existence of a potential serious risk to public health within the meaning of the Guideline on the definition of a potential serious risk to public health in the context of Article 29(1) and (2) of Directive 2001/83 (OJ 2006 C 133, p. 5), published by the Commission. The lack of clinical data adequately demonstrating the efficacy and safety of the medicinal product gives rise to such a risk. In that respect, it is important to bear in mind that one of the objections of the CHMP concerned the fact that the patient population which had been subject to the clinical studies submitted by Abbott was not representative of the whole population of patients in intensive care concerned by the intended indication.

112 Admittedly, in order to respond to the concerns of the CHMP, the applicant carried out additional clinical studies between 2005 and 2010 (see paragraphs 21, 22 and 25 above). However, it is clear that the indication for that medicinal product, which was the subject of those studies and was eventually approved by the Commission in the context of the marketing authorisation for Dexdor, only concerned part of the indication approved by the SUKL. As the applicant explained at the hearing, the indication for the Czech marketing authorisation for Precedex covered, in essence, all postoperative patients in intensive care, while the additional clinical studies it carried out only concerned a specific subset of those patients.

113 In other words, even though, in 2010, the applicant possessed clinical data demonstrating the efficacy and safety of Dexdor for the indication approved by the Commission, such data were and are still lacking in respect of part of the indication referred to by the Czech marketing authorisation for Precedex.

114 Accordingly, the Commission possessed evidence which called into question the fact that the Czech marketing authorisation for Precedex was based on clinical data relevant for the intended indication, as is required by Article 8(3) of Directive 2001/83, read in conjunction with Annex 1 to that directive, and that it had not been withdrawn for public health reasons (see paragraph 110 above).

115 As regards the Commission's claim that it is inaccurate to assume that the concerns of the CHMP were automatically shared by the SUKL, given the different competences of the SUKL and the EMA, it should be observed that the assessment report relating to the Czech marketing authorisation for Precedex does not contain any information from any analysis of the clinical studies submitted by Abbott (see paragraph 13 above).

116 Indeed, as the applicant has stated, without being challenged by the Commission, and contrary to the EPAR prepared in the context of the marketing authorisation applications for Dexdor and Dexmedetomidine Accord (see paragraphs 28, 30 and 47 above), the assessment report relating to the Czech marketing authorisation for Precedex is rudimentary and contains almost no critical assessment of the dossier.

117 Admittedly, scientific advice on one and the same dossier may differ, but it was not open to the Commission to have the opinion of the SUKL simply prevail over that which the CHMP had already issued on the same dossier, without having ascertained whether the SUKL had actually examined the clinical studies and whether that potential examination had called into question the preceding opinion of the CHMP.

118 Furthermore, as regards the Commission's claim that neither it nor the EMA possessed the assessment report relating to the Czech marketing authorisation for Precedex, with the result that, as far as that report was concerned, the Commission was not able to ascertain the accuracy of the applicant's claims on that point, it is sufficient to note that that report was sent by the applicant to the Commission and the EMA on 5 August 2019 (see paragraph 44 above).

119 In those circumstances, it must be concluded that the Commission had, when the contested decision was adopted, evidence which called into question the eligibility of Precedex as a reference medicinal product. Accordingly, the first plea in law must be upheld and, consequently, the contested decision must be annulled, without there being any need to examine the other pleas in law.

Costs

120 Under Article 134(1) of the Rules of Procedure of the General Court, the unsuccessful party is to be ordered to pay the costs if they have been applied for in the successful party's pleadings. Since the Commission has been unsuccessful, it must be ordered to pay the costs, in accordance with the form of order sought by the applicant.

121 Under Article 138(3) of the Rules of Procedure, the Court may order an intervener other than those referred to in paragraphs 1 and 2 of that article to bear its own costs. In the present case, the intervener must be ordered to bear its own costs.

On those grounds,

THE GENERAL COURT (Tenth Chamber, Extended Composition)

hereby:

1. **Annuls Commission Implementing Decision C(2020) 942 (final) of 13 February 2020 granting marketing authorisation under Regulation (EC) No 726/2004 of the European Parliament and of the Council [of 31 March 2004 laying down Union procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency] for the medicinal product for human use 'Dexmedetomidine Accord – dexmedetomidine';**

2. **Orders the European Commission to bear its own costs and to pay the costs incurred by Orion Oyj;**

3. **Orders Accord Healthcare, SL to bear its own costs.**

Papasavvas Porchia Madise

Nihoul Verschuur

Delivered in open court in Luxembourg on 13 November 2024.

V. Di Bucci M. van der Woude
Registrar President