ORDER OF THE PRESIDENT OF THE COURT OF FIRST INSTANCE
28 June 2000 *

In Case T-74/00 R,

Artegodan GmbH, established in Lüchow (Germany), represented by U. Doepner, Rechtsanwalt, Düsseldorf, with an address for service in Luxembourg at the Chambers of Bonn and Schmidt, 7 Val Sainte-Croix,

applicant,

v

Commission of the European Communities, represented by H. Støvlbæk, of its Legal Service, acting as Agent, and B. Wägenbaur, of the Brussels Bar, with an address for service in Luxembourg at the office of C. Gómez de la Cruz, of its Legal Service, Wagner Centre, Kirchberg,

defendant,

* Language of the case: German.

APPLICATION for suspension of operation of the Commission's decision of 9 March 2000 concerning the withdrawal of marketing authorisations of medicinal products for human use which contain amfepramone (C(2000) 453),

THE PRESIDENT OF THE COURT OF FIRST INSTANCE
OF THE EUROPEAN COMMUNITIES

makes the following

Order

Legal context

1 On 26 January 1965 the Council adopted Directive 65/65/EEC on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products (OJ, English Special Edition 1965-1966, p. 20), since amended on several occasions. Article 3 of that directive lays down the principle that no proprietary medicinal product may be placed on the market in a Member State unless an authorisation has first been issued by the competent authority of that Member State in accordance with the directive or an authorisation has been granted in accordance with 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).

2 Article 4 of the directive states that, in order to obtain a marketing authorisation as provided for in Article 3, the person responsible for placing the product on the market is to apply to the competent authority of the Member State. Under Article 5, the authorisation is to be refused if it proves that the proprietary medicinal product is harmful in the normal conditions of use, or that its therapeutic efficacy is lacking or is insufficiently substantiated by the applicant, or that its qualitative and quantitative composition is not as declared, or if the particulars and documents submitted in support of the application do not comply with Article 4. Under Article 10 the authorisation is to be valid for five years and renewable for five-year periods after consideration by the competent authority of a dossier containing in particular details of the data on pharmacovigilance and other information relevant to the monitoring of the medicinal product.

3 The first paragraph of Article 11 provides that the competent authorities of the Member States are to suspend or revoke an authorisation to place a proprietary medicinal product on the market where that product proves to be harmful in the normal conditions of use, where its therapeutic efficacy is lacking, or where its qualitative and quantitative composition is not as declared. According to that provision, therapeutic efficacy is lacking when it is established that therapeutic results cannot be obtained with the proprietary product.

4 Under Article 21, an authorisation to market a proprietary medicinal product may not be refused, suspended or revoked except on the grounds set out in Directive 65/65.

5 The Second Council Directive (75/319/EEC) of 20 May 1975 on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products (OJ 1975 L 147, p. 13), as amended by Council Directive 93/39/EEC of 14 June 1993 amending Directives 65/65, 75/318/EEC and 75/319 in respect of medicinal products (OJ 1993 L 214, p. 22), provides for a number of arbitration procedures before the Committee for Proprietary Medicinal Products (hereinafter 'the CPMP') of the European Agency for the Evaluation of Medicinal Products (hereinafter 'the Agency'). Such a procedure is applied where a Member State considers that there are grounds for

supposing that the authorisation of the medicinal product concerned may present a risk to public health (Article 10 of Directive 75/319 as amended by Directive 93/39), where divergent decisions have been adopted concerning the grant, suspension or withdrawal of national authorisations (Article 11), in specific cases where the interests of the Community are involved (Article 12) and in the case of variations of harmonised authorisations (Articles 15, 15a and 15b). The procedures laid down in Articles 12 and 15a of Directive 75/319 are of particular relevance in the present case.

6 Under Article 12, the Member States among others may, in specific cases where the interests of the Community are involved, refer the matter to the CPMP for application of the procedure laid down in Article 13 before reaching a decision on a request for a marketing authorisation or on the suspension or withdrawal of an authorisation, or on any other variation to the terms of a marketing authorisation which appears necessary, in particular to take account of the information collected in the context of the pharmacovigilance system provided for in Chapter Va of Directive 75/319.

7 Article 15a provides:

'1. Where a Member State considers that the variation of the terms of a marketing authorisation which has been granted in accordance with the provisions of this Chapter or its suspension or withdrawal is necessary for the protection of public health, the Member State concerned shall forthwith refer the matter to the [CPMP] for the application of the [procedures] laid down in Articles 13 and 14.

2. Without prejudice to the provisions of Article 12, in exceptional cases, where urgent action is essential to protect public health, until a definitive decision is adopted a Member State may suspend the marketing and the use of the medicinal product concerned on its territory. It shall inform the Commission and the other Member States no later than the following working day of the reasons for its action.'

Facts and procedure

8 The applicant is the holder of a marketing authorisation, originally issued by the Federal Republic of Germany, for a medicinal product containing amfepramone called 'Tenuate retard'.

9 On 17 May 1995 the Federal Republic of Germany made a referral to the CPMP in accordance with Article 12 of Directive 75/319, as amended by Directive 93/39, expressing its fears as regards anorectics, which include medicinal products containing amfepramone, liable to cause serious pulmonary artery hypertension.

10 The procedure initiated by this referral led to the adoption of Commission Decision C(96) 3608 of 9 December 1996, based on Article 14(1) and (2) of Directive 75/319, instructing Member States to vary certain clinical information which had to appear in the national authorisations to place the medicinal products in question on the market.

11 By letter of 7 November 1997 addressed to the chairman of the CPMP, the Belgian Ministry of Social Affairs, Public Health and the Environment expressed *inter alia* its fears that there was a causal link between cardiac valve disorders and the use of medicinal products containing amfepramone. It therefore requested the CPMP, pursuant to Articles 13 and 15a of Directive 75/319, to issue a reasoned opinion on the medicinal products concerned.

12 On 31 August 1999 the CPMP gave its opinion on medicinal products containing amfepramone. It reached the conclusion that, although the concerns expressed by the Belgian ministry could not altogether be excluded, there was no evidence to substantiate them. However, it concluded that medicinal products containing

amfepramone had an unfavourable benefit/risk balance and recommended that the marketing authorisations for those products should be withdrawn.

13 On the basis of that opinion, the Commission prepared a draft decision which was sent to the applicant amongst others on 20 January 2000. On 9 March 2000 the Commission adopted the decision concerning the withdrawal of marketing authorisations of medicinal products for human use which contain the following substance: 'amfepramone' (C(2000) 453; hereinafter 'the contested decision'). Article 2 of the contested decision refers to the views expressed by the CPMP in the opinion. Article 3 provides that the Member States are to withdraw the marketing authorisations for all the medicinal products mentioned in Annex I to the contested decision within 30 days of its notification.

14 By application lodged at the Registry of the Court of First Instance on 30 March 2000, the applicant brought an action before the Court under the fourth paragraph of Article 230 EC for annulment of the contested decision or, in the alternative, its annulment in so far as it entails withdrawal of the marketing authorisation for its product Tenuate retard.

15 By separate document lodged at the Court Registry on the same day, the applicant brought the present application for suspension of operation of the contested decision, together with an application on the basis of Article 105(2) of the Rules of Procedure of the Court of First Instance for an urgent decision on the claim for interim relief.

16 On 11 April 2000 the President of the Court of First Instance granted the latter application and ordered that operation of the contested decision should be suspended until the making of the order terminating the proceedings for interim relief.

17 The parties presented oral argument at the hearing on 13 April 2000.

18 During that hearing, the applicant was requested to disclose information by 27 April 2000 at the latest providing a full view of its commercial and/or industrial activities and those of undertakings belonging to the same group.

19 On 27 April 2000 the applicant lodged the information requested at the Court Registry.

Law

20 Under the combined provisions of Articles 242 EC and 243 EC and Article 4 of Council Decision 88/591/ECSC, EEC, Euratom of 24 October 1988 establishing a Court of First Instance of the European Communities (OJ 1988 L 319, p. 1), as amended by Council Decision 93/350/Euratom, ECSC, EEC of 8 June 1993 (OJ 1993 L 144, p. 21), the Court may, if it considers that circumstances so require, suspend the operation of the contested measure or prescribe any necessary interim measures.

21 Article 104(2) of the Rules of Procedure provides that applications for suspension of operation must state the circumstances giving rise to urgency and the pleas of fact and law establishing a prima facie case for the relief applied for. These conditions are cumulative, so that an application for suspension of operation must be dismissed if either of them is not fulfilled (order of the President of the Court of Justice in Case C-268/96 P(R) *SCK and FNK* v *Commission* [1996] ECR I-4971, paragraph 30). The court hearing the application will also, where appropriate, balance the competing interests (order of the President of the Court

of Justice in Case C-107/99 R *Italy* v *Commission* [1999] ECR I-4011, paragraph 59; orders of the President of the Court of First Instance in Case T-191/98 R *DSR-Senator Lines* v *Commission* [1999] ECR II-2531, paragraph 22, and in Case T-222/99 R *Martinez and de Gaulle* v *Parliament* [1999] ECR II-3397, paragraph 22).

Prima facie case

Arguments of the parties

22 The applicant puts forward several pleas in law to establish a prima facie case for the interim relief sought.

23 First, the applicant submits that the Commission lacked competence to adopt the contested decision. Article 15a of Directive 75/319 does not provide a legal basis for the procedure used in the present case. Article 15a allows a Member State to initiate the procedure provided for in Articles 13 and 14 of the directive only in the case of marketing authorisations which have been granted in accordance with Chapter III of the directive. However, the authorisation in question is a national authorisation, not an authorisation granted in accordance with that chapter. The fact that it was varied by the decision of 9 December 1996, following a procedure initiated under Article 12 of Directive 75/319, does not affect that conclusion. It follows from the wording of that decision that the various national authorisations covered by it were to be varied only in part. The applicant accordingly claims that this involved supplementing national authorisations as regards the active substances. In addition, that decision was unlawful because a procedure initiated under Article 12 of Directive 75/319 cannot be concluded by a decision of the Commission made under Article 14 of the same directive. An unlawful decision cannot constitute a basis for the powers of the Commission.

24 Secondly, the applicant claims that the application, under Article 15a of Directive 75/319 as amended, of the procedure provided for by Articles 13 and 14 is always contingent on the condition that a Member State submits an application which defines the subject of the procedure. The Belgian authorities requested a review of the risks of cardiac valve disorders caused by the use of medicinal products containing amfepramone and no Member State submitted a request for an assessment of the benefit/risk balance which these medicinal products presented. The recommendation of withdrawal was therefore based on a variation of the subject of the procedure that the CPMP effected on its own authority in the course of the procedure, an action which rendered the contested decision seriously irregular.

25 Thirdly, the applicant alleges that the contested decision infringes the first paragraph of Article 11 of Directive 65/65 governing the withdrawal of marketing authorisation. According to the applicant, where the Commission orders Member States to withdraw a marketing authorisation under Article 14 of Directive 75/319, the Commission must comply with the conditions for withdrawal laid down in Article 11 of Directive 65/65. In the present case, it must therefore be established that medicinal products containing amfepramone are harmful, that they lack therapeutic efficacy or that their qualitative and quantitative composition is not as declared. However, the opinion of the CPMP, adopted by the Commission to justify the contested decision, does not contain any finding relating to those requirements. Rather, the CPMP weighed the benefits against the risks, which Article 11 of Directive 65/65 does not provide for and is therefore unlawful. Nor can the 'Note for Guidance on Clinical Investigations of Drugs Used in Weight Control', which the CPMP also considered, justify withdrawal of a marketing authorisation because it applies only to new authorisations.

26 Fourthly, the applicant submits that the contested decision is contrary to the principle of proportionality. The CPMP considers, in its final opinion, that long-term clinical studies are necessary to assess the efficacy of medicinal products containing amfepramone and the absence of side effects where the products are taken over a long period and concludes that marketing authorisations for these medicinal products must be withdrawn while the studies remain incomplete. According to the applicant, those clinical studies may none the less also be carried

out if the medicinal products remain on the market. In choosing between withdrawal of marketing authorisations and the requirement that the undertakings carry out clinical studies until the next decision on extension of the authorisation, the Commission should have taken into account the fact that withdrawal of marketing authorisations usually constitutes a measure with irreparable consequences, and is therefore the measure which affects the holder of the authorisation the most seriously. The opinion of the CPMP does not contain considerations relating to risks to public health which could, if need be, justify withdrawal of the marketing authorisations. In addition to this, it is alleged that the holders of marketing authorisations failed to comply with requirements which were in practical terms impossible. Thus, the applicant could not have terminated the long-term studies, which the CPMP considers necessary under the guidelines, until March 2003 at the earliest. The measures adopted by the Community institutions accordingly resulted in a requirement which was impossible to meet in practice and so were unlawful.

27 The applicant adds that the contested decision is in fact founded on the sole consideration that the efficacy of medicinal products containing amfepramone is not proved sufficiently in light of the guidelines (the 'Note for Guidance on Clinical Investigations of Drugs Used in Weight Control'). Consideration of altered assessment criteria cannot, however, lead to withdrawal of the marketing authorisations. Such criteria must be taken into account instead in the context of a decision to extend them. This corresponds to the practice of national authorities concerning authorisation. The contested decision failed to have regard to this national practice, which is entirely usual, and as a result disproportionately exceeds the legal requirements.

28 Finally, the applicant submits that the actions of the Commission are unlawful since the contested decision was not formally notified to the Member States and was not simultaneously communicated to the undertakings.

29 The Commission considers that a prima facie case has not been made out.

30 First, it argues that the decision of 9 December 1996 constitutes a marketing authorisation granted in accordance with Chapter III of Directive 75/319. It adds that that decision was adopted on the basis of Article 12 of Directive 75/319 and resulted in harmonisation of the national marketing authorisations for the medicinal products listed in the decision, one of which is that produced by the applicant. The decision varies, on the basis of Community law, the national marketing authorisations in such a way that, following expiry of the period set in Article 3 of the decision, the medicinal products concerned may be marketed only if their presentation includes the clinical information set out in the decision. Moreover, this harmonisation of clinical information resulted in a substantial variation of the national marketing authorisations. Authorisations must be regarded as harmonised in all the Member States where a medicinal product has been the subject of the procedures provided for in Article 12 of Directive 75/319, as is the case here by means of the decision of 9 December 1996. Finally, in the Commission's submission, the applicant's assertion that Article 12 of Directive 75/319 does not refer to Article 14 of the same directive is devoid of relevance given that the procedure governed by Articles 13 and 14 of that directive constitutes one single procedure.

31 Therefore, the contested decision was not procedurally defective. The Commission argues that, as is apparent from the wording of Article 15a(1) of Directive 75/319, the grounds of the request by the Belgian authorities did not preclude the Agency from carrying out a benefit/risk analysis. Under that provision, in order for such an analysis to be carried out it is sufficient for the Member State to consider in its application that the variation, suspension or withdrawal of a marketing authorisation for a specified medicinal product appears necessary for the protection of public health.

32 The Commission denies that the contested decision is unlawful on the ground that the benefit/risk analysis on which it is based is not provided for in Article 11 of Directive 65/65. Provision is made for a benefit/risk analysis in the context of authorisation to market a proprietary medicinal product and it follows that such an analysis is also possible in relation to withdrawal of the authorisation, governed by Article 11 of Directive 65/65. This is also apparent from the purpose of the Community provisions relating to proprietary medicinal products, which have as their fundamental objective the protection of public health. The Agency

clearly established that medicinal products containing amfepramone lack the necessary therapeutic effect. The Commission submits that the applicant's assertion that medicinal products containing amfepramone are not harmful is indefensible. Finally, the Commission argues that the Agency was not only entitled to rely on the guidelines but also required to carry out a benefit/risk analysis with regard to amfepramone in the light of scientific knowledge.

33 The Commission also disputes that the principle of proportionality has been infringed. In its submission, a decision which only suspended the marketing authorisations would not be justified. The applicant's argument amounts to saying that withdrawal of a marketing authorisation for a medicinal product is always disproportionate given the possibility of suspending the authorisation instead. Such an argument is indefensible.

34 Finally, as regards the argument that the contested decision was not formally notified to Member States and was not simultaneously communicated to the undertakings, the Commission observes that the applicant had to expect, at least from notification of the draft of the contested decision, namely from 19 January 2000, that the Commission would adopt such a decision.

Findings of the President of the Court

35 As regards the question of a prima facie case, the pleas raised by the applicant do not prima facie appear to be entirely unfounded. First, it appears that the competence of the Commission to adopt the contested decision depends on the nature of the decision of 9 December 1996, which is open to debate. Second, the Commission has not adduced convincing evidence to explain, in the light of the principle of proportionality, why that decision and the contested decision

reached diametrically opposed results. The pleas raised by the applicant therefore deserve detailed consideration, a consideration which, however, in fact and in law, goes beyond the scope of the present interim proceedings.

36 In those circumstances, the condition requiring a prima facie case to be made out is satisfied here (order of the President of the Court of First Instance in Case T-308/94 R *Cascades* v *Commission* [1995] ECR II-265, paragraphs 49 and 50).

Urgency

Arguments of the parties

37 The applicant submits that if operation of the contested decision is not suspended it will suffer serious and irreparable damage.

38 The withdrawal of marketing authorisation for Tenuate retard would mean the exclusion of that medicinal product from the pharmaceutical trade lists and its removal from the lists of medicinal products used by the medical profession as a basis for advice and prescription practice. After such an extensive withdrawal from the market, combined with a replacement of the product for buyers, any later re-introduction of such a preparation to the market would be practically destined to fail. Consumer confidence and that of doctors and pharmacists in such a product would be undermined once and for all.

39 The applicant adds that, except for Tenuate retard, which is at issue in the present case, it does not have any other product in respect of which a marketing authorisation has been issued. The withdrawal of this authorisation would therefore destroy its commercial activity and endanger its existence.

40 The Commission maintains that the condition relating to urgency is not fulfilled.

41 First, the possibility of a marketing authorisation being withdrawn is one of the normal business risks of any pharmaceutical undertaking. It is for the undertaking concerned to protect itself against the financial consequences of such a withdrawal by an appropriate policy, such as product diversification and adequate turnover.

42 Second, after initiation of the procedure under Article 15a of Directive 75/319 and, in any event, once the final opinion of the CPMP of 31 August 1999 was drawn up, the applicant could have expected the Member States to be asked by the Commission, in the form of a decision, to withdraw marketing authorisations for medicinal products containing amfepramone.

43 Finally, it cannot be determined from the documentation annexed to the application for interim relief whether the applicant's survival would be threatened by withdrawal of the marketing authorisation for its medicinal product.

Findings of the President of the Court

44 It is settled case-law that the urgency of an application for suspension of the operation of a measure must be assessed in the light of the need for an

interlocutory order in order to avoid serious and irreparable damage to the party seeking suspension. In this connection, it is enough, particularly where damage depends on the occurrence of a number of factors, for that damage to be foreseeable with a sufficient degree of probability (see, *inter alia*, the order of the Court of Justice in Case C-280/93 R *Germany* v *Council* [1993] ECR I-3667, paragraphs 32 and 34, and the order of the President of the Court of First Instance in Case T-65/98 R *Van den Bergh Foods* v *Commission* [1998] ECR II-2641, paragraph 62).

45 In the present case, immediate operation of the contested decision entails the complete withdrawal from the market of the medicinal products referred to in Article 1 of the decision. It therefore also entails exclusion of those medicinal products from the pharmaceutical trade lists and their removal from the lists of medicinal products used by the medical profession as a basis for advice and prescription practice. In addition, if operation of the contested decision is not suspended, substitute medicinal products, the existence of which is acknowledged by both parties, will very probably take the place of the products withdrawn. The confidence of consumers, doctors and pharmacists in a medicinal product is particularly sensitive to statements that the product presents a danger to patients' health. Even if those statements are subsequently disproved, it is often impossible to restore confidence in the withdrawn product, other than in special cases where the qualities of the medicinal product are especially valued by users and there is no perfect substitute product, or where the manufacturer enjoys an exceptionally good reputation, so that it cannot be said that he will be unable to repossess the market shares he held before withdrawal. However, such circumstances are not present here.

46 Moreover, if the contested decision were to be annulled by the Court of First Instance and the applicant thus authorised to resume marketing its medicinal product, the financial damage suffered by it because of a fall in sales as a result of loss of confidence in its product could not in practice be quantified sufficiently completely for the purposes of making reparation.

47 Accordingly, the damage which immediate operation of the contested decision could cause would be serious and irreparable.

Balancing of interests

48 Since the applicant has established the existence of serious and irreparable damage, it is necessary to balance, on the one hand, the applicant's interest in obtaining suspension of operation of the contested decision and, on the other hand, the interest of the Community in the immediate withdrawal of the marketing authorisations for the medicinal products in question and, more generally, in the protection of public health.

49 In undertaking that examination, the judge hearing the application for interim relief must determine whether later annulment of the contested measure by the Court when ruling on the main application would allow the situation which would have been brought about by the immediate operation of the measure to be reversed, and, conversely, whether suspension of operation of the measure would prevent it from being fully effective in the event of the main application being dismissed (see, in particular, the order of the President of the Court of Justice in Joined Cases 76/89 R, 77/89 R and 91/89 R *RTE and Others* v *Commission* [1989] ECR 1141, paragraph 15, the order of the Court of Justice in Case C-180/96 R *United Kingdom* v *Commission* [1996] ECR I-3903, paragraph 89, and the order of the President of the Court of First Instance in Case T-41/97 R *Antillean Rice Mills* v *Council* [1997] ECR II-447, paragraph 42).

50 In the present case the balance of interests favours suspension of operation of the contested decision.

51 It appears highly probable that the operation of the contested decision would entail the definitive loss of the applicant's position in the market, even if the court hearing the main application were to annul the decision.

52 In opposition to the commercial interests of the applicant, the Commission submits that suspension of operation of the contested decision could harm public health. On this point, it must be emphasised that in principle the requirements of the protection of public health must unquestionably be given precedence over economic considerations (order in *United Kingdom* v *Commission*, cited above, paragraph 93; judgment in Case C-183/95 *Affish* v *Rijksdienst Keuring Vee en Vlees* [1997] ECR I-4315, paragraph 43; order of the Court of First Instance in Case T-136/95 *Industria del Frio Auxiliar Conservera* v *Commission* [1998] ECR II-3301, paragraph 58; and order of the President of the Court of First Instance in Case T-70/99 R *Alpharma* v *Commission* [1999] ECR II-2027, paragraph 152).

53 However, it must be noted that in this context the mere reference to the protection of public health cannot exclude an examination of the circumstances of the case, in particular of the relevant facts.

54 In the present case, the Commission has indeed established that there is uncertainty as regards the risks associated with medicinal products containing amfepramone, even if those risks are slight. Nevertheless, although the decision of 9 December 1996 and the contested decision are based on identical data, the measures taken by the Commission in 1996 and 2000 for the protection of public health with respect to those risks differ fundamentally. In those circumstances, the Commission was obliged to show that the protective measures in the decision of 9 December 1996 proved to be insufficient to protect public health, so that the protective measures it adopted in the contested decision were not manifestly excessive. However, the Commission has not been able to show this.

55 Moreover, the fact that the health risks which determined the adoption of the contested decision had already been taken into account in the Commission's decision of 9 December 1996 and had resulted in a change to the compulsory information concerning medicinal products supplied on prescription indicates that implementation of the contested decision is not urgent.

56 It follows from all the foregoing considerations that the conditions for the grant of the suspension of operation sought are satisfied.

On those grounds,

THE PRESIDENT OF THE COURT OF FIRST INSTANCE

hereby orders:

1. **Operation of the Commission's decision of 9 March 2000 concerning the withdrawal of marketing authorisations for medicinal products for human use which contain amfepramone (C(2000) 453) is suspended in relation to the applicant.**

2. **Costs are reserved.**

Luxembourg, 28 June 2000.

H. Jung — Registrar

B. Vesterdorf — President