EUROPEAN COMMISSION
Competition DG

CASE AT.40577 – Vifor (IV iron products)

(Only the English text is authentic)

ANTITRUST PROCEDURE
Council Regulation (EC) No 1/2003

Article 9 Regulation (EC) 1/2003

Date: 22/07/2024

EUROPEAN
COMMISSION

Brussels, 22.7.2024
C(2024) 5027 final

COMMISSION DECISION

of 22.7.2024

relating to a proceeding under Article 102 of the Treaty on the Functioning of the European Union (TFEU)

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THE EUROPEAN COMMISSION,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Council Regulation (EC) No 1/2003 of 16 December 2002 on the implementation of the rules on competition laid down in Articles 81 and 82 of the Treaty[1], in particular Article 9(1) thereof,

Having regard to the Commission decision of 20 June 2022 to initiate proceedings in this case,

Having expressed concerns in the Preliminary Assessment of 8 April 2024,

Having given interested third parties the opportunity to submit their observations pursuant to Article 27(4) of Regulation (EC) No 1/2003 on the commitments offered to meet those concerns,

After consulting the Advisory Committee on Restrictive Practices and Dominant Positions,

Having regard to the final report of the Hearing Officer,

Whereas:

1. INTRODUCTION

(1) The present Decision is addressed to Vifor Pharma Participations Ltd. (as the economic successor of Vifor Pharma Ltd.), Vifor Pharma Management Ltd. and Vifor Pharma Deutschland GmbH (together referred to as 'Vifor') and concerns the potential disparagement by Vifor of the intravenous ('IV') iron treatment competing most closely with Vifor's flagship product in Europe.

(2) In its Preliminary Assessment of 8 April 2024, the Commission came to the provisional conclusion that Vifor may have abused its dominant position in a number of national markets within the European Economic Area ('EEA') for the provision of IV iron medicines, namely Austria, Germany, The Netherlands, Sweden, Spain, Finland, Ireland, Portugal and Romania (the 'Relevant Member States'), by disseminating to healthcare

[1] OJ L 1, 4.1.2003, p.1. With effect from 1 December 2009, Articles 81 and 82 of the EC Treaty have become Articles 101 and 102, respectively, of the TFEU. The two sets of provisions are, in substance, identical. For the purposes of this decision (the "Decision"), references to Articles 101 and 102 of the TFEU should be understood as references to Articles 81 and 82, respectively, of the EC Treaty when where appropriate. The TFEU also introduced certain changes in terminology, such as the replacement of "Community" by "Union" and "common market" by "internal market". Where the meaning remains unchanged, the terminology of the TFEU will be used throughout this Decision.

professionals ('HCPs')[2] information that may have been objectively misleading about the safety of a competing IV iron medicine – namely Monofer sold by Pharmacosmos A/S ('Pharmacosmos') – thereby hindering its market entry and/or market uptake and raising concerns as to its compatibility with Article 102 TFEU.

(3) The evidence on the file suggests that Vifor's conduct started in 2010 and was ongoing at least until 2022 (the 'Relevant Period').

(4) While Vifor disagrees with the provisional conclusion of the Commission in its Preliminary Assessment, it nevertheless has offered commitments pursuant to Article 9(1) of Regulation 1/2003 to meet the concerns expressed by the Commission. As further explained below, this Decision finds that Vifor's commitments address the Commission's concerns identified in its Preliminary Assessment and makes those commitments binding on Vifor.

2. THE CONCERNED UNDERTAKING AND PRODUCTS

(5) Vifor is a Swiss-based pharmaceutical company active worldwide in the development, manufacturing and marketing of pharmaceutical products for the treatment of iron deficiency, nephrology and cardio-renal therapies. Vifor Pharma Participations Ltd. is the holding company that fully owns, inter alia, the subsidiaries Vifor Pharma Management Ltd. and Vifor Pharma Deutschland GmbH. In August 2022, Vifor was acquired by CSL, an Australian-based biotechnology group with a portfolio of life-savings medicines, including those that treat haemophilia and immune deficiencies, as well as prevent influenza.[3] In 2023, the CSL group (including Vifor) had worldwide revenues of USD 13 310 million (approximately EUR 12 279 million).

(6) The pharmaceutical products concerned by this Decision are Ferinject (ferric carboxymaltose), which is Vifor's flagship product, and Monofer (ferric derisomaltose or iron (III) isomaltoside 1000), which is commercialised by Pharmacosmos. Ferinject was launched in Europe in 2007 and is currently approved in all the EEA countries, whereas Monofer was launched in Europe in 2010 and is currently approved in 21 EEA countries.[4] Both medicines are IV iron products used to treat iron deficiency ('ID') and iron deficiency anaemia ('IDA').[5]

3. PROCEDURAL STEPS UNDER REGULATION NO 1/2003

(7) On 20 June 2022 the Commission opened proceedings with a view to adopting a decision under Chapter III of Regulation No 1/2003 and on 8 April 2024 adopted a Preliminary Assessment as referred to in Article 9(1) of Regulation No 1/2003 which

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2 For the purpose of this Decision, HCPs refer to healthcare professionals involved in the prescription, procurement or dispensing of IV iron, such as doctors, nurses, midwives and pharmacists, as well as to representatives of tender authorities and other procurement bodies.

3 See Case M.10629 – *CSL/Vifor Pharma*.

4 See Monofer's most recent Package Information Leaflet dated 01/2023 pil.5676.pdf (medicines.org.uk).

5 Both products currently have the same Anatomical Therapeutic Chemical ("ATC") code, which is a unique code assigned to a medicine according to the organ or system it works on and how it works. Initially, Monofer was in class B03AC06 (ferric oxide dextran complexes) and Ferinject in class B03AC01 (ferric oxide polymaltose complex), but as from 2014 the last digits were removed for IV iron, and since then all IV irons have the same ATC code B03AC. The ATC classification system is maintained by the World Health Organization (WHO).

set out the Commission's preliminary competition concerns. The Preliminary Assessment was notified to Vifor on 9 April 2024.

(8) On 16 April 2024, Vifor submitted commitments (the "Initial Commitments") to the Commission in response to the Preliminary Assessment.

(9) On 22 April 2024 a notice was published in the Official Journal of the European Union pursuant to Article 27(4) of Regulation No 1/2003, summarising the case and the Initial Commitments and inviting interested third parties to give their observations on the Initial Commitments within one month following publication.

(10) On 8 May 2024 and 27 May 2024, the Commission informed Vifor of the observation(s) received following the publication of the notice.

(11) On 13 June 2024, Vifor submitted an amended proposal for commitments (the "Final Commitments").

4. REGULATORY FRAMEWORK

4.1. Marketing authorisation

(12) In the EEA, a medicinal product for human use may only be placed on the market after obtaining a marketing authorisation ('MA') attesting its safety, quality and efficacy. The requirements and procedures for obtaining a MA are primarily laid down in Directive 2001/83/EC[6] and Regulation (EC) No 726/2004.[7]

(13) A MA can be obtained either through a centralised procedure before the European Medicines Agency ('EMA') or through national authorisation procedures. National procedures include the decentralised procedure, the mutual recognition procedure and the national procedure. The MAs of both Ferinject and Monofer were obtained in the EEA following a decentralised procedure. This procedure allows the common assessment of an application submitted simultaneously to several Member States, one of them being chosen to take the lead in evaluating the application (the 'Reference Member State'). The Reference Member State prepares and proposes the draft assessment report, summary of product characteristics, labelling and package leaflet, which are then approved by all the concerned Members States. For instance, the decentralised procedure for Monofer was successfully finalised on 26 November 2009. Sweden acted as the Reference Member State and there were at the time 21 other concerned Member States.[8]

4.2. Promotion in the pharmaceutical sector

(14) Advertising of medicinal products is regulated in the European Union ('EU') also by Directive 2001/83/EC. This Directive provides that advertising of such products *"shall not be misleading*"[9] and requires that all the information contained in the documentation transmitted as part of the promotion of a medicinal product to persons qualified to prescribe or supply it must be accurate, up-to-date, verifiable and

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6 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.

7 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 L 136, 30.4.2004, p. 1.

8 Pharmacosmos' complaint, paragraphs 111-112.

9 Article 87 of Directive 2001/83/EC.

sufficiently complete to enable the recipient to form his or her own opinion of the therapeutic value of the medicinal product concerned.[10] Similar requirements are included in the Codes of Conduct of relevant pharmaceutical industry associations.[11]

5. PRELIMINARY ASSESSMENT

(15) This section is based on the Commission's preliminary concerns as set out in the Preliminary Assessment, which the Commission continues to have at the time of adoption of the present Decision.

(16) As set out below, in the Preliminary Assessment, the Commission reached the preliminary conclusion that Vifor may have abused a dominant position (Section 5.2) in a number of national IV iron markets / high-dose IV iron markets (Section 5.1) by disseminating to HCPs information that may have been objectively misleading about the safety of the main competing medicine (i.e. Pharmacosmos' Monofer) resulting in a potential breach of Article 102 TFEU (Section 5.3). The evidence on file suggests that Vifor's conduct (i) started in 2010 and was ongoing at least until 2022 in the EEA (Section 5.4) and (ii) is capable of having an appreciable effect on trade between Member States (Section 5.5).

5.1. Relevant markets

5.1.1. Principles

(17) The main purpose of market definition is "*to identify in a systematic way the effective and immediate competitive constraints faced by the undertakings involved when they offer particular products in a particular area. Market definition leads to the identification of the relevant competitors of the undertaking(s) involved when they offer those products*".[12] In the context of Article 102 TFEU, market definition is carried out to define the boundaries within which it must be assessed whether a given undertaking is able to behave, to an appreciable extent, independently of its competitors, its customers and, ultimately, consumers.[13]

(18) The definition of the relevant market involves defining both the product market and the geographic market:

– *The relevant product market* comprises all the products that customers regard as interchangeable or substitutable to the product(s) of the undertaking(s) involved, based on the products' characteristics, their prices and their intended use.[14] When products can be broadly used for the same purpose but differ in terms of quality, consumer preferences, price or other relevant parameters of competition, they are differentiated. Although differentiated products may 'compete' in some dimensions, a relevant product market in competition cases should only include those differentiated products that are capable of

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10 Article 92(2) of Directive 2001/83/EC.

11 E.g. Code of Practice of the European Federation of Pharmaceutical Industries and Associations, Chapter 1 (https://www.ifpma.org/wp-content/uploads/2022/12/230220-EFPIA-Code.pdf) and Medicines for Europe Code of Conduct, 2020, section 5.3 (code-of-conduct-final-COLORS.cdr (medicinesforeurope.com)).

12 Commission notice on the definition of relevant market for the purposes of Union competition law (C(2023) 6789 final, 08.02.2024) (the "Market Definition Notice"), para. 6.

13 Case T-321/05, *AstraZeneca*, para. 30 and the case law cited.

14 Market Definition Notice, para. 12.

significantly constraining an undertaking's behaviour and of preventing it from behaving independently of an effective competitive pressure;[15]

– *The relevant geographic market* comprises the geographic area in which the undertakings involved supply or demand relevant products, in which the conditions of competition are sufficiently homogeneous for the effects of the investigated conduct to be assessed and which can be distinguished from other geographic areas, in particular because conditions of competition are appreciably different in those areas.[16]

5.1.2. Product market

5.1.2.1. Introduction

(19) ID is a condition resulting from too little iron in the body, which can lead to IDA when the lack of iron causes a drop in the haemoglobin level. ID, with or without anaemia, notably affects women and is also prevalent in patients suffering from chronic conditions, such as Chronic Kidney Disease ("CKD"), Inflammatory Bowel Disease ("IBD"), Chronic Heart Failure ("CHF") and cancer. ID / IDA can cause serious complications, such as heart failures, lung problems, and pregnancy complications. It is a major cause of morbidity and mortality worldwide.

(20) ID / IDA is treated with iron supplementation[17] – which can be administered orally (tablets) or intravenously (intravenous injections or infusions) – to normalise the haemoglobin concentrations and/or to replenish the body iron stores.

(21) Historically, the first generation of IV iron had a worse safety profile than oral iron (in particular, high-molecular weight dextran carried a significant risk of anaphylactic reactions[18] leading to its withdrawal from the EEA in the 1990s). Moreover, oral iron is cheap, effective in most mild-to-moderate cases of ID / IDA and has the advantage of being administered at home, without requiring hospital resources. For these reasons, traditionally, in the EEA, the first step generally consists in treating ID / IDA with oral iron (first-line treatment), while IV iron is usually administered as a second step, after the failure of oral iron or in case of contraindications (second-line treatment). This traditional approach is still generally valid. However, the improvement in the safety profile of IV irons, together with their superior efficacy, has led to a growing use of IV iron as frontline treatment in certain clinical conditions/situations where oral iron is not suitable or effective (e.g. severe ID / IDA, need to deliver iron rapidly, CHF, late-stage CKD, active IBD, late pregnancy).

5.1.2.2. The Commission's Preliminary Assessment

5.1.2.2.1. Oral and IV iron preparations belong to distinct product markets

(22) In the Preliminary Assessment, the Commission reached the preliminary conclusion that oral and IV iron products belong to distinct product markets.[19] This preliminary finding

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15 Case T-251/19, *Wieland-Werke*, para. 40. See also Case COMP/A.37.507/F3 – *AstraZeneca*, para. 370. See also Market Definition Notice, paras. 85-87.

16 Case C-27/76, *United Brands*, para. 44 and Market Definition Notice, para. 12.

17 ID/IDA may also be treated with erythropoiesis-stimulating agent and blood transfusion, which are complementary to iron supplementation rather than substitutes (as they are used in different clinical settings and address different therapeutic needs) and, thus, do not belong to the same product markets.

18 Severe and potentially life-threatening allergic reactions.

19 In case M.6091 - *Galenica/Fresenius Medical Care/Vifor Fresenius Medical Care Renal Pharma JV* (2011), the Commission noted that most of the respondents to the market investigation expressed the

is based on a large body of evidence showing that oral and IV iron preparations have different: (i) profiles in terms of efficacy, safety, tolerability and convenience of use (Section 5.1.2.2.1.1); (ii) therapeutic uses as they are used either sequentially or in different clinical settings (Section 5.1.2.2.1.2); (iii) pricing, IV iron being considerably and persistently more expensive than oral iron (Section 5.1.2.2.1.3) and (iv) prescription requirements since IV iron is only available on prescription contrary to oral iron (Section 5.1.2.2.1.4). The fact that oral iron is not interchangeable and does not compete with IV iron is also well evidenced in Vifor's business documents (Section 5.1.2.2.1.5).

5.1.2.2.1.1. Oral and IV irons have differentiated profiles

(23) ***Superior efficacy of IV iron***: IV iron is a much more effective and quicker treatment than oral iron. This is mainly due to the fact that (i) even under optimal circumstances, the absorption of oral iron by the digestive tract is limited, which means that oral iron treatment requires several months to replenish body iron stores and/or to increase haemoglobin levels; and (ii) ID / IDA is common in patients suffering from chronic diseases impairing the intestinal uptake and absorption of oral iron into the blood stream (e.g. CKD, IBD). Delivering iron directly in the blood through injections/infusion(s) enables to overcome those limitations. Consequently, the use of IV iron allows the fast delivery of high doses of iron and, thus, provides complete treatment within a short period of time. The superiority of the efficacy profile of IV iron was unanimously confirmed by Key Opinion Leaders ("KOLs")[20] and medical associations.[21]

(24) ***Different safety and tolerability profiles****:* although oral and IV irons are both overall safe, they are associated with distinct side-effects, which differ in nature, frequency, and severity. Oral iron commonly gives rise to gastro-intestinal symptoms (e.g. nausea, vomiting, diarrhea), which may result in the patients' low adherence to the (long-term) oral iron treatment and, thus, affect the effectiveness of the treatment.[22] IV iron products are not associated with such side-effects but they all give rise to a minimal risk of hypersensitivity reactions ("HSR") and hypophosphatemia ("HP").[23] HSR is a medical term referring to the overreaction of the immune system to an antigen/allergen. The HSRs to IV iron products are rather uncommon and, most of the time, are mild or moderate but, in rare instances, they can be severe and even life threatening. HP is a condition involving a low level of phosphate in the blood, which is a common, non-fatal, and generally transient side-effect.

(25) ***Convenience of use***: oral and IV irons are further differentiated in terms of convenience of use. Oral iron is typically administered at home and usually requires daily intake for several months, whereas IV iron must be administered by trained staff in hospitals or clinics equipped with resuscitation facilities (as a precaution measure) and requires only a single or a few injections/infusions.[24]

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view that oral and IV irons belong to separate markets but ultimately left open the exact delineation of the market as no serious doubts could arise under any plausible product market definition (paras 33-34). In previous cases, the Commission had defined the relevant product market based on the ATC classification but ultimately left open the market definition.

20 E.g., Minutes of the calls with KOLs, ID1561 (para.22) and ID1586 (para.16).

21 E.g., Reply to question 10 of the Medical Association RFI (ID 1410).

22 E.g., Minutes of the calls with KOLs, ID1531 (para.17) and ID1600 (para.12).

23 E.g., Minutes of the calls with KOLs, ID 1577 (para.13) and ID1589 (para.14).

24 [Information on Vifor's submissions to the Commission].

5.1.2.2.1.2. Oral and IV irons are used either sequentially or in different clinical settings

(26) Oral and IV irons are used either sequentially or in different clinical settings, which reflects their differentiated profiles and shows that they have distinct therapeutic uses.[25] The above is corroborated by a large body of evidence, including notably:

(a) ***IV iron labels****:* the properties and the officially approved conditions of use of a medicine are described in a document called the Summary of Product Characteristic ("SmPC"), which is approved by the relevant authority as part of the market authorisation process. According to their respective SmPCs, the IV iron products marketed in the Relevant Member States are indicated for the treatment of ID either as second-line treatment when oral iron is not effective or not tolerated, or as first-line treatment in situations where oral iron cannot be used / would not be effective (e.g. need to deliver iron rapidly, active IBD);[26]

(b) ***KOLs and medical associations*** unanimously confirmed that oral and IV irons are used sequentially or in different clinical settings and consistently consider that oral and IV irons are not used interchangeably in daily clinical practice;[27]

(c) ***Clinical guidelines***: the relevant guidelines applicable in the EEA generally suggest (i) the use of oral iron as first-line treatment and IV iron as second-line treatments and (ii) the use of IV iron as first-line treatments in specific circumstances where oral iron would not be effective/suitable;[28]

(d) ***National reimbursement restrictions***: in some EEA countries (e.g. Austria)[29] the full reimbursement of IV iron is subject to the use of oral iron as a first-line treatment. Such a requirement to use IV iron only after the failure of oral iron further suggests that these two types of products are not used interchangeably.

5.1.2.2.1.3. IV iron is significantly more expensive than oral iron

(27) Oral iron is considerably cheaper than IV iron. This is apparent from the feedback received from KOLs[30] and from Vifor's internal documents. For example, [Information on the pricing of Vifor's oral and IV iron products].[31] The above is also reflected in the existence of national reimbursement restrictions requiring the use of the cheaper oral iron as first-line treatment (see previous section).

(28) According to para. 48 and to footnote 70 of the Market Definition Notice, price levels may be relevant for market definition purposes since a significant divergence in price between two products may arise where the cheaper product does not exercise any competitive constraint. The specific features characterising competition in the

25 See by analogy Case T-321/05, *AstraZeneca*, paragraphs 66-74.

26 E.g. FERINJECT SmPC; VENOFER SmPC; MONOFER SmPC; FERRLECIT SmPC.

27 E.g., Minutes of the calls with KOLs, ID1437 (paras.20ff) and ID1586 (para.16); Replies to question 10 of the Medical Association RFI (ID1415 and ID1352).

28 E.g., ECCO guidelines on the diagnosis and management of ID and anaemia in IBD (2015) recommend using oral iron in IBD patients with mild IDA, inactive IBD and no previous intolerance to oral iron; and using IV iron in IBD patients with severe IDA, active IBD or previous intolerance to oral iron.

29 [Information on Vifor's submissions to the Commission].

30 E.g., Minutes of the calls with KOLs, ID1586 (para.18) and ID1589 (para.15).

31 [Information on Vifor's internal document]. Although the cumulative iron dose needed from oral iron is typically higher than IV iron (due to the limitations of oral iron absorption – see Section 5.1.2.2.1.1), the disparity in the average selling prices per 100 mg remains valid given (i) the significance of the price gap and (ii) the fact that [Information on Vifor's pricing strategy] (e.g. [Information on Vifor's internal document]). In any case, the need for a higher dose of oral iron is another illustration of the fact that oral and IV irons are not clinically interchangeable.

pharmaceutical sector do not negate the relevance of price-related factors in the assessment of competitive constraints, although those factors must be assessed in their specific context.[32] In this respect, the Commission notes that:

– The relevance of the absence of price competition between oral and IV irons cannot be dismissed on the mere ground that the pricing and reimbursement of drugs are highly regulated. Indeed, even though national regulations may limit price-related interactions between drugs, national healthcare authorities in charge of pricing and reimbursement are also capable of exerting downward pressure on the prices of a type of drugs on account of the lower price of other drugs with the same therapeutic use. In other words, in the present case, national authorities had the power to foster price competition between oral and IV irons, which they did not (as evidenced by the persistent and considerable price gap between oral and IV irons).[33] This implicitly corroborates the preliminary finding that oral and IV irons have distinct therapeutic uses;

– The limited sensitivity of doctors to prices supports the view that oral iron did not exercise, by means of its lower prices, a significant competitive constraint over IV iron, which is reflected by the significant and persistent price difference between those products[34] and confirmed by KOLs.[35]

(29) Therefore, the Commission considers that the fact that IV iron was significantly more expensive than oral iron throughout the Relevant Period shows that the latter likely exerts only a low degree of competitive pressure on the former.[36]

5.1.2.2.1.4. Oral and IV irons are generally subject to distinct prescription requirements

(30) In the EEA, IV irons are available only on prescription whereas oral irons are mostly sold over the counter ("OTC") (i.e. without prescription).[37] The Commission has in the past defined separate markets for prescription and OTC medicines[38] on the ground that medical indications (including side-effects), legal framework, marketing, pricing and distribution all tend to differ between the two categories. Moreover, doctors do not necessarily play a direct role in the purchase of OTC pharmaceuticals and, in most cases, consumers bear the full cost, whereas prescription pharmaceuticals are necessarily prescribed by doctors and generally at least partially reimbursed. Marketing of prescription pharmaceuticals is therefore targeted at the prescribers and not the patients. The above considerations are applicable in the present case (e.g. in many instances, oral irons available OTC are not reimbursed contrary to IV iron).

5.1.2.2.1.5. Vifor's internal documents support the existence of a distinct IV iron market

(31) Vifor's business documents support the existence of a distinct relevant market for IV iron preparations for several reasons. *First*, when assessing internally the competitive situation of Ferinject, [Information on Vifor's internal competitive assessment of the market].[39] [Information on Vifor's internal competitive assessment of the market].[40]

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32 Case T-321/05, *AstraZeneca*, paragraph 183.
33 See by analogy Case T-321/05, *AstraZeneca*, paragraphs 173-175.
34 Case T-321/05, *AstraZeneca*, paragraph.178.
35 E.g., Minutes of the call with a KOL, ID1586 (para.18).
36 Case T-321/05, *AstraZeneca*, paragraph 176.
37 [Information on Vifor's submissions to the Commission].
38 E.g., Case M.9274 – *Glaxosmithkline/Pfizer Consumer Healthcare Business*, paragraphs 18-20.
39 E.g. [Information on Vifor's internal documents].

Vifor also refers to the "*i.v. iron market*" and/or to the "*oral iron market*" in its annual reports;[41] press releases[42] and investor presentations.[43] *Second*, many business documents refer to [Information on Vifor's internal competitive assessment of the market].[44] *Finally*, Vifor's internal documents reveal that oral and IV irons are subject to different competitive dynamics, stressing that the oral iron market is [Information on Vifor's internal competitive assessment of the market].[45] In stark contrast, the IV iron market is a dynamic and expanding market (see Section 5.1.2.2.2.4), characterised by high barriers to entry (see Section 5.2.2.3), where competition is, to a large extent, dominated by a few expensive originator products (see Section 5.2.2.1).

5.1.2.2.2. High-dose IV irons are significantly differentiated from low-dose IV irons and, thus, may constitute a distinct product market

5.1.2.2.2.1. Introduction

(32) The IV iron products marketed in the EEA are typically divided in two groups: low- and high-dose IV irons, which are distinguished by the maximum dose of iron that can be delivered in a single administration and, thus, by how many visits are needed for the treatment. High-dose IV iron can be administered in doses exceeding 500 mg, whereas low-dose IV iron is typically given in 100-200 mg doses.

(33) Low-dose IV iron encompasses various products introduced in the EEA at the end of the 1990s / in the early 2000s, including Ferrlecit (ferric gluconate), Venofer (iron sucrose), and Cosmofer (low-molecular-weight iron dextran).[46] More recently, in 2013, Pharmacosmos launched, in some Member States, Diafer (ferric derisomaltose or iron (III) isomaltoside 1000). With the exception of Diafer, low-dose IV irons are no longer under patent protection and, thus, may face competition from generics. In fact, several iron sucrose similars ("ISS") (i.e. generics of Venofer) were available in the Relevant Member States in the Relevant Period.

(34) High-dose IV iron refers to a newer generation of IV iron compounds[47] launched in the EEA between 2007 and 2012, namely Ferinject (ferric carboxymaltose), Monofer (ferric derisomaltose or iron (III) isomaltoside 1000), and Rienso/Feraheme (ferumoxytol). The latter was withdrawn from the EEA in 2015.

(35) In the Preliminary Assessment, the Commission reached the preliminary conclusion that high-dose IV iron products are significantly differentiated from low-dose IV iron and, thus, may constitute a distinct product market. Indeed, the evidence available on file indicates that, in the Relevant Period, low-dose IV iron exercised limited competitive constraints over high-dose IV iron, whereas Monofer (i.e. Ferinject's only high-dose rival in the EEA since 2015) appears to have exerted significant competitive pressure on Ferinject. This preliminary finding is based on a series of considerations, including (i) the differentiated efficacy profiles of high- and low-dose

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40 E.g. [Information on Vifor's internal document].

41 E.g. Vifor's 2019 Annual Report (pp.23 and 29).

42 E.g., "*Vifor Pharma Group reports strong H1 2018 Results*".

43 E.g., Vifor's Investor Presentation dated April 2020, slide 7.

44 E.g. [Information on Vifor's internal documents].

45 E.g. [Information on Vifor's internal documents].

46 The low-dose IV iron products marketed in the EEA during the Relevant Period are the second generation of IV iron products. The first generation of IV iron products was launched in the EEA in the 1950s before being withdrawn from the market in the 1990s due to serious safety concerns.

47 Also referred as the third generation of IV iron products.

IV iron (Section 5.1.2.2.2.2), (ii) their differentiated therapeutic uses (Section 5.1.2.2.2.3), (iii) the increasing use of high-dose IV iron at the expense of low-dose IV iron since 2010 (Section 5.1.2.2.2.4), (iv) price factors (Section 5.1.2.2.2.5), as well as (v) Vifor's own contemporaneous internal assessment (Section 5.1.2.2.2.6). In any event, the question whether high-dose IV irons constitute a distinct product market or are part of broader IV iron market, including both low- and high-dose IV iron product segments, can be left open since Vifor may have held a dominant position under both plausible market delineations.

5.1.2.2.2.2. Low- and high-dose IV iron have differentiated efficacy profiles

(36) ***Superior efficacy of high-dose IV iron***: A patient typically requires 1-2 g of IV iron in case of IDA and 500 mg of IV iron in case of ID. The high-dose IV iron can provide this dose in 1-2 visits. Conversely, low-dose preparations are typically given in doses of 200 mg or less, which means that ID / IDA correction will generally require at least 5-10 treatment visits depending on the compound and on the extent of the patient's iron need. Thus, using low-dose IV iron prolongs the time it takes for the patient to become iron repleted, causes additional costs of administering, and reduces quality of life for patients. The above superior efficacy and convenience of use of high-dose IV iron is common ground and corroborated by KOLs, medical associations,[48] Vifor's internal documents,[49] head-to-head trials[50] and medical publications.[51]

(37) ***Unclear safety differentiation***: both high- and low-dose IV iron are generally safe and well tolerated. The investigation yielded mixed results as to how high- and low-dose IV iron compare safety-wise, suggesting that there is no clear safety differentiation between them. On the one hand, the evidence suggests that Ferinject and Monofer are to some extent safer than low-dose IV iron as they release in the body less toxic free iron.[52] On the other hand, some medical associations and KOLs expressly stated that low- and high-dose IV irons have comparable safety profiles.[53]

5.1.2.2.2.3. Gradual differentiation of the therapeutic use of low- and high-dose IV iron

(38) As a result of its superior efficacy and convenience of use, high-dose IV iron is very popular. Since their launch in the late 2000s, Ferinject and Monofer have increasingly become the favoured IV iron option in most clinical settings. Conversely, the use of low-dose preparations has been progressively niched in clinical settings where ID / IDA patients need to go to the hospital on a regular basis anyway (e.g. dialysis patients). In other words, over the past 15 years, the therapeutic use of low- and high-dose IV iron has been gradually diverging. This is corroborated by a strong body of evidence. In particular:

(a) **KOLs and medical associations** confirmed that, due to their differentiated profiles in terms of efficacy and convenience of use, high- and low-dose IV iron products are not used in the same clinical settings and, thus, are not

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48 E.g., Minutes of the call with KOLs, ID1589 (paras.16-18) and ID1600 (paras.16-17); Reply to question 11 of the Medical Association RFI (ID1410).

49 E.g., [Information on Vifor's internal documents].

50 [Information on Vifor's internal document].

51 Girelli, *Modern iron replacement therapy: Clinical and pathophysiological insights*, Int J Hematol (2018).

52 E.g., Minutes of the call with a KOL, ID1454 (paras. 23-25); "*Ferinject Growth Strategy – Detailed Assessment*" by LEK (4 July 2014), slides 26 and 29.

53 E.g., Minutes of the calls with KOLs, ID1579 (paras.15-16) and ID1586 (paras.13-14); Reply to question 11 of the Medical Association RFI (ID 1410).

interchangeable.[54] In contrast, they submitted that Ferinject and Monofer are direct substitutes that are fully interchangeable due to (i) their very similar efficacy and safety profiles (apart from the risk of HP, greater with Ferinject than with Monofer, which can be relevant for some patients) and (ii) the fact that they are studied and used in the same clinical settings;[55]

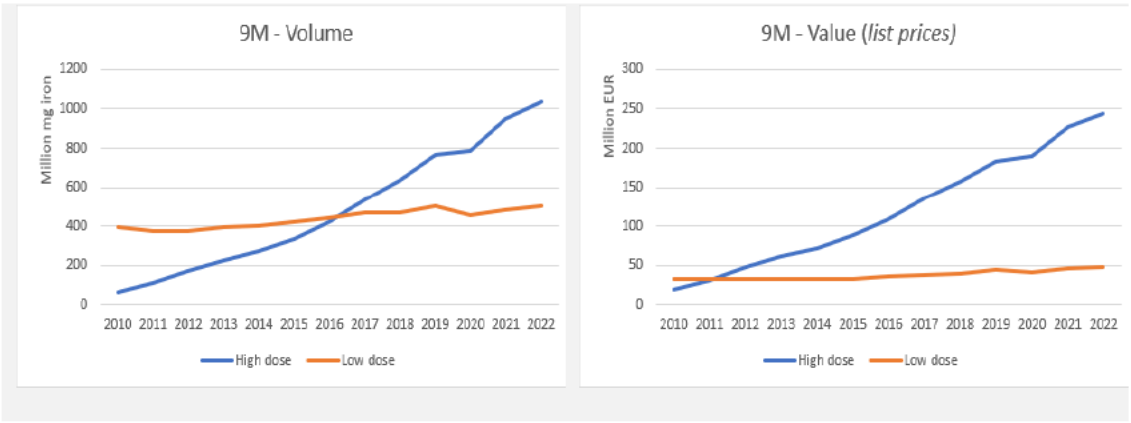
(b) **Vifor's internal documents** reveal that [Information on Vifor's business strategy][56] and that [Information on Vifor's business strategy].[57] Vifor's internal documents also show that [Information on Vifor's business strategy];[58]

(c) **Diafer's restricted label**: from 2013 onwards, Pharmacosmos launched in the EEA a low-dose IV iron (i.e. Diafer) specifically indicated for the treatment of CKD patients on dialysis.[59] The fact that Pharmacosmos deemed necessary to develop and market a low-dose formulation specifically for dialysis patients rather than promoting the use of Monofer for those patients further illustrates the differentiated therapeutic use of low- and high-dose IV iron.

5.1.2.2.2.4. Asymmetrical substitution trend between low- and high-dose IV iron

(39) Actual trends in the consumption of medicines prescribed constitute a key factor in assessing competitive constraints between medicines.[60] In this respect, IV iron sales data reveal the increasing use of high-dose IV iron at the expense of low-dose IV iron since 2010. Indeed, it is apparent from Figure 1 below that, in the Relevant Member States, IV iron sales underwent considerable expansion (both in terms of value and volume), with high-dose IV iron accounting for the bulk of that expansion, whereas the sales of low-dose IV iron remained relatively flat. The above is corroborated by KOLs and medical associations stressing the declining use of low-dose products in daily clinical practice;[61] and by Vifor's internal documents.[62]

Figure 1 - Evolution of the sales of low- and high-dose IV iron in the 9 Relevant Member States in 2010-2022



Source: IQVIA

54 E.g., Minutes of the calls with KOLs, ID1454 (paras.23-25) and ID1579 (paras.15-16).

55 E.g., Minutes of the calls with KOLs, ID1454 (paras.26-29), ID1586 (para.12), ID1531 (paras.15-16) and ID1561 (para.18); Replies to question 5 of the Medical Association RFI (ID1352).

56 [Information on Vifor's internal document].

57 [Information on Vifor's internal documents].

58 [Information on Vifor's internal document].

59 See DIAFER SmPC, Section 4.1.

60 Case COMP/A.37.507/F3 - *AstraZeneca*, para.362; [Information on Vifor's submissions to the Commission].

61 E.g., Minutes of the calls with KOLs, ID1561 (paras.14-17) and ID1823 (para.16).

62 [Information on Vifor's internal document].

(40) This trend of asymmetrical substitution, in conjunction with the repositioning of low-dose IV iron towards the treatment of ID / IDA patients who need to go to the hospital on a regular basis anyway (e.g. dialysis patients) on account of the fact that high-dose IV iron were becoming increasingly dominant on the other clinical settings supports the view that, in the Relevant Period, low-dose IV iron exercised limited competitive constraint over high-dose IV iron.[63]

5.1.2.2.2.5. Limited price competition between low- and high-dose IV iron

(41) ***Limited price competition between high- and low-dose IV iron***: High-dose IV iron is much more expensive than low-dose IV iron. This is apparent from Vifor's average selling prices (per 100 mg of iron) of Ferinject (high-dose) and Venofer (low-dose) during the Relevant Period[64] and from Vifor's business documents.[65] Such a persistent price gap shows that low-dose IV iron products exert a limited price constraint over high-dose IV iron.[66] It also reflects the fact that low-dose IV irons are older compounds that were off-patent during the Relevant Period, unlike Ferinject and Monofer, which further illustrates the fact that low- and high-dose IV irons are subject to different competitive dynamics.

(42) ***Substantial price competition between Monofer and Ferinject***: Conversely, it is well documented that, in the Relevant Period, Pharmacosmos implemented in the EEA an "*aggressive*" pricing strategy which led to Ferinject's price erosion and [Information on Vifor's internal assessment of the competitive landscape].[67] The price difference between Monofer and Ferinject appears moderate (generally ≤ 30% according to IQVIA). In fact, the evidence shows that, throughout the Relevant Period and across the EEA, Vifor defined [Information on Vifor's pricing strategy].[68] In addition, German healthcare authorities promoted automatic substitution between Ferinject and Monofer by pharmacists from 2016 to 2020, which further intensified price competition between high-dose IV iron at national level.

5.1.2.2.2.6. Vifor's internal documents support the preliminary finding that high-dose compounds may constitute a distinct product market

(43) Vifor's internal documents indicate that high-dose IV iron is very differentiated from low-dose IV iron and, thus, may constitute a distinct product market. Indeed, when assessing internally the competitive situation of Ferinject, [Information on Vifor's internal competitive assessment of the market][69] and [Information on Vifor's internal competitive assessment of the market].[70] That being said, in some instances, [Information on Vifor's internal competitive assessment of the market],[71] which suggests that high-dose IV iron may belong to a broader and differentiated IV iron market (including both high- and low-dose preparations) where low-dose IV iron exerts limited competitive constraints on Ferinject and where Monofer is Ferinject's

63 See Case T-321/05, *AstraZeneca,* paragraph 96.

64 E.g., [Information on Vifor's submissions to the Commission] shows that [Information on the pricing of Vifor's IV iron products].

65 [Information on Vifor's internal document].

66 Case T-321/05, *AstraZeneca*, paragraph 176.

67 [Information on Vifor's internal document]. See also e.g. [Information on Vifor's internal document].

68 E.g., [Information on Vifor's internal documents].

69 E.g., [Information on Vifor's internal documents].

70 E.g., [Information on Vifor's internal documents].

71 E.g., [Information on Vifor's internal documents]. See also Vifor's public statements referring to the high-dose segment (e.g. CSL Vifor Investor Briefing dated 17 October 2022, slide 11).

closest competitor. In fact, [Information on Vifor's internal competitive assessment of the market],[72] which also [Information on Vifor's internal competitive assessment of the market].[73]

5.1.2.3. Preliminary conclusion on the relevant product market

(44) In view of the foregoing, the Commission's Preliminary Assessment reached the preliminary conclusion that:

– Oral iron does not belong to the same product market as IV iron products;

– High-dose IV iron is significantly differentiated from low-dose IV iron and, thus, may constitutes a distinct product market. In any event, the question whether high-dose IV iron constitutes a distinct product market (excluding low-dose preparations) or is part of a broader and differentiated IV iron market (including both high- and low-dose preparations) can be left open since Vifor is preliminarily considered dominant under both plausible market delineations.

5.1.3. Relevant geographic market

(45) In the past, the Commission has consistently considered the markets for medicines to be national in scope. This is because the conditions of supply and demand of pharmaceutical products are likely to vary across Member States due to several factors, including (i) different rules on pricing and reimbursement (which remain an exclusive national competence in the EEA); (ii) different purchasing and distribution patterns; and (iii) the fact that competition between pharmaceutical firms still predominantly takes place at a national level. Accordingly, the conditions of competition are likely to differ from one Member State to another. The above considerations also apply in the present case and nothing suggests that the Commission should depart from its established practice.

5.1.4. Preliminary conclusions on market definition

(46) In view of the above, the Commission's Preliminary Assessment reached the preliminary conclusion that, for the purpose of the present Decision, it can be left open whether the relevant market is the IV iron market or the high-dose IV iron market, which are both national in scope.

5.2. Dominance

5.2.1. Principles

(47) According to settled case law, dominance is "*a position of economic strength held by an undertaking which enables it to prevent effective competition from being maintained on the relevant market by giving it the power to behave to an appreciable extent independently of its competitors, its customers and ultimately of consumers*."[74] The existence of a dominant position derives from a combination of factors which, taken separately, are not necessarily determinative.[75] One of them is the existence of very large market shares. In *AstraZeneca*, the Court of Justice held that "*the possession, over a long period, of a very large market share constitutes in itself, save in exceptional circumstances, proof of the existence of a dominant position* [...]" and

72 E.g., [Information on Vifor's internal documents].
73 E.g., [Information on Vifor's internal document].
74 Cases C-457/10 P, *AstraZeneca*, paragraph 175; and C-27/76, *United Brands*, paragraph 65.
75 Case C-27/76, *United Brands*, paragraph 66; Case C-85/76, *Hoffmann-La Roche*, paragraph 39.

that "*market shares of more than 50% constitute very large market shares.*"[76] A share between 70% and 80% is, in itself, a clear indication of dominance.[77] Further, a decline in market shares which still remain very large cannot in itself constitute proof of the absence of a dominant position.[78] Other important factors when assessing dominance are the existence (or lack thereof) of barriers to entry or expansion, as well as countervailing buyer power.

5.2.2. The Commission's Preliminary Assessment

(48) In its Preliminary Assessment, the Commission reached the preliminary conclusion that, during the Relevant Period, Vifor may have held a dominant position in the Relevant Member States under both plausible market delineations (i.e. IV iron and high-dose IV iron).[79] This preliminary conclusion is based on various considerations, namely (i) the very large market shares held by Vifor over a long period of time (Section 5.2.2.1); (ii) Vifor's ability to price its flagship product (Ferinject) higher than all competing products (Section 5.2.2.2); (iii) the existence of high barriers to entry and expansion (Section 5.2.2.3); (iv) the limited countervailing buyer power (Section 5.2.2.4); as well as (v) [Information on Vifor's internal assessment of its own competitive position] (Section 5.2.2.5).

5.2.2.1. Market shares

5.2.2.1.1. Market shares on the relevant national markets for IV iron

(49) Table 1 below lists the main IV iron products commercialised in the Relevant Member States in the Relevant Period, which were marketed locally either by their respective MA holders, their local distributors[80] or parallel importers (in Germany and Sweden).[81]

Table 1 – Main IV iron players active in the Relevant Member States during the Relevant Period

MA holder	Brand	Dosage	Originator/Generic	Relevant Member States
VIFOR	Venofer	low	originator	AU, DE, NL, ES, SE, FI, IE, PT, RO
	Ferinject	high	originator	AU, DE, NL, ES, SE, FI, IE, PT, RO
PHARMACOSMOS	Cosmofer	low	originator	AU, DE, NL, ES, SE, FI, IE, PT
	Monofer	high	originator	AU, DE, NL, ES, SE, FI, IE, PT, RO
	Diafer	low	originator	NL, SE, IE, RO
SANOFI	Ferrlecit	low	originator	DE
MEDICE	Fermed	low	generic	AU, DE
TEVA	Ijzerhydroxide Sacharose	low	generic	NL
ETHYPHARM	Feriv	low	generic	ES
ORIPHARM	Venotrix	low	generic	FI
n.a.	Oxido Ferrico Sacarosa	low	generic	PT

Source: [Information on Vifor's submissions to the Commission] & IQVIA

76 Case C-457/10 P, *AstraZeneca*, paragraph 176.

77 Case T-30/89, *Hilti*, paragraph 92.

78 Case T-340/03, *France Télécom,* paragraph 104.

79 Unless otherwise specified, the preliminary findings in this Section do not materially differ depending on whether the market is defined at a broader IV iron level or at a narrower high-dose IV iron level.

80 In some Relevant Member States, Pharmacosmos' IV irons were marketed indirectly through local partners. For ease of reference, in this Section, those products' sales are attributed to Pharmacosmos (rather than to its local distributors), which has no impact on the market share assessment.

81 In the other Relevant Member States, parallel imports were not material during the Relevant Period.

(50) Table 2 shows that, during the Relevant Period, Vifor had very high market shares by value[82] on the relevant national IV iron markets, consistently above (i) [70-80]% in Austria; (ii) [70-80]% in Finland; (iii) [50-60]% in Germany; (iv) [70-80]% in Ireland (from 2015 onwards); (v) [70-80]% in the Netherlands; (vi) [60-70]% in Portugal (from 2013 onwards); (vii) [80-90]% in Romania; (viii) [60-70]% in Spain; and (ix) [60-70]% in Sweden. According to settled case law, such high market shares are evidence of the existence of a dominant position. The limited number of material competitors in the Relevant Member States, as well as the considerable gap between their market shares and Vifor's, further illustrate the latter's competitive strength on those markets.

Table 2 – Vifor's Market shares (value) for IV iron in the Relevant Member States

	Austria	Finland	Germany	Ireland	the Netherlands	Portugal	Romania	Spain	Sweden
2010	[80-90]%	[80-90]%	[50-60]%	[0-5]%	*n.a.*	[10-20]%	[90-100]%	[60-70]%	[80-90]%
2011	[80-90]%	[70-80]%	[50-60]%	[0-5]%	[90-100]%	[10-20]%	[90-100]%	[60-70]%	[80-90]%
2012	[80-90]%	[80-90]%	[50-60]%	[0-5]%	[90-100]%	[20-30]%	[90-100]%	[70-80]%	[80-90]%
2013	[80-90]%	[80-90]%	[50-60]%	[0-5]%	[80-90]%	[60-70]%	[90-100]%	[70-80]%	[60-70]%
2014	[70-80]%	[90-100]%	[50-60]%	[0-5]%	[70-80]%	[70-80]%	[90-100]%	[80-90]%	[60-70]%
2015	[70-80]%	[90-100]%	[60-70]%	[80-90]%	[70-80]%	[80-90]%	[80-90]%	[80-90]%	[60-70]%
2016	[70-80]%	[90-100]%	[70-80]%	[70-80]%	[70-80]%	[80-90]%	[80-90]%	[70-80]%	[60-70]%
2017	[70-80]%	[90-100]%	[70-80]%	[70-80]%	[70-80]%	[90-100]%	[80-90]%	[80-90]%	[60-70]%
2018	[80-90]%	[80-90]%	[60-70]%	[70-80]%	[70-80]%	[90-100]%	[80-90]%	[80-90]%	[60-70]%
2019	[80-90]%	[80-90]%	[60-70]%	[70-80]%	[70-80]%	[90-100]%	[80-90]%	[80-90]%	[60-70]%
2020	[80-90]%	[80-90]%	[60-70]%	[70-80]%	[70-80]%	[90-100]%	[90-100]%	[80-90]%	[60-70]%
2021	[80-90]%	[80-90]%	[70-80]%	[70-80]%	[70-80]%	[90-100]%	[80-90]%	[80-90]%	[60-70]%
2022	[80-90]%	[80-90]%	[70-80]%	[70-80]%	[90-100]%	[90-100]%	[80-90]%	[90-100]%	[60-70]%

Source: IQVIA

(51) Vifor's market power in the Relevant Members States is further strengthened by the fact that half or most of the main competing products (one out of two in Romania, two out of three in Austria, Spain, Sweden, Finland, Ireland and Portugal, three out of four in Germany, and four out of five in the Netherlands) are low-dose compounds exerting a limited constraint on Vifor's flagship high-dose product (Ferinject). This is notably illustrated by the rapid uptake of high-dose IV iron to the detriment of low-dose IV iron in those countries (see Figure 1).

(52) Moreover, in Germany and Sweden, a material share of Venofer's and Ferinject's sales is accounted for by parallel importers. The Commission considers that, in those markets, (i) the market shares held by parallel importers at a given time overstate their actual market power, whereas (ii) Vifor's market shares (which exclude parallel imports of Ferinject and Venofer – see Table 2 above) understate the strength of its IV iron products on the local market.[83] This is because parallel importers are not engaged in the marketing of products differing from the original reference products: they sell Vifor's products which they have obtained, directly or indirectly, from Vifor in other EEA countries. It follows that parallel importers exclusively compete on price and do not detract from the relative strength of the position of Vifor's products on the market in the import countries (i.e. Germany and Sweden). Indeed, from the perspective of prescribers, the products remain essentially the same

82 In a differentiated market such as the IV iron market, market shares by value more accurately reflect the relative position and strength of each supplier, compared to market shares by volume. Indeed, a purely volume-based measure is unable to reflect the therapeutic differences between IV iron products. Conversely, sales by value reflect both the volumes sold and the prices that are higher for high-dose IV iron due to their superior efficacy (see Case T-321/05, *AstraZeneca*, paras 194-195).

83 Case COMP/A.37.507/F3 – *AstraZeneca*, paragraphs 529-532, 577, 586-587, 590, 594-596.

regardless of whether they are sold by Vifor or by parallel importers. Therefore, in the Commission's view, the total sales of Ferinject and Venofer (including both Vifor's local sales and parallel imports) better reflect the strength of Vifor's products and brands at the point of prescription.[84] In that respect, it appears that, in Germany and Sweden during the Relevant Period, the combined market shares of Venofer and Ferinject (including both Vifor's own sales and parallel imports) were materially larger than Vifor's market shares (considering only the company's own sales), which were already well above [50-60]%.

Table 3 – Ferinject's and Venofer's market shares (value) in Germany and Sweden (including parallel imports)

	GERMANY			SWEDEN		
	Ferinject	**Venofer**	***combined***	**Ferinject**	**Venofer**	***combined***
2010	[40-50]%	[10-20]%	*[50-60]%*	[50-60]%	[30-40]%	*[90-100]%*
2011	[50-60]%	[5-10]%	*[60-70]%*	[60-70]%	[20-30]%	*[90-100]%*
2012	[60-70]%	[5-10]%	*[70-80]%*	[70-80]%	[20-30]%	*[90-100]%*
2013	[70-80]%	[0-5]%	*[70-80]%*	[60-70]%	[10-20]%	*[80-90]%*
2014	[70-80]%	[0-5]%	*[80-90]%*	[60-70]%	10-20]%	*[70-80]%*
2015	[70-80]%	[0-5]%	*[80-90]%*	[70-80]%	[5-10]%	*[70-80]%*
2016	[80-90]%	[0-5]%	*[80-90]%*	[70-80]%	[0-5]%	*[70-80]%*
2017	[80-90]%	[0-5]%	*[80-90]%*	[70-80]%	[0-5]%	*[70-80]%*
2018	[80-90]%	[0-5]%	*[80-90]%*	[70-80]%	[0-5]%	*[70-80]%*
2019	[70-80]%	[0-5]%	*[80-90]%*	[60-70]%	[0-5]%	*[70-80]%*
2020	[70-80]%	[0-5]%	*[70-80]%*	[60-70]%	[0-5]%	*[70-80]%*
2021	[80-90]%	[0-5]%	*[80-90]%*	[60-70]%	[0-5]%	*[70-80]%*
2022	[80-90]%	[0-5]%	*[80-90]%*	[60-70]%	[0-5]%	*[60-70]%*

Source: IQVIA

(53) In light of the above, the Commission's Preliminary Assessment reached the preliminary conclusion that Vifor's very large market shares over a long period of time, in differentiated markets where most competing (low-dose) products exert limited constraints on Vifor's flagship (high-dose) product, are such as to create a strong presumption of dominance on the IV iron market in Austria, Finland, Germany, Romania, Spain, and Sweden in 2010-2022, in the Netherlands in 2011-2022, in Ireland in 2015-2022 and in Portugal in 2013-2022.

5.2.2.1.2. Market shares on the relevant national markets for high-dose IV iron

(54) During the Relevant Period, only two high-dose IV iron products were marketed in the Relevant Member States,[85] namely Vifor's Ferinject (launched locally in 2007 in Germany, 2008 in Finland, Ireland, Portugal and Sweden, 2009 in Austria, the Netherlands and Spain, 2011 in Romania)[86] and Pharmacosmos' Monofer (launched locally in 2010 in Sweden, 2011 in Germany, Finland, Ireland and the Netherlands, and 2012 in Austria, Portugal, Romania and Spain, and *de facto* withdrawn from the Spanish market in 2017).[87] In other words, during the Relevant Period in the Relevant Member States, Ferinject faced at most only one high-dose rival (Monofer) and no competition at all on the potential market for high-dose IV iron in Finland, Germany,

84 This is all the more appropriate given that Vifor's conduct aimed at influencing prescriptions by doctors. For this type of conduct, the share accounted by Ferinject (combining Vifor's own sales and parallel imports) in the total IV iron prescriptions is more relevant than the parallel importers' price-competition.

85 A third compound (i.e. Rienso) was briefly marketed in some of the Relevant Member States in 2012-2014, with marginal sales (according to IQVIA), before being withdrawn from the EEA in 2015.

86 [Information on Vifor's internal document].

87 Pharmacosmos' reply to RFI dated 15 July 2022, Question 6 and Annex 1.

Ireland and the Netherlands in 2010, in Austria and Portugal in 2010-2011, in Romania in 2011, and in Spain in 2010-2011 and 2018-2022.

(55) As shown in Table 4, during the Relevant Period, Vifor consistently accounted for a very large share of the high-dose IV iron market in Austria (≥ [80-90]%), Finland (> [80-90]%), Germany (> [70-80]%), Ireland (> [70-80]% except in 2011 and 2013-2014), the Netherlands (> [70-80]%), Portugal ([90-100%]), Romania (≥ [70-80]%), Spain ([90-100%]), and Sweden (> [60-70]%). According to settled case law, such high market shares evidence in themselves the existence of a dominant position.

Table 4 – Vifor's Market shares (value) for high-dose IV iron in the Relevant Member States

	Austria	Finland	Germany	Ireland	the Netherlands	Portugal	Romania	Spain	Sweden
2010	100%	100%	100%	100%	100%	100%	-	100%	[90-100]%
2011	100%	[90-100]%	[90-100]%	n.a.	[90-100]%	100%	100%	100%	[90-100]%
2012	[90-100]%	[90-100]%	[80-90]%	[90-100]%	[90-100]%	[90-100]%	[80-90]%	[90-100]%	[80-90]%
2013	[80-90]%	[90-100]%	[70-80]%	[0-5]%	[80-90]%	[90-100]%	[80-90]%	[90-100]%	[60-70]%
2014	[80-90]%	[90-100]%	[70-80]%	[5-10]%	[80-90]%	[90-100]%	[70-80]%	[90-100]%	[60-70]%
2015	[80-90]%	[90-100]%	[80-90]%	[90-100]%	[70-80]%	[90-100]%	[70-80]%	[90-100]%	[60-70]%
2016	[80-90]%	[90-100]%	[80-90]%	[70-80]%	[70-80]%	[90-100]%	[70-80]%	[90-100]%	[60-70]%
2017	[80-90]%	[90-100]%	[80-90]%	[70-80]%	[70-80]%	[90-100]%	[70-80]%	[90-100]%	[70-80]%
2018	[80-90]%	[80-90]%	[80-90]%	[70-80]%	[80-90]%	[90-100]%	[80-90]%	100%	[60-70]%
2019	[90-100]%	[80-90]%	[70-80]%	[70-80]%	[80-90]%	[90-100]%	[80-90]%	100%	[60-70]%
2020	[90-100]%	[80-90]%	[70-80]%	[70-80]%	[80-90]%	[90-100]%	[80-90]%	100%	[60-70]%
2021	[90-100]%	[80-90]%	[80-90]%	[70-80]%	[80-90]%	[90-100]%	[80-90]%	100%	[60-70]%
2022	[90-100]%	[80-90]%	[80-90]%	[70-80]%	[80-90]%	[90-100]%	[80-90]%	100%	[60-70]%

Source: IQVIA

(56) Despite its aggressive competition (see Sections 5.1.2.2.2.5 and 5.1.2.2.2.6), Monofer's market share in the Relevant Member States remained substantially lower than Ferinject's throughout the Relevant Period. The considerable gap between the market shares of Ferinject and its only high-dose rival is a clear indication of market strength.

(57) Furthermore, as previously explained, in Germany and Sweden, Vifor's local market shares (excluding parallel imports of Ferinject – see Table 4 above) understate the strength of Ferinject in those two countries. Considering the total sales of Ferinject (including both Vifor's local sales and parallel imports), which better reflect the strength of Vifor's high-dose product, it appears that Ferinject consistently accounted for more than [90-100]% and more than [70-80]% of all the high-dose IV iron sales achieved respectively in Germany and Sweden, in the Relevant Period (based on IQVIA).

(58) In light of the above, the Commission's Preliminary Assessment reached the preliminary conclusion that Vifor's very large market shares over a long period of time are such as to create a strong presumption of dominance on the high-dose IV iron market in Austria, Finland, Germany, the Netherlands, Portugal, Spain, and Sweden in 2010-2022, in Ireland in 2010, 2012 and 2015-2022 and in Romania in 2011-2022.

5.2.2.2. Ferinject's price premium demonstrates Vifor's power to maintain prices above competitive level

(59) As described in Section 5.1.2.2.2.5, high-dose IV iron products (i.e. Ferinject and Monofer) are considerably more expensive than low-dose IV iron products and, within high-dose IV iron, Vifor followed [Information on Vifor's pricing strategy]. Vifor's business documents,[88] as well as Vifor's and Pharmacosmos' actual net sales

[88] E.g. [Information on Vifor's internal document].

data, show that the [Information on Vifor's pricing strategy] was overall successful. When a company is able to sustain prices at a […] higher level compared to the competing products while retaining a much higher market share, it indicates market power and the ability to act, to an appreciable extent, independently of competitors and customers.[89]

(60) Vifor managed to not only sustain a […] premium price compared to all its IV iron rivals, including its closest and only high-dose competitor (Monofer), but also to increase the sales volumes of Ferinject […] in all Relevant Member States over the entire Relevant Period.[90] Monofer did not grow nearly as much despite being cheaper and sales of low-dose IV iron products remained relatively flat, despite them being significantly cheaper (see Sections 5.1.2.2.2.5 and 5.1.2.2.2.4).

(61) Moreover, despite a certain price erosion, the evidence on file reveals that, during the Relevant Period, Vifor's net profit margin for Ferinject steadily increased in at least [some] of the Relevant Member States ([…]) to reach in 2022 a level comprised between […]. As a result, in 2012-2022, Ferinject's net profits increased in […]. This shows that Vifor was able to act independently of its competitors and consumers by not only sustaining a premium price and increase sales volumes for Ferinject but also that sales of Ferinject became increasingly profitable between 2010 and 2022.

5.2.2.3. High barriers to entry and expansion

(62) The preliminary results of the market investigation show that the supply of IV iron, in particular the supply of high-dose IV iron, is characterised by a number of high barriers to entry and expansion owing to (i) the long and costly research and development ("R&D") (Section 5.2.2.3.1), (ii) the manufacturing process of IV iron (Section 5.2.2.3.2, (iii) the inertia characterising the physicians' prescribing choices (Section 5.2.2.3.3), (iv) the fragmentation of the demand regarding the treatment of in ID / IDA (Section 5.2.2.3.4), and (v) the limited attractiveness of the relevant markets in the Relevant Period (Section 5.2.2.3.5). The existence of the above barriers is corroborated by the fact that no material entry/expansion has been observed in the relevant markets in the past 12 years (apart from Pharmacosmos' entry in the Relevant Member States and its moderate expansion in some of them) (Section 5.2.2.3.6).

5.2.2.3.1. Significant R&D barriers

(63) IV iron, especially high-dose IV iron, is characterised by substantial R&D barriers to entry and expansion. Indeed, since both Ferinject and Monofer were still patented in the EEA in 2023, any company willing to enter the high-dose IV iron market in the Relevant Period had to develop and then to secure the regulatory approval of a new innovative compound, which are long and costly processes.[91] Moreover, in order to successfully enter and expand its activities in the relevant markets for IV iron and high-dose IV iron, a company must generate additional post-marketing clinical data showing the effectiveness of its product in the various therapeutic areas where ID / IDA is prevalent (e.g. cardiology, gastroenterology). These data are essential to favour the product's

89 Case T-321/05, *AstraZeneca*, paragraphs 261-266.

90 In the Netherlands (+[…]%), Sweden (+[…]%), Germany (+[…]%), Spain (+[…]%), Austria (+[…]%), Finland (+[…]%) and Romania (+[…]%) from 2012 to 2021, +[…]% in Portugal from 2013 to 2021, and +[…]% in Ireland from 2015 to 2021.

91 [Information on Vifor's submission to the Commission].

adoption in the relevant patient segments and to differentiate it from competition.[92] The conduct of such trials is a multi-year project requiring large investments.[93]

5.2.2.3.2. The IV iron manufacturing process is complex and costly

(64) The manufacturing of IV iron, including high-dose IV iron, constitutes another significant barrier to entry. According to Vifor itself, the production of IV iron (be it low-dose or high-dose) is complex and requires specific expertise. In its view, [Vifor's confidential assessment of IV iron production],[94] which [Vifor's confidential assessment of IV iron production]. The above is corroborated by Vifor's internal documents.[95]

5.2.2.3.3. Doctors' inertia leading to a first-mover advantage

(65) Vifor's internal documents reveal that the prescriptions of (high-dose) IV iron in the Relevant Member States were characterised by a high degree of inertia.[96] The differentiated nature of IV iron compounds and the safety concerns historically associated with the use of this class of medicines (see Section 5.1.2.1) have heightened the caution that normally characterises doctors' attitudes towards new products, thus restricting the constraint exerted by new (high-dose) IV iron products on the incumbent (high-dose) IV iron product(s).[97] Prescribing doctors are generally risk averse and avoid prescribing medicines surrounded by safety concerns or controversies. In such circumstances, they tend to be very conservative about switching to a different medicine than the one they have been treating patients with, which gives a significant competitive advantage to the incumbent product(s).

(66) Venofer and Ferinject are the incumbent products in the Relevant Member States since they were respectively the first low-dose and high-dose IV iron products marketed in those countries and were, thus, likely to benefit from the above-described 'inertia': doctors who had already had occasion to prescribe Venofer and Ferinject would generally favour those compounds for new patients.

5.2.2.3.4. Fragmentation of the demand regarding the treatment of ID / IDA

(67) The supply of (high-dose) IV iron is characterised by another significant barrier to entry / expansion, i.e. the need to reach out to and convince a large number of local prescribers to ensure full market coverage. Indeed, ID / IDA is a blood disorder occurring in a wide variety of therapeutic areas (e.g. nephrology, gastroenterology), which means that, in order to successfully enter and expand its activities in the relevant markets for IV iron and for high-dose IV iron, a company must reach out to and convince a variety of specialist prescribers to ensure full market coverage and, thus, sufficient sales to be profitable. This is resource intensive. In particular, the need to cover a large number of local prescribers requires a substantial (direct or indirect) local presence, involving significant local investments. Vifor's own submissions and business documents show that [Vifor's confidential assessment of IV iron demand].[98]

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92 E.g. [Information on Vifor's internal documents].

93 [Information on Vifor's submission to the Commission].

94 [Information on Vifor's submission to the Commission].

95 E.g. [Information on Vifor's internal documents].

96 E.g., [Information on Vifor's internal documents].

97 Case T-321/05, *AstraZeneca*, paragraph 105, confirmed on appeal in C 457/10 P, paragraph 50.

98 E.g., [Information on Vifor's internal documents].

5.2.2.3.5. Limited attractiveness of the relevant markets

(68) The modest size and, thus, the modest and uncertain potential return on investments characterising the relevant national IV iron markets, and *a fortiori* the relevant national high-dose markets during the Relevant Period limited their attractiveness, creating thus a substantial barrier to entry / expansion.

(69) During the Relevant Period, several factors initially limited the size of the relevant markets, which remained until recently niche markets with limited potential return on investments. Those factors include notably (i) the doctors' limited awareness of ID / IDA and of its treatment (which means that, in many instances, ID / IDA is not being diagnosed, or is diagnosed but not treated with (high-dose) IV iron);[99](ii) the existence of payers/budget restrictions limiting the use of IV iron (which is significantly more expensive than oral iron – see Section 5.1.2.2.1.3) and *a fortiori* of high-dose IV iron (which is much more expensive than low-dose IV iron – see Section 5.1.2.2.2.5);[100] and (iii) the geographic fragmentation of the supply of IV iron in the EEA (which involves significant local investments (see previous Section) in national markets of limited size). Vifor itself acknowledged that [Vifor's confidential assessment of the competitive dynamics in the IV iron market].[101]

(70) The progressive growth of the IV iron market over time had limited impact on potential entries in the Relevant Member States during the Relevant Period for the following reasons. *First*, with respect to low-dose products, the Commission observes that the expansion of the IV iron market was driven by Ferinject, low-dose products being progressively niched in a limited number of clinical setting (see Section 5.1.2.2.2.4). In other words, the sales potential of low-dose IV iron remained limited during the entire Relevant Period. *Second*, the expansion of the demand for high-dose products was gradual (see Section 5.1.2.2.2.4) and not a given in the early years of the Relevant Period given the historical safety concerns affecting the IV iron class (see Section 5.2.2.3.3). In addition, entering the high-dose segment / market does not happen overnight, the development of a new innovative compound being very long (more than 10 years for Ferinject) (see Section 5.2.2.3.1). Therefore, even if one assumes that, at some points in the "*recent years*" of the Relevant Period, a company (other than Pharmacosmos and Takeda – see next Section) may have considered that the high-dose IV iron segment / market was sufficiently large / attractive to envisage the development of a new innovative product (*quod non*), the launch of this product in the EEA would have necessarily occurred well after 2022 and, thus, would not have undermined Vifor's market power during the Relevant Period.

5.2.2.3.6. No or limited past entry both with respect low- and high-dose IV iron

(71) The importance of the barriers to entry and expansion on the (high-dose) IV iron market is corroborated (i) by the fact that, apart from Pharmacosmos' entry in the Relevant Member States and moderate expansion in some of them (see e.g. Section 5.2.2.1.2) and Takeda's failed attempt (2012-2015) to market Rienso in the EEA,[102]

99 [Information on Vifor's submissions to the Commission]. See also e.g. [Information on Vifor's internal document].

100 E.g., [Information on Vifor's internal documents].

101 [Information on Vifor's submissions to the Commission] (emphasis added).

102 See footnote 85 above.

no players tried to enter the high-dose market since 2010 and (ii) by the absence of material low-dose entry in the Relevant Member States in the Relevant Period.[103]

5.2.2.4. Countervailing buyer power

(72) The evidence on file indicates that there was no sufficient countervailing buyer power to offset Vifor's market power in the Relevant Member States in the Relevant Period, the company's customer base being generally fragmented, [Information on Vifor's customer base].[104] The ability of Vifor's customers to switch to other suppliers of (high-dose) IV iron was further impaired by the fact that the entities purchasing IV iron (e.g. wholesalers, retail and hospital pharmacies) have limited control over which products are prescribed since the decision is taken by doctors, who are generally not involved in the procurement process and whose prescribing choices are primarily guided by therapeutic considerations and characterised by a high degree of inertia.

5.2.2.5. [Information on Vifor's internal assessment of its own competitive position]

(73) Vifor's internal documents support the preliminary finding of the company's dominance in the supply of (high-dose) IV iron in the Relevant Member States in the Relevant Period for several reasons. *First*, they emphasise the fact that (i) [Information on Vifor's internal assessment of its own competitive position]][105] and that (ii) [Information on Vifor's internal assessment of its own competitive position].[106] *Second*, [Information on Vifor's internal assessment of its own competitive position],[107] as well as [Information on Vifor's internal assessment of its own competitive position][108] and [Information on Vifor's internal assessment of its own competitive position].[109] *Third*, internal documents reveal that [Information on Vifor's internal assessment of its own competitive position][110] and [Information on Vifor's internal assessment of its own competitive position]. In fact, many internal documents show that [Information on Vifor's internal assessment of its own competitive position].[111] *Fourth*, internal documents evidence the fact that [Information on Vifor's internal assessment of its own competitive position].[112]

5.2.3. Preliminary conclusions on dominance

(74) In view of the foregoing and considering the fact that Vifor's conduct started in 2010 and was ongoing at least until 2022 (see Section 1), the Commission's Preliminary Assessment reached the preliminary conclusion that Vifor may have held a dominant

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103 To the Commission's knowledge, during the Relevant Period, only two new low-dose products were introduced in a couple of Relevant Member States, namely (i) Pharmacosmos' Diafer launched in Sweden in 2013 and in the Netherlands in 2015, and (ii) Rechon Life Science's Järnsackaros Rechon (a Venofer generic) launched in Sweden in 2012. According to IQVIA, the sales of both products were still very modest in 2022.

104 See notably [Information on Vifor's submissions to the Commission].

105 [Information on Vifor's internal document]. See also Case T-321/05, *AstraZeneca*, paragraphs 254 and 260.

106 E.g., [Information on Vifor's internal documents].

107 E.g., [Information on Vifor's internal documents].

108 E.g., [Information on Vifor's internal documents].

109 E.g., [Information on Vifor's internal documents].

110 E.g., [Information on Vifor's internal document].

111 E.g., [Information on Vifor's internal document].

112 E.g., [Information on Vifor's internal document].

position within the meaning of Article 102 TFUE under all plausible market delineations, that is to say:

– on the IV iron market in Austria, Finland, Germany, Romania, Spain, and Sweden in 2010-2022, in the Netherlands in 2011-2022, in Ireland in 2015-2022 and in Portugal in 2013-2022;

– on the high-dose IV iron market in Austria, Finland, Germany, the Netherlands, Portugal, Spain, and Sweden in 2010-2022, in Ireland in 2010, 2012 and 2015-2022 and in Romanian in 2011-2022.

5.3. Practices raising concerns

(75) In the Preliminary Assessment, the Commission conducted a review of Vifor's communications - in particular the two main messages identified in Section 5.3.3 below raising doubts about the safety of Monofer - and reached the preliminary conclusion that Vifor may have abused its dominant position by disparaging its main competing product. If confirmed, this would amount to a breach of Article 102 TFEU.

5.3.1. General principles on the notion of abuse

(76) Article 102 TFEU prohibits as incompatible with the internal market any abuse by one or more undertakings of a dominant position within the internal market or in a substantial part of it, insofar as it may affect trade between Member States.

(77) The concept of abuse under Article 102 TFEU is an objective one referring to "*the behaviour of an undertaking in a dominant position which is such as to influence the structure of a market where, as a result of the very presence of the undertaking in question, the degree of competition is* [already] *weakened and which, through recourse to methods different from those which condition normal competition* […] *has the effect of hindering the maintenance of the degree of competition still existing in the market or the growth of that competition*."[113]

(78) It follows from the nature of the obligations imposed by Article 102 TFEU that, in specific circumstances, undertakings in a dominant position may be deprived of the right to adopt a course of conduct or take measures which would be unobjectionable if adopted or taken by non-dominant undertakings.[114] The actual scope of that special responsibility imposed on a dominant undertaking must be considered in light of the specific circumstances of the case.[115]

(79) Article 102 TFEU lists a number of abusive practices. These are merely examples, not an exhaustive enumeration of the practices that may constitute abuses of a dominant position prohibited by the Treaty or the EEA Agreement.[116] Article 102 TFEU prohibits, among other things, a dominant undertaking from eliminating or marginalising a competitor, thereby hindering the maintenance of the degree of competition still existing in the market or the growth of that competition and

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113 Case T-155-06, *Tomra Systems*, paragraph 206 and the case law cited.

114 Case C-322/81, *Michelin*, paragraph 57; Case T-111/96, *ITT Promedia*, paragraph 139; Case T-301/04, *Clearstream*, paragraph 133.

115 Case C-52/09, *TeliaSonera Sverige,* paragraph 84 and the case-law cited; Case T-612/17, *Google Shopping*, paragraph 165.

116 Case C-6/72, *Europemballage and Continental Can Company*, paragraph 26; Case C-280/08 P, *Deutsche Telekom*, paragraph 173; Case C-52/09, *TeliaSonera Sverige*, paragraph 26.

strengthening its position by using methods other than those which come within the scope of competition on the merits.[117]

(80) When implemented by an undertaking in a dominant position, a practice may be characterised as abusive under Article 102 TFEU if it is capable of producing an exclusionary effect and if it is based on the use of means other than those which come within the scope of competition on the merits.[118]

5.3.2. Specific principles applicable to disparaging conduct on pharmaceutical markets

(81) The dissemination of misleading messages is an example of a conduct falling outside the scope of competition on the merits.[119] In its 2018 *Hoffmann-La Roche* judgment, the Court of Justice ruled that an arrangement *"which concerns the dissemination, in a context of scientific uncertainty, to the EMA, healthcare professionals and the general public of misleading information relating to adverse reactions"* resulting from the use of a competing drug *"for the treatment of diseases not covered by the MA for that product, with a view to reducing the competitive pressure* […] *constitutes a restriction of competition by object"* under Article 101 TFEU.[120] While the *Hoffmann-La Roche* judgment concerned an infringement of Article 101(1) TFEU, Art. 101 and 102 should be interpreted and applied consistently,[121] while also bearing in mind that, under Art. 102 TFEU, dominant undertakings are subject to a "*special responsibility*" not to abuse their market power.[122] That is, *a fortiori*, the case in circumstances where the dominant undertaking disseminates misleading messages in relation to the use of a competing medicine for which there is a marketing authorisation attesting its safety and efficacy.

(82) In view of the special responsibility of dominant undertakings under Article 102 TFEU not to use means outside the scope of competition on the merits, a dominant firm can promote the qualities of its own product but cannot – through that promotion or through other means – disparage a rival pharmaceutical product by creating false perceptions about its material characteristics, including its safety and efficacy, when such disparagement is capable of restricting competition. Accordingly, a campaign by a dominant undertaking to mislead HCPs and other relevant stakeholders by creating, based on its established position with relevant stakeholders, an exaggerated perception of health risks related to the switching to a competing product, is clearly not *"in keeping with the special responsibility of an undertaking in a dominant position"* and not competition on the merits.[123]

(83) Such conduct by a dominant undertaking can constitute an abuse under Article 102 TFEU in circumstances where it (i) consists in the dissemination of objectively misleading information (i.e. inaccurate or incomplete information capable of confusing

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117 Case C-62/86, *AKZO*, paragraph 70; Case C-202/07 P, *France Télécom*, paragraph 106; Case C-457/10 P, *AstraZeneca*, paragraph 75; Case C-377/20, *Servizio Elettrico Nazionale*, paragraph 68-69, 76.

118 Case C-377/20, *Servizio Elettrico Nazionale*, paragraph 103.

119 See in relation to the concept of competition on the merits, Case C-377/20, *Servizio Elettrico Nazionale*, paragraphs 75-79 and case-law cited therein.

120 Case C-179/16, *Hoffmann-La Roche*, paras 92-95. The Court added that *"given the characteristics of the medicinal products market, it is likely that the dissemination of such information will encourage doctors to refrain from prescribing that product thus resulting in the expected reduction in demand for that type of use"*, see paragraph 93. See also AG Saugmandsgaard Øe in that case paras 158 and 160.

121 Case C-333/21, *SuperLeague,* paragraph 119.

122 Case C 413/14 P, *Intel*, paragraph 135.

123 See, by analogy, Case T-321/05, *AstraZeneca*, paragraphs 355-361.

its addressees, that is capable of discrediting a competing product);[124] (ii) is capable of producing exclusionary effects;[125] and (iii) is not objectively justified.[126]

5.3.2.1. Objectively misleading information

(84) Misleading information is not only information that is inaccurate but also information that is strictly speaking correct, though presented in an incomplete manner that is capable of confusing and manipulating the public perception around the safety risks of a competing medicine.[127]

(85) A communication is misleading where, because of the manner in which it is presented, it is likely to mislead those who receive it.[128] This may include instances where a company omits to state that the risks created by using the medicines are uncertain or exaggerates such risks with a lack of objectivity with regard to the available evidence.[129]

(86) In addition, the misleading nature of representations must be assessed from an objective perspective. This means that there is no need to establish that the misleading information had the actual effect of misleading the targeted stakeholders.[130] Instead, it is sufficient to show that the disseminated information was of such nature that it was capable of misleading the relevant stakeholders, irrespective of how these eventually reacted to the disseminated information.

5.3.2.2. Capability to produce exclusionary effects

(87) In pharmaceutical markets, HCPs are key drivers of demand as the uptake of prescription medicines depends largely on their prescribing practices, procurement decisions and dispensing practices. A disparagement campaign that methodically covers these main stakeholders and targets a material aspect of a prescription medicine such as its safety or efficacy is capable of weighing heavily on the decisions of HCPs and thereby capable of steering demand away from the medicine targeted by such campaign.

(88) HCPs tend to be conservative about switching to a different medicine than the one they have been treating patients with, in the absence of a pressing medical need.[131] Further, prescribing doctors are primarily guided by considerations of therapeutic appropriateness/efficacy and the safety of medicines,[132] rather than costs.

(89) These features make pharmaceutical markets particularly vulnerable to disparagement practices. The potential exclusionary effect of a disparagement campaign by a dominant undertaking is all the more likely if the dominant

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124 Case C-179/16, *Hoffmann-La Roche*, paras 92-95.

125 Case C-377/20, *Servizio Elettrico Nazionale*, paragraph 103.

126 Case C-377/20, *Servizio Elettrico Nazionale*, paragraph 84.

127 See Case C-179/16, *Hoffmann-La Roche*, paragraph 92. Further, the pharma legislation requires the promotion information to be accurate and complete: Article 92(2) of Directive 2001/83 states that any documentation relating to a medicinal product which is transmitted as part of the promotion of that product to persons qualified to prescribe or supply it shall be accurate, up-to-date, verifiable and sufficiently complete to enable the recipient to form his or her own opinion of the therapeutic value of the medicinal product concerned.

128 Opinion of AG Saugmandsgaard Øe in Case C-179/16, *Hoffmann-La Roche*, paragraph 158.

129 Ibid, paragraph 160.

130 Case T-321/05, *AstraZeneca*, paragraphs 360-361. See also Case C-457/10 P, *AstraZeneca*, paragraph 99.

131 Case T-321/05, *AstraZeneca*, para.105. See also Case C 457/10 P, *AstraZeneca*, paragraph 50.

132 Case C-179/16, *Hoffmann-La Roche*, paragraph 65.

undertaking enjoys a strong reputation. Through this reputation and its strong presence on the market, as well as its established relationship with HCPs, a dominant incumbent has unrivalled capacity to influence HCPs.[133]

5.3.2.3. Objective justification

(90) Conduct may escape the prohibition of Article 102 TFEU if the dominant undertaking can provide an objective justification for its behaviour or it can demonstrate that its conduct produces efficiencies which outweigh the negative effect on competition. The burden of proof for such an objective justification or efficiency defence is on the dominant company.[134]

5.3.3. Application to this case

(91) The evidence on the Commission's file suggests that, when Monofer was launched in Europe in 2010, Vifor engaged in a communication campaign capable of leading HCPs into believing that administering Monofer entails serious health risks and that Monofer has a worse risk profile compared to Ferinject.

(92) To promote this overarching claim, Vifor disseminated two main messages that were capable of discrediting Monofer. Those messages were that (i) Monofer bears the serious safety risks historically associated with IV iron dextran compounds, in particular high molecular weight ("HMW") IV iron dextrans; and (ii) Monofer has more frequent HSRs compared to Ferinject. Each of these main messages is preliminarily assessed in the sections that follow.

5.3.3.1. ***"First Message"***: Monofer is a dextran and/or *"dextran-derived"*/*"dextran-based"* and may cause dextran-induced anaphylactic reactions ("DIARs").

(93) One of the two main messages in Vifor's communication campaign about the safety of Monofer was that, despite being based on a new chemical composition (iron (III) isomaltoside 1000, currently known as ferric derisomaltose), Monofer is a *"dextran"* or *"dextran-derived"/"dextran-based"* medicine, playing on the fact that this compound carries the historic negative safety connotations of HMW IV iron dextrans (which are no longer marketed in Europe).[135]

(94) To properly assess the full implications of this message it is important to understand that it is highly toxic and, thus, not safe to inject iron or iron salts directly into the blood stream, making it necessary to wrap the iron in a carbohydrate shell to enable a slow and controlled release of iron and to avoid toxicity.[136]

(95) There are different types of carbohydrate shells that are used or have been used as carriers in IV iron medicines. In the 1950s, the first-generation IV iron products were characterised by shells of sucrose or HMW dextran to avoid the toxicity of labile iron. The HMW dextran complexes were immunogenic and led to severe HSRs, most

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133 See also Case C 457/10 P, *AstraZeneca*, paragraph 50 where the Court concluded that *"enjoying a solid brand image and reputation, was further supported by the fact that doctors generally require time in order to learn about a new medicinal product and thus that they will hesitate to prescribe PPIs of other producers entering that market."*

134 Case C-377/20, *Servizio Elettrico Nazionale*, paragraph 84 and case law cited therein.

135 To support this message, Vifor relied on Monofer's Public Assessment Report, the WHO ATC classification at the time and Monofer's US patent. In addition, Vifor relied on Vifor-sponsored studies, co-authored by Vifor employees, to claim in its communications that Monofer may react with anti-dextran antibodies and trigger DIARs.

136 Pharmacosmos' complaint, paragraph 164.

notably (potentially fatal) anaphylactic shocks requiring emergency medical intervention (which ultimately led to their withdrawal from the European markets in the 1990s).[137] The available IV iron products during this period were therefore associated with an unacceptably high rate of serious adverse events.[138]

(96) Accordingly, IV iron dextran compounds have historically been, and still are, widely associated with very serious health risks.

5.3.3.1.1. Examples of the First Message and its dissemination

(97) When Monofer was launched in various Members States in 2010, Vifor developed and disseminated to HCPs a message linking Monofer with the toxicity historically associated with IV iron dextrans. The essence of such message, as set out by Vifor's [Information on the source of Vifor's internal communication], was as follows: *"Isomaltozide"* [Monofer's molecule] *does not exist. Monofer is a Dextran!"* Therefore, the *"key issue* [is] *to create the awareness that Monofer is a Dextran"* because *"Ferinject is not a Dextran therefore if you want to avoid dextran toxicity use Ferinject.*"[139]

(98) To create such awareness, Vifor's [Information on the source of Vifor's internal communication] agreed, inter alia, to *"*[f]*ormulate and communicate to* [Sales] *Field Force our "Dextran Message""* and *"*[e]*quip field forces with Monofer 'Objection Handler'."*[140]

(99) This strategy was also reflected in [Information on the source of Vifor's internal communication], whose *"Key Competitive Message"* in relation to Monofer was that it was *"*[j]*ust another iron Dextran."*[141]

(100) This dextran message was formulated in various ways and evolved over time.

(101) For instance, various of the early presentations and objection handlers prepared by Vifor's headquarters referred to Monofer as *"a 4th generation dextran IV iron solution"*[142] or a *"low molecular weight dextran"*[143]*;* or held that Monofer's molecule (iron (III) isomaltoside 1000) is *"a dextran – nomenclature is Dextran 1"*[144] and that *"it cannot be excluded that Isomaltoside 1000 consists of higher molecular weight dextran."*[145]

(102) Vifor even suggested (incorrectly) in documents produced by its headquarters[146] and in training materials used in Germany in 2011[147] that this was also the perspective of health authorities: *"*[f]*rom the perspective of health authorities, this is just another dextran."*

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137 [Information on Vifor's submissions to the Commission].

138 Michael Auerbach and Iain C. Macdougall, *"Safety of intravenous iron formulations: facts and folklore"*, Blood Transfus. 2014 Jul; 12(3): 296–300.

139 [Information on Vifor's internal document].

140 Ibid. Objection handlers are documents prepared to help sales personnel deal with concerns raised by customers and, in the case of pharmaceutical markets, by HCPs. They are used to train staff and provide them with the lines to take with external stakeholders in case certain objections that can be anticipated are raised.

141 [Information on Vifor's internal document].

142 [Information on Vifor's internal document].

143 [Information on Vifor's internal document].

144 [Information on Vifor's internal document].

145 [Information on Vifor's internal document].

146 [Information on Vifor's internal document].

147 [Information on Vifor's internal documents].

(103) Vifor also claimed (incorrectly) that *"Ferinject is the only high-dose i.v. iron that is non-dextran based."*[148]

(104) In addition, Vifor introduced a *"dextran vs. non-dextran naming"* to compare the different IV iron products, which it sought to *"communicate actively"* targeting *"ALL HCP."*[149] Sales representatives were equipped with relevant publications containing the *"dextran vs non-dextran nomenclature"*, which were used as *"fact building"* whist trying to avoid referring explicitly to Monofer in its promotional pieces.[150]

(105) This dextran message evolved over the years, so that Monofer was no longer described simply as a dextran. Instead of *"fighting that battle"*, Vifor tried to refine its positioning of Monofer: "*we almost certainly COULD defend a definition that Monofer is a dextran, but do we really need to? Our aspirational positioning is that HCPs believe it to be dextran-derived…so why fight that battle?"*[151]

(106) Whilst Vifor may no longer have claimed that Monofer was a dextran as a means to differentiate it from its Ferinject, it developed a similar narrative that dextran-containing, dextran-derived or dextran-based IV iron medicines, such as Monofer, were riskier than Ferinject because they could cause DIARs, which Ferinject did not since it did not contain dextran nor was dextran-derived or dextran-based. In Vifor's own words: *"what we want our customers to believe: "All IV irons are not the same" and Ferinject is the iron therapy leader with a superior benefit: risk profile"* […] *"While Monofer is a dextran derivative with increased hypersensitivity concerns and limited clinical data for patients."*[152]

(107) In other words, Vifor still wanted HCPs to associate Monofer with *"dextran toxicity"*, whilst using a more refined terminology.

(108) For this purpose, Vifor devised an additional, intermediate class of IV iron products, which resulted in its classifying IV iron products in the following way: (i) a *"Dextran"* class (which included Cosmofer, a low molecular weight - "LMW" – low-dose IV iron dextran); (ii) a *"Dextran-derived"* class (which included iron (III) isomaltoside 1000, the active substance in Monofer) and (iii) a *"Non-dextran-based"* class (which included, *inter alia*, ferric carboxymaltose, the active substance in Ferinject).[153]

(109) Furthermore, Vifor supported its dextran-derived messaging with Vifor-sponsored studies,[154] co-authored by Vifor employees. Although these *in vitro* studies had no clinical relevance (as expressly acknowledged by the authors and consistent with EMA's views), Vifor used them to suggest unsubstantiated increased safety risks due to the alleged dextran-derived composition of Monofer. Indeed, as early as in 2010,

148 [Information on Vifor's internal document].
149 [Information on Vifor's internal document].
150 [Information on Vifor's internal documents]
151 [Information on Vifor's internal document].
152 [Information on Vifor's internal documents].
153 See, for instance, [Information on Vifor's internal documents].
154 Neiser S, Wilhelm M, Schwarz K, Funk F, Geisser P and Burckhardt S, *"Assessment of dextran antigenicity of intravenous iron products by an immunodiffusion assay"*, Port J Nephrol Hypert 2011; 25(3): 219-224 and Neiser S, Koskenkorva T, Schwarz K, Wilhelm M and Burckhardt S, *"Assessment of Dextran antigenicity of intravenous iron preparations with enzyme-linked immunosorbent assay (ELISA)"*, Int. J. Mol. Sci. 2016, 17, 1185.

Vifor established as an action point the need to *"*[g]*enerate further evidence to show that Monofer react*[s] *with dextran antibodies.*[155]

(110) The main purpose of these studies was to characterise Monofer as reacting with pre-existing anti-dextran antibodies which could trigger DIARs.[156] As captured in contemporaneous internal evidence, *"Vifor Pharma*['s] *position* [was that] *Monofer is a dextran-1-based compound and reacts with anti-dextran antibodies in vitro."*[157] At the same time, Vifor would claim (or at least imply) that Ferinject has a superior safety profile because *"Ferinject is specially engineered to have a low immunogenic potential:* [a]*s a non-dextran-based preparation, it does not react with dextran antibodies"*[158] or even that *"Ferinject is the only intravenous iron preparation that can be administered at a high dose, that does not react with anti-dextran antibodies."*[159]

(111) These studies were regarded by Vifor as *"a very valuable tool to support the importance of stating that Ferinject is dextran-free whereas Monofer is a dextran-containing preparation"* and, as such, should be distributed *"to all relevant stakeholders*."[160]

(112) Internal contemporaneous evidence clearly shows that the dextran message, in its various formulations and dimensions, was disseminated externally to relevant stakeholders, in particular HCPs. Just by way of example, in the Nordic region in 2012, Vifor stated that *"*[m]*ost of the time the customers ask us "What do You know about the other/The new drug?" the only thing we says* [sic] *here is "It's a dextran as Cosmofer"."*[161] Or in 2015, Vifor reported internally that *"I told a doctor that Monofer is a dextran. Now he would like some documentation to verify it himself. How do I do that? […] do we already have a "skunk" package for this?"* [unofficial translation].[162]

(113) External seminars were also used by Vifor as a platform to disseminate Monofer's alleged dextran-derived nature and implied health risks. For example, in [Date of the event], Vifor Pharma Austria organized [Name of the event] for HCPs to listen to a lecture given by *"*[o]*ur KOL".*[163] The latter's presentation (which was distributed to participants afterwards with Vifor's approval)[164] stated that there are *"*[f]*atalities from*

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155 [Information on Vifor's internal document].

156 See, for instance, the abstract of Neiser S, Koskenkorva T, Schwarz K, Wilhelm M and Burckhardt S, *"Assessment of Dextran antigenicity of intravenous iron preparations with enzyme-linked immunosorbent assay (ELISA)"*, Int. J. Mol. Sci. 2016, 17, 1185: *"The results strongly support the hypothesis that, while the carbohydrate alone (isomaltoside 1000) does not form immune complexes with anti-dextran antibodies, iron isomaltoside 1000 complex reacts with anti-dextran antibodies by forming multivalent immune complexes."*

157 [Information on Vifor's internal document].

158 [Information on Vifor's internal document].

159 [Information on Vifor's internal document].

160 [Information on Vifor's internal document].

161 [Information on Vifor's internal document].

162 [Information on Vifor's internal document], email dated [Information on Vifor's internal document] from [Information on Vifor's internal document] to various Vifor employees regarding *"Wie zeige ich möglichst einfach, dass Monofer ein Dextran ist?"* [unoffical translation: How do I show as simply as possible that Monofer is a dextran?]: *"Ich habe einem Arzt erzählt, dass Monofer ein Dextran ist. Nun hätte er gerne ein paar Unterlagen dazu um das selber zu verifizieren. Wie mache ich das? […] haben wir eventl bereits dazu ein „skunk" Paket?"*.

163 [Information on Vifor's internal document]

164 [Information on Vifor's internal document].

anaphylactic reactions due to dextran-contained iron preparations"[165] while identifying Monofer as a *"Iron(III)oxid Dextran complex[…]"* [unofficial translation].[166] At the same time, the presentation emphasised that there were *"no fatalities from Ferinject (because dextran-free)"*[167] and that an *"optimal IV Iron preparation* [is] [f]*ree of dextran and dextran-derivatives"* [unofficial translation].[168] Similarly, in [Date of the event], Vifor suggested to a speaker at the [Name of the event] Congress and Vifor Symposium in [Place of the event] that he *"may want to orally mention in* [his] *presentation that Ferumoxytol and Isomaltoside contain dextran."*[169]

(114) Further, Vifor regularly used digital pharmaceutical sales content tools with external stakeholders, such as eDetailers, when alerting HCPs of Monofer's alleged dextran-derived HSR: *"Iron(III) isomaltoside (MonoFer) is dextran-based, binding of anti-dextran antibodies occurred in vitro* [….] *possibility of dextran-induced anaphylactic reactions"* and that *"Ferinject is dextran-free, no binding of anti-dextran antibodies occurred in vitro"* while in a footnote mentioning that *"*[d]*extran-containing preparations have the potential to react with preformed anti-dextran antibodies and cause dextran-induced anaphylactic reactions (DIAR)"* [unofficial translation].[170]

5.3.3.1.2. Preliminary Assessment of the inaccurate and/or incomplete nature of the First Message

(115) For the reasons set out below, in the Preliminary Assessment the Commission reached the preliminary view that the First Message is based on inaccurate and/or incomplete information.

(116) <u>*First*</u>, from a chemical perspective, Monofer is not a dextran. Whilst expert consultants commissioned by Vifor in the context of the present investigation may argue the existence of certain similarities between Monofer and a small fraction of dextran,[171] it differs significantly from both the historic HMW IV iron dextrans (withdrawn from the EEA in the 1990s) and the only LMW IV iron dextran currently marketed in the EEA (i.e. Cosmofer) as it is significantly lighter and has a significantly different molecular structure.

(117) The significant differences between Monofer and Cosmosfer are illustrated in Figure 2 below. Whilst the molecular structure of Monofer (ferric derisomaltose or iron (III) isomaltoside 1000) is short, non-branched and linear, with an average molecular weight of 1000 Dalton and an average of 3-5 glucose units, the molecular structure of Cosmofer is long, branched and non-linear, with an average molecular weight of 5000 Dalton and

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165 [Information on Vifor's internal document]: "[…] *Todesfälle durch anaphylaktische Reaktion durch dextranhältiges Fe- Präparat."*

166 Ibid, page 3: *"Eisen(III)oxid-Dextran-Komplexe: - COSMOFER 50 mg/ml – Injektionsloesung und Infusionsloesung; - MONOFER 100 mg/ml – Injections- oder Infusionsloesung."*

167 Ibid, page 2: *"N.B.: durch Ferinject bisher keine Todesfälle gegeben hat (weil dextranfrei)."*

168 Ibid, page 3: *"Was zeichnet ein optimales iv Eisenpräparat aus? […] Frei von Dextran und Dextran-Derivaten."*

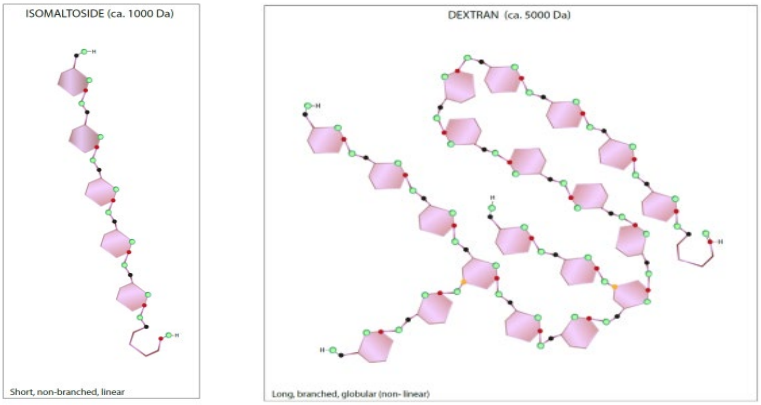
169 [Information on Vifor's internal document].

170 [Information on Vifor's internal document]: *"Eisen(III)-Isomaltosid (MonoFer) ist Dextran-basiert, es kam in vitro zur Bindung von Anti-Dextran-Antikörpern* […] *Möglichkeit von Dextran-induzierten anaphylaktischen Reaktionen" while "Ferinject ist Dextran-frei, es kam in vitro zu keiner Bindung von Anti-Dextran-Antikörpern."* Footnote: *"Dextran-haltige Präparate haben das Potential, mit prä-formierten Anti-Dextran-Antikörpern zu reagieren und Dextran-induzierte anaphylaktische Reaktionen (DIAR) auszulösen."*

171 [Information on Vifor's submissions to the Commission].

an average of 25 glucose units. In addition, the end group in iron (III) isomaltoside 1000 is a glucitol which is different from the aldehyde end group in dextran.

Figure 2: Iron (iii) Isomaltoside 1000 (Monofer) vs Dextran 5000 (Cosmofer)



Source: [Information on Vifor's submissions to the Commission]

(118) *Second*, the characterisation of Monofer as a dextran has no basis in the regulatory findings by relevant health authorities.

(119) As explained by the EMA to the Commission, medicinal products are characterised and described based on the information contained in the respective SmPC. Monofer's SmPC does not refer to dextran, thus it is not considered a dextran. Formally it is a complex of ferric irons and iron (III) isomaltoside 1000 (currently known as ferric derisomaltose) and the fact that it originates from a LMW dextran fraction does not make it a dextran.[172]

(120) This is consistent with the position adopted in the 2020 Intravenous Iron Post-Authorisation Safety Study ("PASS") (recommended by EMA to further evaluate the HSR risk associated with IV irons)[173] which categorised both Monofer and Ferinject as *"non-dextrans."*[174] Similarly, in December 2016 the French *Haute Autorité de Santé* published a summary opinion where it described Monover's (i.e. the local brand for Monofer) chemical structure as *"dextran-free iron."*[175]

(121) The mere fact that Monofer's Public Assessment Report recognised that Monofer's carbohydrate originates from a chemical modification of isomalto-oligosaccharides present in a dextran fraction does not make it a dextran medicine from a chemical perspective. On the contrary, Monofer's Public Assessment Report is clear that the active substance in Monofer is iron(III) isomaltoside 1000 which is reflected in Monofer's SmPC.[176]

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172 Consolidated minutes of the Meetings with the EMA, 10 May 2022 and 14 September 2022, p.3.

173 See paragraphs (166)-(167) below.

174 *"Intravenous Iron Post-authorisation Safety Study (PASS): Evaluation of the Risk of Severe Hypersensitivity Reactions"* (EUPAS20720), 20 November 2020, p.38, Fig.9, available at IV_Iron PASS_Final Report_Revised V1.3_20Nov2020_Redacted.pdf (europa.eu).

175 Haute Autorité de Santé, Brief Summary of the Transparency Committee Opinion, 2016, p.1, available at MONOVER_SUMMARY_CT15570 (has-sante.fr).

176 The same applies to Vifor's reliance on Monofer's US patent. The mere fact that Monofer may originate from a dextran fraction which is then hydrolysed and reduced in a multi-step process, does not make it a dextran medicine from a chemical perspective. This is consistent with EMA's views and the national rulings in the Netherlands and Germany briefly summarised below. Likewise, the fact that the WHO ATC classification until 2014 classified Monofer at the ATC 5th level as *"B03AC06 Ferric oxide dextran*

(122) *Third*, this matter has been the subject of disputes at national level and the outcome in those proceedings has generally been consistent with the finding that Monofer is not a dextran.

(123) As early as 2011, the Dutch Ethical Standards Board of the Foundation for Advertising Medicinal Products ("GCR") found that *"…the mere fact that Dextran I can be used as a building block does not imply that Monofer (iron isomaltoside 1000) is a dextran or a dextran derivative"* (unofficial translation).[177] In this ruling dated 30 November 2011, Vifor's local subsidiary was ordered to stop disseminating in the Netherlands, with immediate and full effects, any messages equating iron (III) isomaltoside 1000/Monofer to dextran 1000 or any other statement implying that Monofer is a dextran or that the active ingredient of Monofer is something other than iron (III) isomaltoside 1000.

(124) Similarly, in Germany there have been a number of judicial proceedings where the chemical composition of both Ferinject and Monofer have been considered.

(125) Of particular relevance are the Order of the Hamburg Regional Court issued in case 315 O 301/18 and the Order of the Hamburg Higher Regional Court in case 3 W 48/19, where both courts found that Cosmofer was the only medicinal product on the market of IV iron products with an active substance containing dextran.[178] Further, the Judgment of the Hamburg Regional Court in case 416 HKO 156/20 found that describing Monofer as dextran-free *"…is not untrue as regards the composition of the medicinal product. As is undisputed between the parties, the preparation no longer contains any dextran in the chemical sense. Nor does the alleged classification of parenteral iron preparations into "dextran-containing", "dextran-based" and "dextran-free" render the statement untrue because the Applicant* [Vifor] *has not submitted any prima facie evidence for its allegation that this classification is scientifically relevant…"* (unofficial translation).[179]

(126) Although Vifor initially appealed this latter decision (case 3 U 4/21), it ultimately withdrew such appeal upon instructions by the Hamburg Higher Regional Court at the oral hearing, which made clear that even though dextran is the starting material of Monofer, that does not render the claim that Monofer is "dextran-free" misleading as

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complex" does not provide an appropriate basis to support Vifor's claim. As clearly set out in the Guidelines for ATC classification and Defined Daily Dose (DDD) assignment, *"*[t]*he main purpose of the ATC/DDD system is as a tool for presenting drug utilization statistics with the aim of improving drug use. This is the purpose for which the system was developed and it is with this purpose in mind that all decisions about ATC/DDD classification are made. Consequently, using the system for other purposes can be inappropriate.*" (*Guidelines for ATC classification and DDD assignment* (2023), pp.33-34).

177 Ruling of the Ethical Standards Board (Chamber I) in cases K11.006 and K11.008, p.17: *"Uit het enkele feit dat dextran-I als bouwsteen wordt gebruikt kan naar het oordeel van de Codemmissie niet worden afgeleid dat Monofer (ijzerisomaltoside 1000) een dextraan of een afgeleide van dextraan is. Dit onderdeel van de klacht is ongegrond."*

178 Order of the Regional Court of Hamburg in case 315 O 301/18, p.7-8 and Order of the Hamburg Higher Regional Court in case 3 W 48/19, p.2.

179 Judgment of the Regional Court Hamburg in case 416 HKO 156/20, p.5: *"Die angegriffene Werbung „Dextran-frei " mit der auflösenden Fußnote „ Fachinformationen MonoFer® Stand Februar 2020" ist nicht unwahr mit Blick auf die Zusammensetzung des Arznei mittels. Wie zwischen den Parteien unstreitig, ist in dem Präparat im chemischen Sinne kein Dextran mehr vorhanden. Auch ergibt sich die Unwahrheit nicht aus einer vermeintlichen Eintei lung der parenteralen Eisenpräparate in „Dextran-haltig", „Dextran-basiert" und „Dextran-frei", da die Antragstellerin die wissenschaftliche Relevanz dieser Einteilung angesichts der von der An tragsgegnerin vorgebrachten Studie AG 14 nicht glaubhaft gemacht hat."*

dextran is then hydrolysed and reduced in the production process. Accordingly, in the Court's view, Monofer does not contain dextran from a chemical perspective.[180]

(127) *Fourth*, the description of Monofer as dextran-free is consistent with the definition of dextran contained in the Compendium of Chemical Terminology (the "Gold Book") of the International Union of Pure and Applied Chemistry ("IUPAC"),[181] which characterises dextran as a branched molecule, a feature that is not present in the iron (III) isomaltoside compound: *"[b]ranched poly-α-d-glucosides of microbial origin having glycosidic bonds predominantly C-1 → C-6.*"[182]

(128) The fact that the carbohydrate component of iron (III) isomaltoside 1000 did not fit within the IUPAC definition of dextran – due to the absence of branched units and aldehyde groups – was one of the many reasons why PLOS ONE (a peer-reviewed, open-access, online science publication) refused to publish the Vifor-sponsored study by *Neiser et al*[183] in 2016.[184]

(129) *Fifth*, contemporaneous internal evidence shows that Vifor was fully aware that its description of Monofer as a dextran was failing to persuade national courts: *"…The times Vifor with stubbornness has claimed that IIM* [iron isomaltoside] *is a dextran, we have come to court, with disappointing results".*[185]

(130) Even the refined positioning of Monofer as dextran-derived was internally perceived as a *"stretch"*. It was more about creating the *"perception"* that this was the case: *"Dextran derived, or as we say in the Ehlken* [study] *'the dextran heritage of iron (III) isomaltoside 1000' is perhaps as far as you dare to stretch…A clear and unambiguous scientific support is not so easy to come up with, here it is often more about giving a "perception" that this is the case.*"[186]

(131) Indeed, Vifor was fully aware that the task of finding a good solid reference that Monofer is a dextran and/or dextran-derived/dextran-based was *"quite complicated.*"[187]

(132) Vifor also knew that it lacked an appropriate scientific basis to associate Monofer with *"dextran toxicity"* and/or suggest it may react with pre-existing anti-dextran antibodies: *"we had a* [teleconference]*... to discuss how to present ISM* [isomaltoside] *in the context of dextran and related HSRs. I think it was confirmed*

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180 [Information from Vifor's confidential summary notes of the oral hearing] (see [Information on Vifor's submissions to the Commission]).

181 The IUPAC is the world authority on chemical nomenclature, terminology (including the naming of new elements in the period table), standardized methods for measurement, atomic weights and many other critically-evaluated data.

182 Compendium of Chemical Terminology, 2nd ed. (the "Gold Book"), compiled by A. D. McNaught and A. Wilkinson. Blackwell Scientific Publications, Oxford (1997), online version (2019-) created by S. J. Chalk. ISBN 0-9678550-9-8, available at https://doi.org/10.1351/goldbook.

183 Neiser S, Koskenkorva TS, Schwarz K, Wilhelm M, Burckhardt S, *"Assessment of Dextran Antigenicity of Intravenous Iron Preparations with Enzyme-Linked Immunosorbent Assay (ELISA)"*, Int. J. Mol. Sci. (2016), 17(7), 1185.

184 [Information on Vifor's internal document]: *"Finally the authors distinguish between dextran based and non-dextran based iron complexes and they include iron dextran, ferumoxytol and iron isomaltoside 1000 in the dextran-based group. Yet based on the IUPAC definition of dextran, the carbohydrate component of isomaltoside has no signs of branched units and no aldehyde groups. and thus does not fit to the IUPAC definition of 'dextrane'* [sic]*."*

185 [Information on Vifor's internal document].

186 Ibid.

187 [Information on Vifor's internal document].

that there is NO evidence supporting the link between ISM [isomaltoside] *being dextran derivative and HSRs of pure dextran products.*"[188]

(133) In fact, both Vifor and the authors of the *in vitro* Vifor-sponsored studies accepted that these had significant limitations, in particular the lack of any clinical relevance[189] as the results could not be extrapolated to the clinical setting[190] and the fact that DIARs are only one of the possible mechanisms that may trigger a HSR, so that a broader set of assays are required.[191] They also recognised that *"*[t]*o date, no antibody-mediated DIARs have been reported for IIM* [iron isomaltoside]."[192]

(134) More importantly, the successive reviews of IV iron medicines by EMA have never been able to establish a difference in safety profiles between the available IV iron complexes. More specifically, when EMA reviewed the first of those *in vitro* studies sponsored by Vifor, amongst other criticism, its ultimate conclusion was that non-clinical data (such as *in vitro* testing) *"…cannot answer to mechanism of the hypersensitivity reactions; therefore the conclusions should mainly rely on the clinical evaluation for the safety issue.*"[193]

(135) German courts have also found that there is no legitimate basis to support the claim that Monofer has the potential to cross-react with antidextran antibodies and to potentially trigger DIARs. In particular, in case 416 HKO 156/20 the Hamburg Regional Court found that *"*[n]*or does the alleged classification of parenteral iron preparations into "dextran-containing", "dextran-based" and "dextran-free" render the statement* [that Monofer is dextran-free] *untrue because the Applicant* [Vifor] *has not submitted any prima facie evidence for its allegation that this classification is scientifically relevant…"* [unofficial translation].[194]

(136) As the Court explained, *"…the formal chemical composition is not of particular interest to doctors in their work. What is of paramount importance to doctors treating patients are the possible side effects of a medication. In this respect, however, the Applicant* [Vifor] *has not submitted any prima facie evidence for this allegation that Monofer® has a comparable side effect profile to a preparation containing dextran. The studies cited in this regard…are not sufficient"* [unofficial translation].[195]

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188 [Information on Vifor's internal document].

189 [Information on Vifor's internal document].

190 See, for instance, Burckhardt S, *"Reply to Comment on Neiser et al. Assessment of Dextran Antigenicity of Intravenous Iron Preparations with Enzyme-Linked Immunosorbent Assay (ELISA)",* Int. J. Mol. Sci. 2017, 18, 122, p.1.

191 Neiser S, Koskenkorva T, Schwarz K, Wilhelm M and Burckhardt S, *"Assessment of Dextran antigenicity of intravenous iron preparations with enzyme-linked immunosorbent assay (ELISA)"*, Int. J. Mol. Sci. 2016, 17, 1185, p.7.

192 Ibid.

193 Assessment report for iron containing (IV) medicinal products, 13 September 2013, p.6.

194 Judgment of the Hamburg Regional Court in case 416 HKO 156/20, p.5: *"Auch ergibt sich die Unwahrheit nicht aus einer vermeintlichen Eintei lung der parenteralen Eisenpräparate in „Dextran-haltig", „Dextran-basiert" und „Dextran-frei", da die Antragstellerin die wissenschaftliche Relevanz dieser Einteilung angesichts der von der An tragsgegnerin vorgebrachten Studie AG 14 nicht glaubhaft gemacht hat."*

195 Ibid., pp. 6-7: *"…da die formale chemische Zusammensetzung für den Arzt in seiner Tätigkeit nicht von sonderlichem Interesse sei. Von höchster Bedeutung für die Ärzte sind bei ihrer Behandlung vielmehr die möglichen Neben wirkungen eines Medikaments. Diesbezüglich hat die Antragstellerin jedoch nicht glaubhaft gemacht, dass MonoFer® ein vergleichbares Nebenwirkungsprofil wie ein Dextran-haltiges Präpa rat hat. Die hierzu angeführten Studien (ASt. 8, 15) sind hierzu nicht hinreichend."*

(137) Although Vifor initially appealed this latter decision (case 3 U 4/21), it ultimately withdrew such appeal upon instructions by the Hamburg Higher Regional Court at the oral hearing. In addition to the reasoning set out in paragraph (126) above, the Court found that Vifor had not sufficiently shown that Monofer has the potential to cross-react with antidextran antibodies and to potentially trigger dextran induced anaphylactic reactions, as the *in vitro* studies cited in this regard only produced *"hypothesis"* and *"theories*."[196]

(138) For all the reasons set out above, in the Preliminary Assessment the Commission reached the preliminary conclusion that the First Message is based on inaccurate and/or incomplete information.

5.3.3.1.3. Vifor's First Message was capable of confusing HCPs

(139) Because of its inaccuracy and/or the incomplete manner in which it was presented, Vifor's First Message was also capable of confusing HCPs.

(140) In particular, Vifor's inaccurate and/or incomplete messages regarding Monofer's chemical composition were capable of confusing HCPs and other relevant addressees by suggesting that chemically speaking, Monofer was a dextran or derived from dextran, relying on the fact that this compound carries the historic negative safety connotations of HMW IV iron dextrans. This ability to confuse the relevant addressees was compounded by the fact that any possible association with dextran, even if demonstrated, has not been appropriately shown to be clinically relevant, which Vifor omitted and ignored in its communications.

(141) Similarly, Vifor's inaccurate and/or incomplete messages regarding Monofer's unproven and uncertain risk of reacting with anti-dextran antibodies and triggering DIARs were capable of confusing HCPs, by associating Monofer with *"dextran toxicity"* and all the related historic safety concerns, without a legitimate clinical and scientific basis.

5.3.3.1.4. Vifor's First Message was capable of discrediting Monofer

(142) By disseminating messages that may have been objectively misleading about essential characteristics of its competitor's product, Vifor was not striving to raise awareness of therapeutic and clinical characteristics of its own product.

(143) HCPs are very sensitive to any information that points to health risks for a given medicine, especially when such evidence about health risks is provided by the long established (and trusted) incumbent in the market. The capability to discredit Monofer is particularly acute in this case given the serious safety concerns historically linked with IV iron dextrans, which were associated with an unacceptably high rate of serious adverse events, most notably anaphylactic shocks. This is well known by HCPs who were traditionally taught that IV iron is dangerous[197] and for whom *"…the dextran topic and related debate is of major interest and value to HCPs aware of the limitations of earlier dextran-based IV irons*."[198]

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196 [Information from Vifor's confidential summary notes of the oral hearing before the Hamburg Higher Regional Court] ([Information on Vifor's submissions to the Commission]).

197 Michael Auerbach and Iain C. Macdougall, *"Safety of intravenous iron formulations: facts and folklore"*, Blood Transfus. 2014 Jul; 12(3): 296–300.

198 [Information on Vifor's submissions to the Commission].

(144) Therefore, by merely (in Vifor's own words) *"planting the seed of doubt"*[199] about Monofer's safety, Vifor's dextran-related messages were capable of discrediting Monofer in the eyes of HCPs and capable of misleading them and influence their prescription practice. Although not necessary for the finding of an abuse, in this case the evidence shows that Vifor was actually pursuing commercial objectives by instilling doubts concerning the safety of Monofer.

5.3.3.1.5. Preliminary conclusion on the misleading nature of Vifor's First Message

(145) In view of the above, in the Preliminary Assessment the Commission reached the preliminary conclusion that Vifor's messaging describing Monofer as a "*dextran*" or as a "*dextran-derived*"/"*dextran-based*" compound, and associating it with *"dextran toxicity"* by implying it could trigger DIARs, may have been objectively misleading and not reflective of competition on the merits.

(146) In particular, these messages were based on inaccurate and/or incomplete information not supported by appropriate scientific evidence, which was presented in a manner that was capable of confusing HCPs, instilling doubts in their minds as to Monofer's safety.

(147) In addition, these messages were capable of creating a negative perception of Monofer's safety and, as such, of discrediting it in the eyes of HCPs.

5.3.3.2. "***Second Message***": Monofer has more frequent HSRs compared to Ferinject

(148) In addition and in parallel to the dextran message, Vifor also disseminated messages suggesting that Monofer was more dangerous for patients than Ferinject because of an alleged increased risk of HSRs with Monofer, irrespective of whether or not these HSRs were linked to dextran.

(149) As explained in Section 5.1.2.2.1.1 above, HSR is a medical term referring to the overreaction of the immune system to an antigen/allergen. It encompasses mild, moderate and severe reactions, including anaphylactic/anaphylactoid reactions, which are amongst the more serious HSRs.

(150) In the Preliminary Assessment and as set out below, the Commission reached the preliminary view that the Second Message is based on inaccurate and/or incomplete information. Vifor's claim that Monofer is associated with a higher risk of HSRs than Ferinject is not reflective of the key findings and conclusions by relevant healthcare authorities (in particular EMA), ultimately set out in Ferinject's and Monofer's respective SmPCs. Vifor did not rely on sufficiently robust scientific evidence apt to substantiate its claim. Instead, Vifor relied on a biased selection of studies and national reports that are inapt to support it – due to a number of limitations preventing any sound comparative analysis between the safety profiles of Ferinject and Monofer (which Vifor was fully aware of) – and not representative of all the scientific evidence available at the time.

5.3.3.2.1. Examples of the Second Message and its dissemination

(151) In order to *"*[r]*e-define* [Vifor's] *corporate response to Pharmacosmos,"* it developed a "*HSR Strategy Project,"* whose objective was to *"*[d]*efine and roll out competitive*

[199] [Information on Vifor's internal document]: *"Project Description: Support ILC board to decide Corporate positioning against Pharmacosmos and Monofer […] Key outcome: Corporate messaging to win and pre-empt Monofer […] Call attention to the safety profiles in order to create an unmet need. Connect preparation of Ferinject® to superior safety and support with safety data […] Plant the seed of doubt / There is an opportunity to raise a red flag relating to safety by comparing the 2 profiles."*

messaging" targeting *"Authority bodies, HCPs, Hospital Pharmacists and internal company."*[200] Vifor wanted to *"*[p]*lant the seed of doubt"* because *"*[t]*here is an opportunity to raise a red flag relating to safety by comparing the 2 profiles."*[201] Vifor saw Ferinject's alleged *"safety benefit"* as a *"key differentiator"* and recommended internally to *"*[p]*ro-actively include HSR in communication in a smart way."*[202]

(152) As part of this strategy, Vifor disseminated information based in particular on four studies (including two studies sponsored and funded by Vifor)[203] to support its claim that Monofer was associated with a higher risk of HSRs. For instance, Vifor prepared internal materials stating that *"a recent study* [Mulder MB et al (2019)] *showed hypersensitivity reactions occurred 4x more frequently with Monofer than Ferinject"* and that *"*[s]*evere hypersensitivity reactions were reported ~10x more frequently with Monofer vs Ferinject."*[204]

(153) Vifor also prepared Objection Handlers that were used externally with HCPs and pharmacists in a number of Member states, in which Vifor stated that *"*[s]*tudies have demonstrated hypersensitivity reactions occurred significantly more frequently with IIM* [Iron Isomaltoside] *than Ferinject"*, *"Ferinject demonstrated an approximately 75% lower risk of hypersensitivity than IIM*, *"Hypersensitivity reactions were less severe with Ferinject than IIM"* and that *"*[o]*ver 7 years, the rate of severe hypersensitivity reactions have been between 3-18 times greater with IIM vs Ferinject.*"[205] Similar messages were included in educational slide decks on objection handling shared internally and also externally at least in Austria and the Netherlands.[206]

(154) To further substantiate Monofer's alleged increased risk of HSRs when compared to Ferinject, Vifor disseminated information based on two national reports/health warnings regarding adverse drug reactions with Monofer: (i) the report by the Dutch Pharmacovigilance Centre (the "Lareb report") which found that there *"were 23 reports of HSRs with Monofer between 2012 and 2015, 5 with Diafer in 2015, and 7 with Ferinject between 2011 and 2013"*;[207] and (ii) the health warning issued by the Spanish Agency of Medicines and Medical Devices (the "AEMPS health warning") which found that *"*[u]*ntil 5 July 2017, 108 reported cases of severe anaphylaxis were identified in*

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200 [Information on Vifor's internal document].

201 Ibid, [Information on Vifor's internal document].

202 Ibid, [Information on Vifor's internal document].

203 Vifor relied in particular on four studies, namely (i) Bager *et al*, "*Drug-specific hypophosphatemia and hypersensitivity reactions following different intravenous iron infusions*", Br J Clin Pharmacol (2017); (ii) Mulder *et al*, "*Comparison of hypersensitivity reactions of intravenous iron: iron isomaltoside-1000 (Monofer®) versus ferric carboxy-maltose (Ferinject®). A single center, cohort study*", Br J Clin Pharmacol (2019); (iii) Ehlken *et al*, "*Evaluation of the Reported Rates of Severe Hypersensitivity Reactions Associated with Ferric Carboxymaltose and Iron (III) Isomaltoside 1000 in Europe Based on Data from EudraVigilance and VigiBase™ between 2014 and 2017*, Drug Safety (2019); and (iv) Nathell *et al*, "*Reported Severe Hypersensitivity Reactions after Intravenous Iron Administration in the European Economic Area (EEA) Before and After Implementation of Risk Minimization Measures*", Drug Safety (2020). The Ehlken (2019) study and the Nathell study (2020) were both sponsored and funded by Vifor.

204 [Information on Vifor's internal document].

205 See for instance [Information on Vifor's internal document]. Vifor recognised [Information on Vifor's submissions to the Commission] that this Objection Handler was used externally at least in Austria, Germany and Sweden with HCPs/pharmacists.

206 See for instance [Information on Vifor's internal document]. Vifor informed the Commission, [Information on Vifor's submissions to the Commission], that this document was used externally at least in Austria and the Netherlands with HCPs/pharmacists.

207 [Information on Vifor's internal document].

association with i.v. irons. Forty-four were related to iron isomaltoside, and the report stated that this was a higher rate than for other i.v. iron preparations."[208]

(155) In addition, Vifor also disseminated information based on a 2013 report published by the Swiss Agency for Therapeutic Products (the "Swissmedic report") in documents comparing Ferinject with Monofer, even though this report had nothing to do with Monofer but concerned instead the number of HSRs in Switzerland following the administration of another IV iron drug manufactured by a different pharmaceutical company: i.e. Rienso (Ferumoxytol), which has since been discontinued in Europe.[209]

(156) The Lareb report, the AEMPS health warning and the Swissmedic report were referenced in various Objection Handlers that were shared internally as well as externally with HCPs in a number of Member States.[210]

5.3.3.2.2. Preliminary Assessment of the inaccurate and/or incomplete nature of the Second Message

(157) For the reasons set out below, in its Preliminary Assessment, the Commission reached the preliminary view that the Second Message is based on inaccurate and/or incomplete information.

(158) *First*, there is no basis to differentiate Ferinject and Monofer's HSR profile based on the information contained in the respective SmPCs. Both drugs have been approved by health authorities as safe to use for the treatment of ID and IDA[211] and the respective SmPCs (which have also been approved by health authorities and are part of the respective official marketing authorisation) include the same special warnings and precautions for use relating to HSRs.[212]

(159) Those special warnings and precautions for use have been fully aligned since early 2014. Prior to that, they were not exactly the same but there was no suggestion of any meaningful distinction in terms of special warnings and precautions between the two drugs with regard to HSRs.

(160) They were also aligned with regard to the frequency of HSRs, with hypersensitivity in general classified as uncommon (≥1/1,000 to <1/100) and specifically anaphylactoid and anaphylactic reactions classified as rare events ((≥1/10,000 to <1/1,000).[213] Such frequency classifications have been entirely consistent between both SmPCs since 2018. Prior to that there were only some non-significant variations.

(161) Therefore, the information contained in Monofer's and Ferinject's SmPCs demonstrates that relevant healthcare authorities considered that there was no

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208 Ibid.

209 Ibid, [Information on Vifor's internal document].

210 See, for instance, [Information on Vifor's internal documents]. Vifor informed the Commission, in response to the Commission's Article 18(3) decision of 22 November 2022, that all these materials were used externally with HCPs/pharmacists.

211 Both Monofer and Ferinject are marketed on the basis of marketing authorisations confirming their quality, safety and efficacy (as required by Directive 2001/83/EC and Regulation (EC) No 726/2004). Further, even if Vifor's messages would not have not concerned a listed indication but an off-label use of Monofer, its messages would have been equally misleading. Indeed, in light of the *Hoffmann-La Roche* judgment, disparagement aimed at off-label uses of a medicine can be anticompetitive. Accordingly, this is all the more the case for indications that form part of the marketing authorisation of a medicine.

212 See section 4.4 of the respective SmPCs.

213 See section 4.8 of the respective SmPCs.

appropriate basis to distinguish the two products with regard to the risk and frequency of HSRs.

(162) That was also the view reached in the context of two ongoing cases in the UK, where the Prescription Medicines Code of Practice Authority ("PMCPA") was required to assess messages by Vifor regarding the risks and frequency of HSRs with Monofer which were very similar, if not exactly identical, to the ones illustrated in the previous section in a non-exhaustive way.[214]

(163) As evidenced by internal documents, Vifor was fully aware of the above (e.g. *"*[b]ut *now looking at the actual tables in the respective SmPCs, of course we cannot use this, since the products have the same frequency* [of HSRs]")[215] but, nevertheless, ignored it when communicating to HCPs that Monofer had a poorer HSR profile than Ferinject.

(164) *Second*, Vifor's messages alleging that Monofer was associated with an increased risks of HSRs compared to Ferinject[216] also failed to reflect - let alone to be reconciled with - the conclusions reached by EMA in a number of successive post-marketing authorisation reviews of the safety of IV iron products.

(165) Indeed, IV iron medicines available in European markets have been subject to a number of post-marketing authorisation reviews in which the EMA has analysed and compared their respective safety risks. In all these reviews, the EMA has never been able to establish, based on the available data, a difference in the safety profiles of the examined IV iron medicines, including those of Monofer and Ferinject.

(166) The first of such reviews was triggered by a referral under Article 31 of Directive 2001/83/EC from the French National Agency for the Safety of Medicine and Health Products ("ANSM"), following a national review in 2010. Such review concluded that *"…differentiation between these iron complexes in terms of hypersensitivity reactions could not be identified"*[217] but recommended additional measures such as a post-authorisation safety study ("PASS") to further evaluate the safety concerns stemming from the HSRs produced by the use of IV irons, as well as other periodic monitoring measures.[218]

(167) The final report of this PASS was issued in 2020, following a number of annual interim reviews. It found that conclusions cannot be drawn, based on the available data and due to methodological limitations, as to the existence of differences between the different IV iron medicines in terms of HSRs.[219] Subsequent to this report, the PRAC explicitly confirmed in 2021 that "[t]*he obligation to perform the PASS is considered fulfilled… routine pharmacovigilance is appropriate to monitor the risk of hypersensitivity and closely monitored in future* [Periodic Safety Update Reports]."[220]

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214 See PMCPA's interim case report in case AUTH/3199/5/19, pp. 23-24. See also PMCPA's interim case report in case AUTH/3224/7/19, p. 32. The reason why these reports are still interim is not because of pending appeals but because the PMCPA's Panel reported Vifor to the Appeal Board, who ordered multiple audits of Vifor's procedures which are still ongoing.

215 [Information on Vifor's internal document].

216 Such as the comparative messages exemplified in paragraphs (152) and (153) above.

217 Assessment report for: Iron containing intravenous (IV) medicinal products, EMA, p. 26.

218 Assessment report for: Iron containing intravenous (IV) medicinal products, EMA, pp. 26-28.

219 See *Intravenous Iron Post-authorisation Safety Study (PASS): Evaluation of the Risk of Severe Hypersensitivity Reactions* (EUPAS20720), 20 November 2020, p.38.

220 Minutes of PRAC meeting on 30 Aug - 02 Sep 2021, p.50.

(168) This means that, since 2011 and up until today, the EMA has conducted numerous safety monitoring procedures, which included comprehensive reviews of all available data (including the studies and national reports relied upon by Vifor) and comparisons of all available IV iron products in Europe. The EMA Referral Procedure which presents the highest authoritative evidence available on hypersensitivity risk of IV irons, confirmed that Monofer cannot be claimed to have a higher risk of HSRs compared to Ferinject, and this has also never been established in any of the subsequent monitoring procedures. Accordingly, EMA took no action to update the information on the risk and frequency of HSRs included in Ferinject's and Monofer's respective SmPCs.

(169) *Third*, Vifor disseminated information based on a selection of studies and national reports which were inapt to support Vifor's claims.

(170) Indeed, to provide support for the Second Message, Vifor relied in particular on the four studies and on the three national reports mentioned in the previous section, which are all based on spontaneous reporting of HSRs by HCPs and/or marketing authorisation holders. However, unlike head-to-head randomised controlled trials, which are specifically designed to compare two medicines, the spontaneous reporting of adverse events such as HSRs (also called 'real-world evidence'), is subject to a number of biases and as such is unreliable to estimate precise frequencies of adverse events and to compare safety profiles of different drugs.

(171) Whilst real-world evidence may have some value in generating potential pharmacovigilance safety signals that require further investigation, its substantial limitations, for example for comparing with other medicines, are a well-known fact that has been expressly acknowledged by EMA on several occasions, including in the context of its post-marketing authorisation review of the safety of IV iron products. For instance, in 2013, EMA "*pointed out limitations of comparative analyses based on spontaneous reporting rates alone*", stressing that "*spontaneous reporting rates cannot be used to compare the benefit risk of products*"[221] (unlike clinical data derived from head-to-head randomised controlled trials). It is also expressly acknowledged in some of the above-mentioned studies and reports. For example, the *Ehlken* study reads: "*reporting of AEs [adverse events] does not necessarily reflect the occurrence of events in clinical practice, and therefore the presented results do not allow a conclusion to be drawn about the absolute and relative risk for severe HSRs associated with ferric carboxymaltose and iron (III) isomaltoside 1000. Although AE reporting can be used to estimate the relative rates of events with*

221 This is because "*the data has not been presented in a similar way for the different products and the exposure data are based on estimations. Further, there are differences in the time for which different products have been on the market and it can be expected that reporting rates are higher for a new product compared to those which have been marketed for a longer time. Differences in geographical distributions of the consumption of the products may also add uncertainty to the reporting rates as it can be expected that routines for spontaneous adverse events reporting may vary in different countries. Thus, given the low total number of life-threatening and fatal events it is noted that the estimated rates are quite sensitive to even slight levels of under-reporting and differences in methodology for calculating these rates could also have an impact*" (EMA's *Assessment report for: Iron containing intravenous (IV) medicinal products,* 13 September 2013, pp.18-19, emphasis added). See also the statement made by EMA's Head of Pharmacovigilance and Epidemiology in 2018 that "*to conclude that one product is safer than the other, based on numbers of spontaneous suspected adverse reaction reports alone, without consideration of all other relevant data, including clinical trials and epidemiological studies, is in our view ostensibly simplistic, invalid and misleading*" (EMA Rapid response to BMJ. Re: Pandemrix vaccine: why was the public not told of early warning signs? (EMA/659264/2018), emphasis added)

individual products, head-to-head data remain the gold standard because they capture exposure and outcome in a standardized manner and circumvent effects of differential prescribing and reporting. […]".[222]

(172) Despite the foregoing, Vifor relied on the above-mentioned studies and reports to convey the message that Monofer was associated with a higher risk of HSRs than Ferinject, omitting to mention that such real-world evidence is inapt to support any comparative analysis between Ferinject's and Monofer's safety (which Vifor was fully aware of).[223]

(173) It should also be noted that EMA reviewed the above studies and reports as part of its numerous post-marketing authorisation reviews of IV iron medicines and, based on the available data, it has never been able to establish differences in the safety profile of the different IV iron medicines, including in relation to risk of HSRs. Consequently, EMA considered that those studies and report did not warrant an update of the HSR information included in Ferinject's and Monofer's SmPCs. The only report that has not been assessed by EMA is the Swissmedic report, as this falls outside EMA's jurisdiction. This report is nevertheless irrelevant as it concerned HSRs of another IV iron medicine - Rienso (Ferumoxytol) - in Switzerland. It thus had nothing to do with the safety of Monofer. Yet, despite its irrelevance, Vifor used it on several occasions as part of communications aimed at comparing the safety profile of Monofer and Ferinject.

(174) In addition, the selection of studies and reports relied upon by Vifor is biased as there are various other studies and relevant findings at national level by health bodies and other organisations on the safety of IV iron products pointing to a different conclusion:

(a) Vifor omitted the existence of numerous other studies finding that the risk of HSRs with Monofer was lower or at very least comparable to Ferinject.[224]

(b) Vifor also omitted in its HSR messages other relevant findings at national level suggesting a similar safety and efficacy profile between Ferinject and Monofer, such as those issued by the Danish Council for the use of Expensive Medicines ("RADS")[225] and the French *Haute Autorité the Santé*,[226] as well as the "Wise List"[227] from the Stockholm County Medicines (Formulary) Committee.[228]

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222 Ehlken *et al*, *Evaluation of the Reported Rates of Severe Hypersensitivity Reactions Associated with Ferric Carboxymaltose and Iron (III) Isomaltoside 1000 in Europe Based on Data from EudraVigilance and VigiBase™ between 2014 and 2017*, Drug Safety (2019).

223 See e.g. [Information on Vifor's internal document]: "*Vifor concurs with* [the] *position* [of EMA regarding the limitation of spontaneous reporting]" ([Information on Vifor's internal document]).

224 See, for instance, Kalra P and Bhandari S, *Safety of intravenous iron use in chronic kidney disease*, Curr Opin Nephrol Hypertens (2016), 25(6), pp. 529-535; Pollock RF and Biggar P, *Indirect methods of comparison of the safety of ferric derisomaltose, iron sucrose and ferric carboxymaltose in the treatment of iron deficiency anemia. Expert Review of Hematology* (2020), Vol. 13, No. 2, pp. 187-195; Achebe M and DeLoughery TG, *Clinical data for intravenous iron - debunking the hype around hypersensitivity, Transfusion* (2020), Volume 60, Issue 6, pp. 1154-1159; Blumenstein I, Shanbhag S, Langguth P, Kalra PA, Zoller H, Lim W, *Newer formulations of intravenous iron: a review of their chemistry and key safety aspects - hypersensitivity, hypophosphatemia, and cardiovascular safety*, Expert Opinion on Drug Safety (2021), Vol. 20, No. 7, pp. 757-769; and Kennedy NA, Achebe MM, Biggar P, Pöhlmann J, Pollock RF, *A systematic literature review and meta-analysis of the incidence of serious or severe hypersensitivity reactions after administration of ferric derisomaltose or ferric carboxymaltose*, International Journal of Clinical Pharmacy (2023), 45(3), pp. 604-612.

225 In 2018 RADS found that *"[a]ll preparations seem equal in terms of side effects and for all the preparations apply that there is a risk of developing anaphylaxis and an observation period of 30*

(175) The Commission acknowledges that these other studies and positions at national level also contain their own limitations. But they show that the relevant evidential and scientific basis is much wider and mixed than the biased selection presented by Vifor to HCPs and, when considered in its totality by the expert health authority (i.e. EMA), it has never been possible to establish differences in the safety profile of the available IV iron medicines based on the available data, contrary to Vifor's claims.

(176) *Fourth and finally*, the internal contemporaneous evidence shows that Vifor was aware it had no appropriate basis to claim that Ferinject had a superior safety profile compared to Monofer: *"But now looking at the actual tables in the respective SmPCs, of course we cannot use this, since the products have the same frequency* [HSRs]. *Which brings us back to the fact that there are no solid data to show that Ferinject has a better safety profile than Monofer. I don't know how many times over the years we have tried to come up with such arguments, but never been really successful*."[229]

(177) Vifor itself recognised that *"[t]he relative safety of FERINJECT vs Monofer has not been definitively established*"[230] and that, at least in 2018, it did not consider it had the data compared to other IV iron therapies to claim a superior benefit risk profile: *"I don't think we can ever claim to have a superior benefit risk profile. different maybe, superior…."*; *"Just be aware that there was talk of adding 'superior' wording for which we have no data compared to other iv iron therapies. Just in case it comes up again. Medical feels we do not have the data at this time to support such statement.*"[231]

(178) In fact, Vifor internally recognised that […].[232]

(179) For the reasons set out in this section, in the Preliminary Assessment the Commission reached the preliminary view that Vifor's message suggesting that Monofer has higher risks of HSRs compared with Ferinject is based on inaccurate and/or incomplete information as it is contrary to the regulatory findings as reflected in the SmPCs of both Monofer and Ferinject and in the outcome of the several post-marketing authorisation reviews by the EMA on the safety of the different IV iron medicines.

(180) To support its claim, Vifor relied on a biased selection of scientific studies and national reports purportedly showing Monofer as less safe than Ferinject, but which

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minutes after the administration of all preparations is recommended…" and that *"there is no indication of significant differences in side effects and risks between the accessible iron preparations, so the drugs are at par"* (Pharmacosmos' complaint, paragraphs 41 and 180).

226 In December 2016, the French Haute Autorité de Santé issued a summary of the Transparency Committee Opinion in relation to Monover (Monofer's brand in France), in which it explicitly stated that *"[t]he safety profile of MONOVER seems to be similar to that of other iron sucrose-based proprietary medicinal products, with a risk of severe hypersensitivity reactions common to all injectable irons"* (Haute Autorité de Santé, Brief Summary of the Transparency Committee Opinion, 2016, p. 2).

227 The Wise List contains drugs that are recommended for treatment of common diseases in primary care, specialised outpatient care and tertiary care. The recommendations are based on scientific evidence of efficacy and safety, pharmaceutical effectiveness, cost-effectiveness and environmental aspects.

228 In 2018, the "Wise List" stated that *"[t]he price of Ferinject is considerably higher than that of Venofer and pharmacy selling price is approximately 20 percent higher compared to Monofer that is equal in effect, safety and indication. Monofer can be given in higher dose than Ferinject in one visit which may lead to fewer hospital visits when treating iron deficiency. Since the risk of hypersensitivity reactions increases with the number of administrations, fewer administrations provide an advantage"* (Pharmacosmos' complaint, paragraphs 42 and 183).

229 [Information on Vifor's internal document].

230 [Information on Vifor's internal documents].

231 [Information on Vifor's internal document].

232 [Information on Vifor's internal document]. See also [Information on Vifor's internal document].

were not reflective of the regulatory position and were inapt to allow any comparative conclusions between the two medicines with regard to the risk of HSRs, due to their selective nature and significant limitations.

5.3.3.2.3. Vifor's Second Message was capable of confusing HCPs

(181) Because of its inaccuracy and/or the incomplete manner in which it was presented, Vifor's Second Message was also capable of confusing HCPs.

(182) In particular, Vifor's inaccurate and/or incomplete messages were capable of confusing HCPs by suggesting that Monofer is associated with a higher risks of triggering HSRs compared to Ferinject, both in terms of frequency and seriousness, which has never been established and does not reflect the regulatory position. This ability to confuse HCPs in relation to a key factor such as safety was compounded by the following facts. First, Vifor used this message in combination and/or in addition to the other message associating Monofer with "dextran toxicity", implicitly or explicitly associating such misleading feature with a higher risk of HSRs, be it dextran-induced or otherwise. Second, Vifor disseminated information based on a biased selection of scientific studies purportedly showing Monofer as less safe than Ferinject without drawing HCPs' attention to their significant limitations and relevant findings by EMA - it should have been, and actually was, aware that these studies were methodologically inapt to draw any comparative conclusions.

5.3.3.2.4. Vifor's Second Message was capable of discrediting Monofer

(183) By disseminating messages that may have been objectively misleading about essential characteristics of its competitor's product, Vifor was not striving to raise awareness of therapeutic and clinical characteristics of its own product.

(184) HCPs are very sensitive to any information that points to health risks for a given medicine, especially when such evidence about health risks is provided by the long established (and trusted) incumbent in the market. The capability to discredit Monofer by suggesting, without adequate substantiation, an increased risk of HSRs is particularly strong in circumstances where HCPs have an acute sensitivity to safety issues due to the historic experience with early IV iron products, which were associated with an unacceptably high rate of serious adverse events, most notably anaphylactic shocks.[233]

(185) Therefore, by striving to create a *"big emotional impact on prescribers"*[234] concerning HSRs and potentially leading HCPs into developing a negative perception of Monofer (i.e. that its safety, a key feature for the successful therapeutic and commercial uptake of a drug, was inferior), Vifor's messages suggesting an increased risk of HSRs with Monofer (without an adequate substantiation) were capable of discrediting the main competing product in the eyes of HCPs and capable of misleading them and influencing their prescription practice. Although not necessary for the finding of an abuse, in this case the evidence shows that Vifor was actually pursuing commercial objectives by instilling doubts concerning the safety of Monofer.

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233 Michael Auerbach and Iain C. Macdougall, *Safety of intravenous iron formulations: facts and folklore*, Blood Transfus. 2014 Jul; 12(3): 296–300.

234 [Information on Vifor's internal document].

5.3.3.2.5. Preliminary conclusion on the misleading nature of Vifor's Second Message

(186) In view of the above, in the Preliminary Assessment the Commission reached the preliminary conclusion that Vifor's messaging suggesting higher risks of HSRs with Monofer compared to Ferinject may have been objectively misleading and not reflective of competition on the merits.

(187) In particular, these messages were based on inaccurate and/or incomplete information not supported by appropriate scientific evidence, which was presented in a manner that was capable of confusing HCPs, instilling doubt in their minds as to Monofer's safety.

(188) As a result, these messages were capable of creating a negative perception of Monofer's safety and, as such, of discrediting it in the eyes of HCPs.

5.3.3.3. Capability to produce exclusionary effects

(189) In the Preliminary Assessment, the Commission reached the preliminary view that Vifor's communication campaign was capable of influencing the demand and uptake for Monofer and, therefore, of foreclosing Ferinject's closest competitor on the IV iron market and only rival on the high-dose IV iron market. This preliminary finding was based on the following considerations: (i) the addressees of Vifor's communication campaign (i.e. HCPs) are key drivers of the demand for high-dose IV iron (Section 5.3.3.3.1); (ii) the First and Second Messages questioning Monofer's safety were capable of weighing heavily on the latter's decisions (Section 5.3.3.3.2); (iii) Vifor's privileged market position, in particular its established and trusted relationships with HCPs, as well as its unrivalled direct local presence across the EEA, ensured the successful dissemination of the misleading messages (Section 5.3.3.3.3); and (iv) the dissemination of the misleading messages to the HCPs was extensive and systematic (Section 5.3.3.3.4).

5.3.3.3.1. Vifor's communication campaign targeted key drivers of the high-dose IV iron demand

(190) Vifor's objective was to hinder competition from Monofer by methodically targeting multiple categories of HCPs who are the main drivers of the demand for high-dose IV iron. Vifor was striving to influence (i) their prescribing practices by discouraging the use of Monofer; (ii) the procurement of high-dose IV iron to avoid notably the implementation of measures favouring price competition between Ferinject and Monofer; and (iii) the dispensing practices of pharmacists who had, in some instances, the ability to substitute Ferinject with Monofer (and *vice-versa*).

(191) **Prescription of high-dose IV iron**: The uptake of prescription medicines, like Monofer, depends largely on the prescribing practices of HCPs. Vifor's campaign sought to influence individual prescribers of high-dose IV iron on a sufficiently large scale to steer the overall demand away from Monofer through a broad HCP coverage. Vifor's efforts were not limited to doctors prescribing high-dose IV iron, but also included other HCPs involved in the administration of high-dose IV iron, such as nurses and midwives.[235] While doctors take the final decision as to which IV iron product to prescribe, nurses, as well as midwives in the context of pregnancies and childbirth, are the ones administering the treatment and/or reporting HSRs to the

[235] [Information on Vifor's submissions to the Commission].

doctors, which may give them a certain degree of influence on doctors and, thus, the ability to steer the choice of treatment.[236]

(192) **Procurement of high-dose IV iron**: In addition to prescribing HCPs, Vifor targeted HCPs involved in the procurement process of high-dose IV iron products, such as hospital pharmacists, as well as representatives of tender authorities, and other procurement bodies, who are also key drivers of the demand as they decide on mechanisms capable of introducing price competition (e.g. by organising tenders where Ferinject and Monofer compete with each other in a single lot). By targeting those HCPs, Vifor's goal was to prevent decisions/measures that would lead to direct price competition within high-dose IV iron and, thus, imperil Ferinject's market position. The above is well documented in Vifor's internal documents.[237]

(193) **Dispensing of high-dose IV iron**: Pharmacists may also play a role in determining which product is ultimately dispensed to the patient. This was notably the case in Germany where the relevant authorities promoted substitution between Monofer and Ferinject from 2016 to 2020.[238] Accordingly, German pharmacists could in certain cases decide to dispense Monofer instead of Ferinject (or *vice versa*). From this perspective, in Germany in 2016-2020, pharmacists were, after doctors, the last resort in terms of HCPs that could directly influence actual substitution of medicines.

5.3.3.3.2. The First and Second Messages were capable of influencing demand by HCPs

(194) By disseminating messages that may have been objectively misleading about the safety of the only high-dose alternative to Ferinject, Vifor's communication campaign was capable of weighing heavily on the HCPs' decisions. This is because doctors are primarily guided by therapeutic considerations[239] and generally tend to be conservative (or "inert") about switching to a medicine in the absence of a pressing medical need.[240] The above is particularly relevant in IV iron where the safety concerns historically associated to the use of this class of medicines have heightened the caution that normally characterises doctors' attitudes towards new products (see Section 5.2.2.3.3). For similar reasons, HCPs involved in the procurement of high-dose IV iron may refrain from implementing mechanisms capable of introducing price competition between Ferinject and another medicine surrounded by safety controversies.

(195) In addition, HCPs, such as doctors and pharmacists, are unlikely to have the time or the capacity to undertake a detailed scientific assessment of the information disseminated by a disparaging undertaking. When presented with misleading scientific information coming from an established and well-reputed player, most HCPs will, in practice, not be able or willing to question, complement or correct such information, especially if there are diverging conclusions from clinical studies, and will tend to adopt the approach surrounded by least controversy.[241]

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236 E.g., [Information on Vifor's internal documents].

237 E.g., [Information on Vifor's internal documents].

238 E.g., [Information on Vifor's internal documents].

239 Case C-179/16, *Hoffmann-La Roche,* para. 65.

240 Cases T-321/05, *AstraZeneca,* para.105 and C-457/10 P*, AstraZeneca*, para. 50.

241 Accordingly, Art. 92(2) of Directive 2001/83/EC requires that all the information transmitted as part of the promotion of a medicine "*shall be accurate, up-to-date, verifiable and sufficiently complete to enable the recipient to form his or her own opinion of the therapeutic value of the medicinal product concerned*."

5.3.3.3.3. Vifor enjoyed a special position in its communication with HCPs

(196) As shown in Section 5.2.2, Vifor appears to have been dominating the supply of (high-dose) IV iron for more than a decade thanks to the success of Venofer and Ferinject.[242] According to its own internal documents, [Information on Vifor's own internal assessment of its market position][243] and [Information on Vifor's own internal assessment of its market position].[244] In addition, Ferinject being Vifor's flagship product in the Relevant Period, the company invested heavily in its marketing and distribution in Europe.[245] As a result, Vifor has established and trusted relationships with HCPs, as well as an unrivalled direct local presence across the EEA. This privileged market position enabled Vifor to strengthen the impact of its misleading Dextran and HSR messages on HCPs and to ensure an extensive coverage of the relevant HCPs in the EEA. According to Vifor's customer relationship management ("CRM") database, during the Relevant Period in the Relevant Member States, Vifor visited almost 200 000 relevant HCPs treating ID/IDA patients or prescribing IV iron products.[246]

5.3.3.3.4. Extensive and systematic dissemination of the First and Second Messages

(197) Vifor's campaign focused on disseminating messages that may have been objectively misleading to the relevant HCPs with a view to reducing competitive pressure from Monofer. To achieve this, Vifor created a set of centrally approved communication and training materials to be used across Europe to educate relevant stakeholders on its First and Second Messages, including objection handlers. The latter were used, either in their original form or in national variations, for the training of Vifor's various market-facing teams at national level[247] and were central to steer their communications with HCPs.[248] Vifor communicated its misleading messages directly to HCPs through numerous face-to-face meetings (e.g., […]), as well as contacts via phone, email,[249] or at external events.[250]

(198) Vifor further amplified the dissemination of the First and Second Messages to HCPs by funding studies published in medical journals (such as the above-mentioned *Neiser, Ehlken* and *Nathell* studies which, as already explained, were inapt to draw any comparative conclusion between Ferinject and Monofer) and by hiring KOLs.[251] Such seemingly neutral and independent communications were capable of influencing the broader public perception amongst HCPs concerning the safety profile of Monofer.

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242 Internal documents indicate that [Information on Vifor's own internal assessment of its market position] (e.g., [Information on Vifor's internal document]).

243 [Information on Vifor's internal document]. See also Case T-321/05, *AstraZeneca*, paragraphs 254 and 260.

244 E.g., [Information on Vifor's internal documents].

245 [Information on Vifor's submissions to the Commission].

246 [Information on Vifor's submissions to the Commission].

247 Vifor organises its sales and market contacts through [Information on Vifor's internal sales and marketing organisation] ([Information on Vifor's internal document]).

248 By Vifor's own admission, some of those objection handlers, were used externally in the EEA ([Information on Vifor's submissions to the Commission]).

249 E.g., [Information on Vifor's internal document].

250 E.g., [Information on Vifor's internal documents].

251 [Information on Vifor's internal documents].

5.3.3.3.5. Preliminary conclusion on the capability to produce exclusionary effects

(199) In view of the above, in the Preliminary Assessment the Commission reached the preliminary conclusion that Vifor's communication campaign about the safety of Monofer was capable of foreclosing Ferinject's closest competitor on the IV iron market and only rival on the high-dose IV iron market in the Relevant Member States.

5.3.3.4. No objective justification

(200) As shown above, by disseminating messages that may have been objectively misleading about essential characteristics of its competitor's product, Vifor was not striving to raise awareness of therapeutic and clinical characteristics of its own product, which could have been a legitimate objective. There is also no evidence to suggest that Vifor was seeking to pursue genuine and evidence-based public health objectives.

(201) Instead, the evidence shows that Vifor was pursuing commercial purposes by instilling doubts concerning the safety of Monofer. Essentially, Vifor intended to *"[p]lant the seed of doubt"* in the minds of HCPs about whether Monofer is safe to use (*"raise a red flag relating to safety"*),[252] despite the fact that Monofer had been approved as effective and safe to use by health authorities. Moreover, the studies and national reports on which Vifor relied were ultimately found by the EMA to be insufficient and/or unsuitable to support its claims.

(202) In the light of the above, in the Preliminary Assessment the Commission reached the preliminary view that there was no objective justification for Vifor's conduct.

5.4. Duration and geographic scope

(203) Having reviewed the available evidence and information, in the Preliminary Assessment the Commission reached the preliminary view that Vifor disseminated to HCPs in the Relevant Member States the First and Second Messages on a continuous and regular basis since 2010 and at least until 2022, although it may have started at different points in time in some of the Relevant Member States.

5.5. Substantial part of the internal market and effect on trade between Member States

(204) The conduct concerned by this Decision covered a number of different Member States and sought to influence individual prescriptions of IV iron medicines on a sufficiently large scale by targeting an extensive number of HCPs. As such, Vifor's campaign has taken place in a substantial part of the internal market and was capable of having an appreciable effect on trade between Member States.

5.6. Conclusion of the Preliminary Assessment

(205) Since 2010 and at least until 2022, Vifor developed a communication campaign capable of leading HCPs into believing that administering Monofer could entail serious health risks and that Monofer had a worse risk profile compared to Ferinject. In particular, Vifor disseminated two main messages implying that (i) Monofer bears the serious safety risks historically associated with IV iron dextran compounds, and (ii) Monofer is associated with a higher risk of HSRs than Ferinject.

(206) In view of the considerations summarised in Sections 5.1 to 5.5, in the Preliminary Assessment the Commission reached the preliminary conclusion that the

[252] [Information on Vifor's internal documents].

dissemination of the First and Second Messages may constitute an abuse of the dominant position that Vifor may have held in the markets for IV iron / high-dose IV iron in the Relevant Member States. If confirmed, this would amount to a breach of Article 102 TFEU. Indeed, the Commission takes the preliminary view that the above messages may have been (i) objectively misleading and not reflective of competition on the merits as they were based on inaccurate and/or incomplete information not supported by appropriate scientific evidence, which was presented in a manner that was capable of confusing HCPs by creating a negative perception of Monofer's safety; (ii) capable of influencing the demand and uptake for Monofer and, therefore, of foreclosing Ferinject's closest IV iron competitor and only high-dose IV iron rival; and (iii) not objectively justified.

6. PROPOSED COMMITMENTS

6.1. The Initial Commitments

(207) On 16 April 2024, Vifor offered commitments (the "Initial Commitments") consisting of two main obligations, i.e. the so-called *"Required Conduct"* and the *"Prohibited Conduct"* which can be summarised as follows:

(a) ***The Required Conduct***[253] is a comprehensive, multi-channel communication campaign, the main purpose of which is to rectify and undo the potential effects of the messages previously disseminated by Vifor regarding the safety of Monofer. As part of the Required Conduct, Vifor commits to (i) disseminate a succinct and factual clarificatory communication (the "Stakeholder Communication")[254] to a significant number of HCPs in the Relevant Member States[255] via email, mail and in-person meetings; (ii) publish prominently on Vifor's website(s) the Stakeholder Communication for a period of 36 months; (iii) publish the Stakeholder Communication in leading medical journals in each of the Relevant Member States;[256] and (iv) allow third parties to use the Stakeholder Communication. Vifor further commits to respond to any follow-up questions received from HCPs in relation to the content of the Stakeholder Communication in line with a Q&A document annexed to the commitments.[257]

(b) ***The Prohibited Conduct***[258] prevents Vifor, for a period of 10 years across the entire EEA, from engaging in external promotional and medical communications, in writing and orally, about Monofer's safety profile containing information that is neither based in Monofer's SmPC nor derived from randomised, controlled clinical head-to-head trials. Vifor also commits to implement a number of measures and safeguards to ensure compliance with the Prohibited Conduct, including setting up (i) internal mechanisms to ensure that all relevant external promotional and medical communications, as well as internal training materials are in line with the commitments prior to their use; (ii) internal mechanisms to address any isolated unauthorised miscommunications

253 Initial Commitments, Section II.
254 Initial Commitments, Appendix 1.
255 Initial Commitments, Appendices 3 and 4.
256 Initial Commitments, Appendix 5.
257 Initial Commitments, Appendix 2.
258 Initial Commitments, Section III.

deviating from the commitments;[259] (iii) a dialogue process between Vifor and Pharmacosmos, as well as the trustee in charge of monitoring Vifor's compliance with the commitments, to enable Pharmacosmos to raise and discuss any potential deviations from the commitments and (iv) annual internal compliance trainings and annual certification of compliance with the Prohibited Conduct.

(208) In addition to the above, Vifor would be prohibited from circumventing, directly or indirectly, any obligations contained in the Initial Commitments. In particular, Vifor would not, directly or through third parties, generate, sponsor, publish, or promote comparative studies/publications on Monofer's safety that would infringe the Prohibited Conduct. Vifor may however generate, sponsor, publish, and promote real-world evidence related to Ferinject only or demonstrating the non-inferiority of Ferinject compared to Monofer. Vifor may also generate and sponsor (but not publish or promote directly or through third parties) comparative real-world evidence, with the sole aim of submitting that evidence to EMA for a regulatory evaluation and potential inclusion in the SmPC.[260]

(209) Finally, the Initial Commitments included reporting obligations on Vifor's implementation of the commitments,[261] as well as the monitoring of Vifor's compliance with the commitments by an independent monitoring trustee.[262]

6.2. Commission Notice Pursuant to Article 27(4)

(210) On 22 April 2024, the Commission published a notice pursuant to Article 27(4) of Regulation No 1/2003 inviting interested third parties to provide their observations on the Initial Commitments within one month following publication. In response, the Commission received one submission from an interested third party.

(211) The respondent generally welcomed the Initial Commitments, which it believed would address the preliminary concerns expressed by the Commission, subject to a couple of minor clarification comments.

(212) *First*, the respondent suggested to amend the non-circumvention clause to clarify that Vifor may generate, sponsor, publish, and promote comparative real-world evidence demonstrating the non-inferiority of Ferinject compared to Monofer[263] as long this real-world evidence does not show or suggest superiority of Ferinject compared to Monofer.

(213) *Second*, the respondent suggested to amend the text of the Q&A document annexed to the Initial Commitments (Appendix 2) in order to ensure consistency with the Stakeholder Communication (Appendix 1).

6.3. The Final Commitments

6.3.1. Description of the Final Commitments

(214) On 13 June 2024, Vifor modified its Initial Commitments with a revised proposal (the "Final Commitments") implementing the comments received in response to the Article

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259 The implementation of such internal mechanisms to address unauthorized miscommunications is without prejudice of the general application of EU competition rules and any other applicable rules governing the promotion and/or advertising of pharmaceutical products.

260 Initial Commitments, Section IV.

261 Initial Commitments, Section V.

262 Initial Commitments, Section VI.

263 Initial Commitments, paragraph 9(b).

27(4) Notice (see previous Section), as well as a few additional amendments concerning mainly:

– the legal entities concerned by the Final Commitments to reflect a recent corporate change within the CSL Group (Vifor Pharma Ltd. having been merged into Vifor Pharma Participations Ltd.);

– the timing of the Required Conduct to ensure the effectiveness of the communication campaign by making sure that Vifor's emails and mails to HCPs are not sent over the summer and winter holiday periods;

– the fact that the Stakeholder Communication will be sent by mail one extra time to the HCPs for whom no email address is available;

– the publication of the Stakeholder Communication in medical journals to include in the commitments (i) a deadline for the publication and (ii) a mechanism to identify alternative leading medical journals in 4 Member States where publication in the medical journals identified in Appendix 5 of the Initial Commitments appears not to be feasible;

– the deadline for Vifor to address unauthorised miscommunications to specify that this deadline is expressed in working days rather than calendar days and to include the possibility for Vifor to ask for a deadline extension.

6.3.2. Assessment of the Final Commitments

6.3.2.1. Principles

(215) In the context of Article 9 of Regulation No 1/2003, the Commission must verify that the commitments in question address the concerns expressed in the Preliminary Assessment (effectiveness assessment) and that the undertaking concerned has not offered less onerous commitments that also address those concerns adequately (proportionality assessment). When carrying out that assessment, the Commission must take into consideration the interests of third parties.[264] The Court also held that the Commission enjoys a wide discretion when assessing whether it is appropriate to accept the proposed commitments.[265]

6.3.2.2. Application in the present case

(216) ***As regards effectiveness***, in view of the market test results, the Commission considers that the Final Commitments are sufficient to address its preliminary competition concerns for the following reasons.

(217) *First*, the Required Conduct will address any potential anticompetitive effects that Vifor's past conduct may have on the market in the Relevant Member States through the implementation of a restorative communication campaign dispelling the safety risks associated with Monofer. This is all the more important given that, since the prescription of high-dose IV iron is characterised by high degree of inertia, HCPs are reluctant to switch to new IV iron products surrounded by safety concerns or controversies (see Section 5.2.2.3.3), which means that the First and Second Messages previously disseminated by Vifor could possibly have long-term exclusionary effects. Addressing those is key to limit the potential harm to healthcare systems and patients, which is growing as the market expands.

264 Case C-441/07 P, *Alrosa*, paras. 41 and 61; and Case C-132/19 P, *Groupe Canal +*, paras. 105-106.
265 Case C-441/07 P, *Alrosa*, para. 94.

(218) The effectiveness of the above restorative communication campaign will be ensured by:

- *The concise and straightforward nature of the Stakeholder Communication* pursuant to which Vifor clearly and unambiguously acknowledges that (i) there is no scientific basis to consider that Ferinject is safer than Monofer; (ii) there is no basis to suggest that Monofer has a limited evidence base that would call into question its safety; (iii) Monofer is not a dextran, dextran-derived, or dextran-based product; and (iv) Monofer does not have an increased risk of HSRs compared to Ferinject;[266]
- *The extensive coverage of the HCPs targeted by the Required Conduct*, i.e. almost 200 000 HCPs covering all the HCPs procuring, prescribing or dispensing IV irons contacted by Vifor in the Relevant Member States since 2010[267] (including not only doctors but also pharmacists, nurses, midwives, etc.), as well as physician/pharmacist organizations in Germany, and tender authorities and other procurement bodies in the Relevant Member States.[268] The Stakeholder Communication will be disseminated to each HCP on several instances via email, mail and in-person meetings;
- *The multi-channel nature of the communication campaign*, which is designed to have a widespread effect as it also includes (i) the publication of the Stakeholder Communication on a prominent place of Vifor's global and national websites in the EEA for 3 years, (ii) the publication of the Stakeholder Communication in leading medical journals in each of the Relevant Member States; and (iii) the third parties' right to use the Stakeholder Communication, which would notably enable Pharmacosmos to further advertise the letter across the EEA.

(219) Second, the Prohibited Conducted is designed to prevent the future dissemination of misleading messages, directly or indirectly (e.g. through third parties), with a 10-year ban across the entire EEA of any oral or written communications on Monofer's safety that is (i) neither based on Monofer's SmPC, (which is approved by the relevant regulatory authorities), (ii) nor derived from head-to-head randomised controlled trials (which are specifically designed to compare two medicines, unlike real-world evidence).[269] This will notably prohibit any communications suggesting that Monofer is a dextran/dextran-derived/dextran-based product or subject to a higher risk of HSRs than Ferinject (as this is not supported by Monofer's SmPC) and will prevent Vifor from misusing real-word evidence to imply that Monofer has a poorer safety profile than Ferinject.

(220) In addition to the above, Vifor committed to a number of measures and safeguards, which will not only ensure compliance with the Prohibited Conduct (e.g. internal mechanisms to address isolated unauthorised miscommunications, dialogue process allowing Pharmacosmos to raise and discuss any potential deviations of the commitments) but will also raise awareness on good promotional and medical communications practice within the company (e.g. through annual internal

266 Final Commitments, Appendix 1.

267 Identified based on the records of Vifor's Customer Relationship Management system, i.e. the software system used by Vifor to manage interactions with customers.

268 Final Commitments, Appendices 3 and 4.

269 As explained in Section 5.3.3.2.2, unlike head-to-head trials, real-world evidence are unreliable to compare the safety profiles of different drugs.

compliance training and internal mechanisms ensuring that external communications, as well as internal training materials are in line with the Final Commitments prior to their use), which would further minimise the risk of misconduct in the future.

(221) Further, to the extent that Vifor's potential disparagement against Monofer has not been fully terminated, which cannot be excluded at the time of this Decision, the Prohibited Conduct would be a quick and effective way to bring the conduct to an end.

(222) ***As regards proportionality***, Vifor has not offered less onerous commitments in response to the Preliminary Assessment that would also address the Commission's concerns adequately.

6.3.2.3. Conclusion on the Final Commitments

(223) The Commission considers that the Final Commitments effectively address the preliminary competition concerns identified in the Preliminary Assessment and Section 5 above and are proportionate.

(224) The Commission has taken into consideration the interests of third parties, including in particular Pharmacosmos,[270] analysing carefully all the comments received. To the extent that they contribute to meeting the preliminary competition concerns identified in the Preliminary Assessment and are proportionate, those comments were discussed with Vifor and are reflected in the Final Commitments.

(225) In view of the foregoing, the Commission concludes that the Final Commitments and this Decision declaring them binding, adequately address its preliminary concerns and comply with the principle of proportionality.

7. CONCLUSION

(226) By adopting a decision pursuant to Article 9(1) of Regulation No 1/2003, the Commission makes the Final Commitments, offered by the undertaking concerned to meet the Commission's concerns expressed in its Preliminary Assessment, binding upon them. In line with Recital (13) of the Preamble to the Regulation No 1/2003, this decision does not conclude whether or not there has been or still is an infringement.

(227) The Commission's assessment of whether the Final Commitments offered are sufficient to meet its concerns is based on its Preliminary Assessment, representing the preliminary view of the Commission based on the underlying investigation and analysis, and the observations received from third parties following the publication of a notice pursuant to Article 27(4) of Regulation No 1/2003.

(228) In light of the Final Commitments, the Commission considers that there are no longer grounds for action on its part and, without prejudice to Article 9(2) of Regulation No 1/2003, the proceedings in this case should therefore be brought to an end.

(229) The Commission retains full discretion to investigate and open proceedings under Article 102 of the Treaty and Article 54 of the EEA Agreement as regards practices that are not the subject matter of this Decision.

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[270] Vifor and Pharmacosmos have recently reached a commercial settlement agreement. The Commission is not a party to the settlement (which is a private agreement between the two companies), nor was it directly involved in those settlement discussions. However, since Vifor's alleged disparagement has been specifically and exclusively targeting Pharmacosmos' drug Monofer, the existence of a settlement agreement solving the companies' dispute was taken into consideration by the Commission in its decision to explore the commitments procedure in this case.

HAS ADOPTED THIS DECISION:

Article 1

The Final Commitments as listed in the Annex shall be binding on Vifor Pharma Participations Ltd, Vifor Pharma Management Ltd, Vifor Pharma Deutschland GmbH and all other legal entities of the CSL group involved in the promotion, marketing, or sale of Ferinject in the EEA for a period of 10 years from the date of the notification of this Decision.

Article 2

This Decision brings an end to the proceedings in this case.

Article 3

This Decision is addressed to:

Vifor Pharma Participations Ltd.
Rechenstrasse 37
9014 St. Gallen
Switzerland

Vifor Pharma Management Ltd.
Flughofstrasse 61
8152 Glattbrugg
Switzerland

Vifor Pharma Deutschland GmbH
Gmunder Str. 25
81379 Munich
Germany

Done at Brussels, 22.7.2024

For the Commission

Signed

Margrethe VESTAGER
Executive Vice-President