Completed acquisition by ProStrakan Group PLC of Archimedes Pharma Limited

ME/6465/14

The CMA's decision on reference under 22(1) given on 14 November 2014. Full text of the decision published on 1 December 2014.

Please note that [✂] indicates figures or text which have been deleted or replaced in ranges at the request of the parties for reasons of commercial confidentiality.

Summary

1. ProStrakan Group plc (**ProStrakan**) and Archimedes Pharma Limited (**Archimedes**) (together the **Parties**) are both specialty pharmaceutical companies. They both supply fast-acting fentanyl products in the UK, which are licensed for the management of breakthrough cancer pain (**BTCP**) namely Abstral and PecFent respectively.

2. The Competition and Markets Authority (**CMA**) considers that the Parties' businesses ceased to be distinct as ProStrakan acquired the entire issued share capital of Archimedes (the **Merger**), that the share of supply test is met, and that therefore a relevant merger situation has been created.

3. The CMA has assessed the competitive impact of the Merger on the basis of the supply of fast-acting fentanyl products to patients in the UK.

4. The CMA is of the view that Archimedes did not materially constrain ProStrakan in the supply of fast-acting fentanyl products before the Merger, primarily because of its relatively small share of supply and the limited extent to which Archimedes' PecFent is considered a close substitute to ProStrakan's Abstral. The CMA notes the presence of other credible suppliers of fast-acting fentanyl products, which will continue to constrain the merged entity, and the absence of substantiated third party concerns.

5. The CMA considers that these constraints, taken together, are sufficient to ensure that there is no realistic prospect that the Merger will result in a substantial lessening of competition.

6. This Merger will therefore **not be referred** under section 22(1) of the Enterprise Act 2002 (the **Act**).

Assessment

Parties

7. ProStrakan is a specialty pharmaceutical company incorporated in Scotland. It is controlled by Kirin Holdings Company Limited, a Tokyo-based international specialty pharmaceutical group. ProStrakan's worldwide turnover was approximately £155 million and its UK turnover was around £47 million in 2013.

8. Archimedes is a specialty pharmaceutical company focused on oncology and pain relief. It was incorporated in England and formerly owned by Novo A/S. Archimedes' worldwide turnover was approximately £42 million and its UK turnover was around £19 million in 2013.

Transaction

9. ProStrakan acquired the entire issued share capital of Archimedes on 5 August 2014. The CMA imposed an initial enforcement order pursuant to section 72(2) of the Act on the same date.

Jurisdiction

10. The CMA notified ProStrakan that its Merger Notice was satisfactory on 19 September 2014 and the initial period as defined in section 34ZA(3) of the Act commenced on 22 September 2014. The 40 working day statutory deadline for a decision under section 34ZA(1) of the Act is therefore 14 November 2014. The Merger was completed on 5 August 2014 and the statutory four month period within which the CMA may make a reference following completion of the Merger expires on 5 December 2014, after the 40 working day statutory deadline referred to above.

11. As a result of the Merger, the enterprises of ProStrakan and Archimedes have ceased to be distinct.

12. The Parties overlapped in the supply of fast-acting fentanyl products for the management of BTCP in the UK, with a combined share of supply of [20-30]% by value ([30-40]% by volume) with an increment of approximately [0-5]% ([0-5]% by volume). As a result, the CMA considers that the share of supply test in section 23 of the Act is met.

13. The CMA therefore believes that it is or may be the case that a relevant merger situation has been created pursuant to section 23(2) of the Act.

Frame of reference

14. The CMA considers that market definition provides a framework for assessing the competitive effects of the Merger and involves an element of judgement. The boundaries of the market do not determine the outcome of the analysis of the competitive effects of the Merger, as it is recognised that there can be constraints on merging Parties from outside the relevant market, segmentation within the relevant market, or other ways in which some constraints are more important than others.[1]

15. Prior to the Merger, both Parties supplied fast-acting fentanyl products for the management of BTCP in the UK. BTCP is often acute, short in onset and duration, and moderate to severe in intensity and is not alleviated by the patient's normal pain management. This pain occurs in cancer patients who are already receiving a regular scheduled opioid regimen (such as morphine) for the management of so called 'background pain'.

16. Fast-acting fentanyl is a potent, synthetic opioid analgesic with a rapid onset and short duration of action. It is stronger than morphine and used to complement the regular pain management treatment when patients suffer short periods of acute pain.

Product frame of reference

17. In previous decisions,[2] the CMA's predecessor, the Office of Fair Trading (**OFT**), and the European Commission (**EC**) noted that pharmaceuticals may be subdivided into therapeutic classes by reference to the 'Anatomical Therapeutic Chemical' classification (**ATC**), developed and maintained by the European Pharmaceutical Marketing Research Association (**EphMRA**).

18. The third ATC level (**ATC3**), specifying the therapeutic indication, has generally been used as a starting point for defining product scopes. The OFT and the EC have previously departed from the ACT3 level when market testing indicated that another product scope was more appropriate, for example the active pharmaceutical ingredient (molecule) or medicines used

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[1] *Merger Assessment Guidelines*, A joint publication of the Competition Commission and the Office of Fair Trading, OFT1254/CC2, September 2010, paragraph 5.2.2. The *Merger Assessment Guidelines* have been adopted by the CMA (see Annex D to CMA2 *Mergers: Guidance on the CMA's Jurisdiction and Procedure*, January 2014).
[2] See for example ME/6331/13 *Shire/Viropharma* decision of 10 February 2014; M.5999 *Sanofi Aventis/Genzyme* decision of 12 January 2011; M.5865 *Teva/Ratiopharm* decision of 3 August 2010; and M.1835 Monsanto/Pharmacia & Upjohn decision of 30 March 2000.

for the treatment of a particular disease.[3]

19. ProStrakan submitted that the Parties overlapped in the manufacture and supply of pharmaceuticals at EphMRA ATC3 classification 'N2A' (opioids), ATC product classification 'N02AB03' (fentanyl) and, more specifically, fast-acting fentanyl products. The overlap products are Abstral, produced by ProStrakan, and PecFent, manufactured by Archimedes. Each of the above brands has a different mode of administration. Abstral is a sublingual tablet and PecFent is administered by a nasal spray.

20. ProStrakan submitted that it considers the product scope to include all fast-acting fentanyl products for the management of BTCP.

Fast-acting fentanyl v. non-fentanyl opioid analgesics

21. The ATC3 classification N2A includes a wide range of products produced with different molecules, some of which may be available in an immediate release formulation.[4] ProStrakan submitted that non-fentanyl opioids (such as morphine) have slower onset of action, therefore providing less rapid pain relief. ProStrakan considered that fast-acting fentanyl products for the management of BTCP constitute a product market distinct from non-fentanyl opioid analgesics.

22. Respondents to the CMA's market testing indicated that fast-acting non-fentanyl products are usually the first-line treatment, with fast-acting fentanyl products used when this is not effective or appropriate. Fast-acting fentanyl products may be the preferred treatment in some situations because they have certain advantages (for example a more rapid onset) over other non-fentanyl opioid analgesics.

23. The CMA does not conclude on this point and, on a cautious basis, does not include (immediate release) non-fentanyl opioid analgesics into the product scope for the purpose of this analysis.

Fast-acting fentanyl v. slow-release fentanyl products

24. ATC product classification 'N02AB03' (fentanyl) includes both fast-acting and slow-release fentanyl products. Slow-release fentanyl products are designed to deliver chronic pain relief over prolonged periods.

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[3] See footnote 2 above.
[4] The N2A class includes ProStrakan's product Zomorph, which is a non-fentanyl opioid analgesic. The Parties note that Zomorph does not overlap with Abstral and PecFent although falling in the same ATC3 classification. Zomorph differs in both application and indication, as a sustained release capsule formulation of morphine sulphate indicated for the treatment of severe chronic pain or pain resistant to other analgesics.

25. ProStrakan submitted that it does not consider these products and fast-acting fentanyl products to be substitutable. Respondents to the CMA's market testing suggested that fast-acting fentanyl products may have certain advantages over slow-release fentanyl products in some situations.

26. For the purpose of this analysis, the CMA has not found it necessary to conclude on this point as it does not affect the outcome of the competitive assessment and, on a cautious basis, does not include slow-release fentanyl opioid analgesics into the product scope.

Fast-acting fentanyl – modes of administration

27. ProStrakan submitted that it considers the product scope to comprise all fast-acting fentanyl products for the management of BTCP regardless of their mode of administration. Internal documents from ProStrakan and respondents to the CMA's market testing confirm this.

28. If the product scope were delineated by mode of administration, no overlap would exist between the Parties' product offerings.

29. The CMA does not conclude on this point and, on a cautious basis, does not distinguish fast-acting fentanyl products on the basis of their mode of administration.

Distribution channel

30. The CMA may consider individual distribution channels or customer groups separately if the effects of the Merger on competition to supply a distribution channel or group of customers may differ from its effects on other channels or groups of customers, and require a separate analysis.[5]

31. In this case, the relevant products are supplied to patients either via a hospital pharmacy or community-based pharmacy. [✂] Pharmacies dispense the clinicians' prescriptions which are based on the clinician's medical assessment and on a patient-by-patient basis. [✂] The CMA's market testing did not provide any reasons to distinguish distribution channels in defining frames of reference.

32. Based on this evidence, the CMA considers that the competitive conditions the Parties face do not vary significantly by distribution channel or customer group.

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[5] *Merger Assessment Guidelines*, paragraph 5.2.28.

33. The CMA does not conclude on whether competitive conditions vary by customer group as no concerns arise in any distribution channel or any plausible subset of customers.

Conclusion on product frame of reference

34. For the reasons set out above, the CMA, on a cautious basis and for the purpose of this assessment, considers the impact of the Merger on the basis of the supply of fast-acting fentanyl products to patients.

Geographic frame of reference

35. ProStrakan submitted that the appropriate geographic frame of reference for the products in question is national due in particular to differences in national approval and reimbursement schemes, and differences in national clinical guidelines and medical views. The CMA notes that this is in line with previous EC and OFT decisions.[6] The CMA received no evidence to suggest that the geographic frame of reference should be wider in this case.

36. The CMA has considered whether the geographic scope should be narrower but has found that the competitive conditions do not warrant such an approach.

37. The CMA therefore considers the impact of the Merger on the UK for the purpose of this assessment.

Conclusion

38. As no competition concerns arise on any of the possible product and geographic frames discussed above, the CMA does not consider it necessary to conclude on the relevant frame of reference. The CMA has used the following frame of reference for the purpose of this assessment: the supply of fast-acting fentanyl products to patients in the UK.

Counterfactual

39. The CMA assesses the Merger's impact relative to the situation that would prevail absent the merger (that is, the counterfactual).[7] The CMA received no evidence to suggest that the prospect of the pre-Merger conditions continuing is not realistic absent the merger. Accordingly, the CMA considers the pre-

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[6] See footnote 2 above.
[7] See *Mergers Assessment Guidelines*, paragraph 4.3 ff.

Merger conditions of competition to be the relevant counterfactual.

Horizontal unilateral effects

Shares of supply

40. ProStrakan submitted data on shares of supply of fast-acting fentanyl products to patients for the management of BTCP in the UK.[8] These are shown in Table 1.

TABLE 1 Share of supply of fast-acting fentanyl products for the management of BTCP in the UK based on IMS data on a moving annual total basis (ending May 2014)

	Volume		**Value**	
ProStrakan (Abstral)	[✂]	[20-30]%	[✂]	[20-30]%
Archimedes (PecFent)	[✂]	[0-5]%	[✂]	[0-5]%
Combined	[✂]	**[30-40]%**	[✂]	**[20-30]%**
Teva (Actiq and Effentora)	[✂]	[60-70]%	[✂]	[70-80]%
Takeda (Instanyl)	[✂]	[0-5]%	[✂]	[0-5]%
Meda Pharm. (Breakyl)	[✂]	[0-5]%	[✂]	[0-5]%
Grünenthal (Recivit)	[✂]	[0-5]%	[✂]	[0-5]%
TOTAL	[✂]	**100%**	[✂]	**100%**

41. There are four suppliers of fast-acting fentanyl products in the UK (the Parties, Teva and Takeda) and two recent entrants which did not have any significant sales at the time of collecting this data. Meda Pharmaceuticals introduced its product Breakyl in January 2014 and Grünenthal launched Recivit in April 2014.[9]

42. The CMA accepts the Parties' estimate of a combined share of supply of fast-

[8] The data was based on independent third party's data by Intercontinental Medical Statistics (**IMS**).
[9] Grünenthal confirmed to the CMA that it has realised sales 'in the low thousands'. Meda Pharmaceuticals did not provide any information, however, third party testing confirmed Meda Pharmaceuticals' presence in market.

acting fentanyl products in the UK[10] of approximately [30-40]% by volume and [20-30]% by value with a [0-5]% by volume and [0-5]% by value increment.[11]

43. The CMA notes that fast-acting fentanyl products are differentiated, in particular due to the product's different modes of administration and other features such as the time of onset and duration, packaging and taste. The CMA has therefore considered closeness of substitution between the Parties' products, as the share of supply is a less meaningful indicator of unilateral effects in the supply of differentiated products.[12]

Closeness of competition

44. ProStrakan submitted that it does not consider Abstral and PecFent to compete closely with each other. ProStrakan's internal documents support its submission that nasal and oral products do not compete closely with each other.[13]

45. ProStrakan noted that it considers [✂] to be its closest competitor. This is based on the IMS data which ProStrakan uses to monitor competitors' performance. ProStrakan considered that [✂] competes most closely with Archimedes' PecFent, which is also a nasal spray. This view is supported by ProStrakan's internal documents.[14]

Evidence from third parties

46. One competitor submitted that the fast-acting fentanyl products PecFent and Instanyl are more similar to each other than the Parties' products are to each other. PecFent and Instanyl are both nasally administered, with relatively quick action and short duration. Abstral is more similar to Actiq and Effentora. They are all orally administered products, and their effect lasts longer. Another competitor mentioned that Abstral and Recivit are very similar, since they are both sublingual products.

47. Hospitals which responded to the CMA's questionnaires submitted that nasal formulations are used for patient groups for which oral or buccal formulations

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[10] The CMA considers the shares of supply of fast-acting fentanyl products in the UK do not significantly vary from the shares of supply of fast-acting fentanyl products for the management of BTCP in the UK. The Parties and third party testing confirm that off-label prescription appears to be minimal relative to licensed applications (ie, for the management of BTCP).
[11] The Parties also submitted shares of supply by hospital channel and retail channel. The combined shares of supply are higher in the 'hospitals channel': [50-60]% with an increment of [5-10]% by value, and [50-60]% with an increment of [5-10]% by volume. The CMA considers that the competitive conditions the Parties face do not vary significantly by distribution channel or customer group. See paragraphs 30-32 above on distribution channels.
[12] See *Merger Assessment Guidelines*, paragraph 5.4.6 ff.
[13] [✂].
[14] [✂].

are unsuitable (for example because of mouth wounds). Some hospitals let their patients choose between oral and nasal formulations.

Guidelines and formularies

48. NHS National Institute for Health and Clinical Excellence (**NICE**) publishes guidance containing recommendations, based on the best available evidence, to guide decisions for a particular area of health, public health or social care.[15] NICE guidelines are not mandatory; healthcare professionals are expected to consider them when exercising their clinical judgement, but it does not override their responsibility to make decisions appropriate to the circumstances and wishes of the individual patient.

49. NICE guidelines do not recommend fast-acting fentanyl products, and therefore do not influence the level of competition and closeness of competitors in the market. Scottish Medicines Consortium published that it does not recommend a buccal film fast-acting fentanyl product, Breakyl. This possibly weakens the position of this specific product in the market. However, guidelines in each country do not lead to Abstral and PecFent becoming each other's closest alternatives, as none of the guidelines take a view on PecFent.

50. Several hospitals have arrangements in place that restrict the set of fast-acting fentanyl products that can be prescribed to one or two products. Such decisions have been taken based on budgetary and clinical considerations. In the examples of such arrangements that came to the CMA's attention, nasal formulations and oral formulations were not considered as substitutes for the majority of patients but rather as complements for different patient groups.

Central purchase agreements and prescription behaviour

51. The relevant bodies in each of England, Wales, Scotland and Northern Ireland are responsible for national procurement of secondary-care pharmaceuticals and organise tenders when certain thresholds are met. Suppliers of medicines can voluntarily take part in these tenders and are able to offer its regulated list prices from the Pharmaceutical Price Regulation Scheme (**PPRS**)[16] or discounted prices.

52. The Parties' products [✂]. In addition, the parties have not competed to become part of one of these contracts. These contracts have therefore not

[15] Drugs do not have to be appraised by NICE for them to be available through the NHS. The vast majority of drugs that are available have never been appraised by NICE and in these situations, decisions about funding are taken by local organisations.
[16] Manufacturers must ensure overall price neutrality under the PPRS. That is, price increases of one product must be set off by a price decrease in respect of another product within its portfolio.

increased the constraint that the Parties' products impose on each other.

Constraints from outside the frame of reference

53. NICE has published guidance on the treatment of pain in palliative care of adults.[17] This advocates the prescription of immediate-release non-fentanyl opioids for the management of BTCP, and expressly rules out the prescription of fast-acting fentanyl as a first-line rescue medication for patients who can take oral opioids. ProStrakan submitted that, due to the prescribing clinicians' familiarity with immediate-release non-fentanyl opioids, in conjunction with the NICE guidance, these non-fentanyl opioids impose a competitive constraint upon fast-acting fentanyl products from outside the proposed product scope.

54. The CMA has received examples of local/regional prescription algorithms which show that prescribers are advised to try to optimise the dose and formulation of immediate-release non-fentanyl opioid analgesics to control the BTCP before fast-acting fentanyl products are considered. These non-fentanyl opioids (such as morphine or oxycodone) are supplied by generic manufacturers and the cost of an equivalent dose is significantly lower than that of fast-acting fentanyl.

55. As there are no competition concerns even if the supply of fast-acting fentanyl products is considered in isolation, the CMA does not consider it necessary to conclude on this possible constraint from outside the frame of reference.

Conclusion on horizontal unilateral effects

56. Based on the evidence set out above, the CMA is of the view that Archimedes did not materially constrain ProStrakan in the supply of fast-acting fentanyl products pre-Merger, because of its relatively small share of supply and the limited extent to which PecFent is considered a close substitute to Abstral (primarily due to different modes of administration). The CMA notes the presence of other credible suppliers of fast-acting fentanyl products, namely Takeda and Teva (who has a larger share of supply than the merged entity), which will continue to constrain the merged entity post-Merger, and the absence of substantiated third party concerns.

57. Accordingly, the CMA does not believe that there is a realistic prospect that the Merger will result in a substantial lessening of competition as a result of horizontal unilateral effects in relation to the supply of fast-acting fentanyl

[17] *Opiods in palliative care: safe and effective prescribing of strong opioids for pain in palliative care of adults*; paragraph 1.1.15.

products to patients in the UK.

Barriers to entry and expansion

58. Entry, or expansion of existing firms, can mitigate the initial effect of an acquisition on competition, and in some cases may mean that there is no substantial lessening of competition. In assessing whether entry or expansion might prevent a substantial lessening of competition, the CMA considers whether such entry or expansion would be timely, likely and sufficient.[18]

59. ProStrakan submitted that there were two recent entrants into the supply of fast-acting fentanyl products in the UK in January and April 2014, namely Breakyl and Recivit respectively. Third party testing confirmed this statement.

60. As there are no competition concerns even in the absence of entry or expansion, the CMA does not consider it necessary to conclude on entry or expansion in this market.

Third party views

61. The CMA contacted clinicians and pharmacists in different hospitals across the UK (including hospitals in each of the four devolved nations), competitors, potential competitors and wholesalers, as well as NICE, Medicines and Healthcare Products Regulatory Agency, Commercial Medicines Unit at the Department of Health, NHS Wales (All Wales Medicines Strategy Group, and NHS Wales Shared Services Partnership), Scottish Medicines Consortium, NHS Northern Ireland (Health and Personal Social Services, and Health and Social Care Northern Ireland), Association for Palliative Medicine of Great Britain and Ireland, and the Faculty of Pain Management of the Royal College of Anaesthetists.

62. Only a very small minority of the third parties raised some concerns. They related to the risks of price increases and reduction in choice, however, these were not substantiated in more detail.

63. Third party comments have been taken into account where appropriate in the competitive assessment above.

Decision

64. Consequently, the CMA does not believe that it is or may be the case that the Merger has resulted or may be expected to result in a substantial lessening of

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[18] See *Merger Assessment Guidelines*, paragraph 5.8.1 ff.

competition within a market or markets in the United Kingdom.

65. This Merger will therefore **not be referred** under section 22(1) of the Act.

Nelson Jung
Director of Mergers
Competition and Markets Authority
14 November 2014