

THE AVASTIN-LUCENTIS CASE: AN ILLICIT AGREEMENT BETWEEN ROCHE AND NOVARTIS CONDEMNED BY THE ITALIAN COMPETITION AUTHORITY

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1 INTRODUCTION

On 27 February 2014, the Italian Competition Authority (ICA) closed its proceedings I/760 by finding that the parent companies of the Roche and Novartis groups, together with their Italian subsidiaries, infringed article 101 TFEU for an illicit agreement related to the sales in Italy of Avastin and Lucentis, two medicines having wide applications for treating several severe eye diseases.²

The proceedings was launched owing to the complaints submitted by an association of private healthcare clinics and by the Italian Ophthalmological Society: both complainants claimed that Roche and Novartis Groups were colluding for impeding the use of a product, Avastin, in order to illicitly advantage the commercial performance of the much more expensive Lucentis. The same complaints were subsequently supported during the proceedings by an Italian region, Emilia-Romagna, and by a consumer's association.

At the end of its investigation, the ICA held liable for the infringement the Swiss companies F. Hoffmann-La Roche Ltd. and Novartis AG, together with the Italian companies Novartis Farma S.p.A. and Roche S.p.A., and consequently imposed relevant pecuniary sanctions; as for Genentech Inc., a Californian company pertaining to the Roche group that was also part of the proceedings, the ICA did not ascertain any liability according to the EU competition law. Roche and Novartis groups rejected the ICA's findings and appealed; a resolution by the competent administrative court (TAR Lazio) is expected probably in November 2014.

¹ Italian Competition Authority.

²See ICA, proceedings I/760, *Roche-Novartis/farmaci Avastin e Lucentis*; decision No. 24823 of February 27, 2014 (http://www.agcm.it/trasp-statistiche/doc_download/4112-i760-provvedimento.html).

2 PRODUCTS, RELEVANT MARKETS AND CONDUCTS

Avastin and Lucentis are two biotech medicines based on the same operating mechanism, namely the neutralization of the vascular endothelial growth factor (VEGF) at the basis of the physiological process of blood-vessel formation called angiogenesis: as a matter of fact, Lucentis's active ingredient, ranibizumab, is an engineered fragment of Avastin's active ingredient, bevacizumab. Both medicines were developed by Genentech when the company was already part of Roche Group.

More in detail, Avastin was destined to oncologic applications, while Lucentis proved to be effective in treating the wet Age-related Macular Degeneration (AMD), an eye disease leading to blindness. Genentech eventually retained the commercial rights on Avastin and Lucentis within the United States, while worldwide commercial rights were awarded respectively to Roche and Novartis by means of two separate agreements. As regards the EU, Avastin was approved by the European Medicines Agency (EMA) in 2005 for the treatment of specific forms of metastatic cancers by means of infusion in the blood, while Lucentis was approved in 2007 for treating AMD by means of injection in the eye. However, before Lucentis's approval, an unregistered (so called "off-label") use of Avastin was already established among ophthalmologists for treating AMD by splitting the medicine's vial and inject a small portion of it in the eye. Cost differences of the two ophthalmic therapies were (and still are) noteworthy: in fact, to take the case of Italy, Lucentis entered the market in 2007 with a price per injection of €1,700 - only at the beginning of 2013 it lowered to €900 - while the cost per injection of Avastin used off-label was €81 at its maximum.

Due to this relevant cost difference, the Italian National Healthcare System (NHS) used Avastin for treating AMD and other eye diseases, instead of Lucentis. This happened due to the Italian legal framework (namely Law n. 648/1996) that allows off-label uses under the condition of the non-existence of a medicine already registered for the same treatments. While Lucentis, together with a few other drugs, was obtaining its registrations for eye-treatments, the off-label ophthalmic uses of Avastin covered by the NHS were subsequently diminished. Roche never registered Avastin for ophthalmic applications: this notwithstanding an increasing amount of studies supporting the medicine's efficacy in treating AMD. Moreover, from 2011 results of independent comparative studies carried out at the expense of public healthcare organizations (so-called CATT study in the US and IVAN study in the UK) started to support the conclusion of an equivalence of the two medicines also under a safety profile, as finally recognized by the EMA's scientific committee in 2012.

As regards the antitrust side of the story, the ICA opened its investigation in February 2013 and closed it a year later by detecting what was considered an anti-competitive collusion between the Roche and Novartis Group within the Italian relevant market of drugs used for treating vascular ocular diseases. This national market, whose value in 2012 was estimated at €100 million, comprises medicines used for

treating AMD and other widespread eye illnesses: as for market shares, off-label uses of Avastin and registered uses of Lucentis held more than 40% and 50% respectively.

In the ICA's view, Roche and Novartis colluded by raising and spreading concerns related to the safety of the ophthalmic uses of Avastin in order to boost the sales of Lucentis, from which both groups were expecting their own returns. In fact, while Novartis was directly gaining from the sale of the product, Roche was obtaining indirect revenues from the royalties recognized by Novartis on the same sales to Genentech; as further evidence of relevant intertwining interests, the ICA also took into account that Novartis holds more than 33% of Roche.

The main undertaking's conducts that the ICA considered as having an antitrust relevance started as of June 2011, when Roche, being the sole legitimate subject to deal with EU regulatory matters related to Avastin, requested EMA to modify its Summary of Product Characteristics (SmPC), the official document stating all the relevant information for each drug. Such modification was aimed at obtaining an extra-wording related to the drug's ophthalmic risks that, according to what was scheduled by the parent companies and highly expected by their own national subsidiaries, should have been proactively communicated to healthcare professionals. EMA, however, did adopt several changes to Avastin's SmPC that differed from the ones requested by Roche, and refused to allow the sending of a formal warning to the medical community. EMA also modified the Lucentis' SmPC in order to make it clear that systemic health risks are common to all anti-VEGF drugs.

The ICA's final resolution was based on several pieces of evidence of the anti-competitive plan developed by the two groups. This is the case, for instance, of email exchanges that occurred among the CEOs of the Italian branches of Roche and Novartis, explicitly referring to the artificiality of the product differentiation in connection with the modification of the Avastin's SmPC (cf. §193); several messages circulated inside Roche's national branch, in their own turn, indicating as dubious the same pharmacovigilance issues previously recalled (cf. §§106-108). Moreover, internal documents of Novartis' parent company referred to generating and communicating safety concerns related to Avastin's ophthalmic uses, also by means of financing symposia, scientific papers devoted to the revision of the independent comparative studies, as well as cooperation with patient groups (cf. §§196-199). These plans were developed while the results of the independent comparative studies started to be issued: according to other Novartis internal documents, this was at risk to make ophthalmologists more confident in using Avastin, but the impact of such studies was successfully minimized by the companies (cf. §116). At the bottom line of these general activities carried on by the parent companies, the Italian branches of Roche and Novartis jointly managed what they considered to be national emergencies, such as a temporary governmental approval of the off-label ophthalmic uses of Avastin, coordinating their own public communication activities (cf. §§216-219).

3 CONCLUSIONS

The ICA ascertained a collusion between Roche and Novartis having an illicit object; it also underlined several effects of the infringement, focusing on the modification of the demand attitudes towards the off-label uses of Avastin with direct consequences both on healthcare's expenditures and access to treatments. According to the ICA's estimates, the shift that occurred during 2012 within public hospitals from the ophthalmic off-label uses of Avastin to the registered products (basically Lucentis) caused an economic harm to the NHS corresponding to an additional cost of about €45 million.

At the end of its evaluations, the ICA considered the undertakings' conducts as a very serious infringement of the EU competition law. Taking into account the duration, the relevance of the parties involved and the sophisticated design of their conduct, the fines imposed were €92,028,750 for Novartis and €90,593,369 for Roche.

Apart from the antitrust consequences, it is noteworthy to consider that after the ICA's resolution the healthcare legal system was revised, a recent law (No. 79/2014, substantially amending a previous law decree, No. 36/2014) was adopted in order to allow general off-label ophthalmic uses of Avastin. Finally, as of June 2014, such uses have been effectively approved within the NHS.³

³ Arnaudo L., *The Avastin-Lucentis Case: an illicit agreement between Roche and Novartis condemned by the Italian Competition Authority*.
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