AUTORITÀ GARANTE DELLA CONCORRENZA E DEL MERCATO

# Pharmaceutical antitrust enforcement in Italy

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**23rd EU-China Competition week**
**31st March, 2022**

# The strategic use of pharmaceutical patents: the Pfizer case

# The Italian Pfizer case

- 2003: Pfizer became the owner of a patent on a blockbuster drug, *Xalatan* (Lactanoprost), leader in the market for the treatments of glaucoma (reduction of the blood pressure of the eye through the drainage of the aqueous humor).
- Xalatan was covered by a **patent expiring on Sep 2009**. In 1997 Pharmacia **obtained a SPC** for all the EU Member States, **except Italy.** Therefore, while in Italy the patent on Xalatan was valid until Sep 2009, in the **rest of Europe such expiry was extended until July 2011**.
- In 2002, Pharmacia **applied for a *divisional patent*** based on the compound patent covering Xalatan. The divisional patent was supposed to **last until Sep 2009**.
- On Jan 2009 Pfizer (new owner of the patent) **applied for a SPC on the divisional patent which extended the protection to July 2011** and aligned the patent expiry for Xalatan **in Italy** to the other EU countries.

# The Italian Pfizer case

- Ratiopharm, a generic company relied on the initial expiry date of the compound patent and in 2007 got a MA for the generic version of Xalatan and started producing the product.
- Pfizer sent cease and desist letters inviting Ratiopharm to refrain from marketing the generic version of Xalatan before July 2011.
- Ratiopharm sent a complaint to the ICA. The investigation started.
- *On May 2012 EPO revoked the divisional patent as this was exceeding the scope of the compound patent.*
- The ICA sanctioned Pfizer for having abused its dominant position through a misuse of the right of asking for patent protection, since this foreclosed the entry of generics in the Italian market

# ICA's view

- Pfizer gained almost two and a half more years of patent protection.
- This **delayed the entry of generics** in the market
  - **Lost savings for the Italian NHS estimated in 14 millions Euros.**
- The obstruction of generics' entry in the market for the treatment of glaucoma as a means to preserve profits was the real aim behind the legal strategies adopted by Pfizer.
- This was confirmed by the *revocation of divisional patent* (no true innovative activity behind patent activity – lack of business rationale).
- *The conscious enforcement of an illegitimate patent was thus an indicia of the exclusionary intent.*
- For this reason, the ICA decided that Pfizer's conduct constituted an abuse of dominant position and sanctioned it.

# The First Instance Judge's view

- Pfizer merely acted to protect its own commercial interests. This is not sufficient to substantiate an antitrust violation.
- In order to prove the infringement **necessary to *prove exclusionary intent* on the basis of *additional elements*** that allow to 'colour' with the taint of illegitimacy behaviour otherwise lawful.
- The AGCM had failed to prove the existence of such additional elements, since
  - *on May 2012 the EPO Board of Appeal annulled the revocation decision and declared the divisional patent valid*
  - the illegitimacy of Pfizer's conduct could not be derived from the illegitimacy of its patent filing activity, as the latter was just assumed and not proved
- This circumstance invalidated the whole logics behind the ICA's infringement decision.

# The Supreme Administrative Court's Judgement in Pfizer

- The **legitimacy of the divisional patent is irrelevant**
- The abuse of dominant position is a type of **abuse of right**, which is proved when
  - Existence of a right
  - Many possible ways of exercising such right
  - Concrete exercise is formally compliant with the norms on which the right was attributed, but not coherent with the aim for which it was granted (e.g. exclusion of competitor is not a valid aim that can be attached to the right)
  - Disproportionate benefit to the right owner compared to the counterparty

# Disparagement of rival drugs: the Roche-Novartis case

# The two *biotech* products

- ***Avastin*** (bevacizumab)
  - anti-VEGF drug developed by Genentech, part of Roche Group, marketed worldwide by Roche, excluding US, based on a 1999 general licensing agreement with Genentech
  - registered use: treatment of some forms of metastatic cancer
  - ***off-label use***: treatment of wAMD and other ophtalmic diseases
  - cost (calculated per eye injection obtained by splitting the vial): € 15-80
- ***Lucentis*** (ranibizumab)
  - anti-VEGF drug developed by Genentech, marketed worldwide by Novartis, excluding US, based on a 2003 licensing agreement with Genentech
  - registered use: treatment of AMD
  - price (per vial/eye injection): € 1,700 (lowered to € 900 since 2013)

# The off-label use of Avastin in Italy

- *Avastin* was included in the 648 List in 2007 for the treatment of several types of macular degeneration diseases (including Age-related MD)
- *Lucentis* entered the market at the end of 2008
- The Italian Medicine Agency then limited the *off label* use of Avastin a smaller number of MD
- In 2010 Avastin could not be used to treat patients that were previously treated with the drug (switch to *Lucentis*)
- At the end of 2012 the IMA decided to completely eliminate Avastin from the 648 list (*delisting*)

# Avastin *vs* Lucentis

- Despite the delisting, the ophtalmic *off-label use of Avastin continued* and the drug became a *competitor of Lucentis*
- Regions continued to prefer *Avastin* to Lucentis even after the registration of the latter since the former was *much cheaper*
- *Avastin remained the principal anti-VEGF medicine used in Italy in the treatment of ocular vascular pathologies*
- Starting from June 2011 Roche funded and supported research activities on the superiority of Lucentis
- Roche criticised independent comparative studies proving that Avastin and Lucentis are similar in terms of efficacy profiles
- Roche also requested the EMA to modify Avastin's SmPC in order to obtain an «extra-wording» related to its ophthalmic risks of the *off label* use (blindness)

# The proceedings opened by the ICA

- The competition from Avastin on Lucentis contrasted Roche's and Novartis' expectation of selling the two products on two different therapeutic markets
- Thus Roche and Novartis **shared and pursued an «artificial differentation strategy»** aimed at manipulating the perception of the risks associated to Avastin in order impede its *off label* use
- This aimed that conditioning the choice of doctors
- Novartis acted to generate Avastin's safety concerns and to communicate it to health authorities («*generate concern*»)
- Pharmacovigilance concerns related to ophthalmic use of Avastin were baseless (scientific uncertainty)
- Roche did not seem to be interested in solving real dangers, but rather in leveraging all available data for raising concerns

# The agreement restrictive of competition

- In order to avoid competition, Roche and Novartis colluded to keep Avastin out of the ophthalmic sector in order to protect Lucentis sales
- The final goal was the **maximisation of profits for both companies each in its therapeutic area** (this explained why Roche did not register the new indication)
- The arrangements between Roche and Novartis constituted an unlawful **market-sharing agreement that had as its *object* the restriction of competition**, aiming at preventing the use of the cheaper product
- On February 2014 the ICA fined Roche and Novartis for having violated art. 101 TFEU respectively 90,5 and 92 million Euros

# The decision of the CJEU in Jan 2018 (1)

- Drugs that may be used for the same therapeutic indications belong, in principle, to the same product market.
- In assessing substitutability, the regulation which governs the drugs' MA is relevant.
- If it is established by a national court/authority that a product was unlawfully prescribed/sold *off label*, it cannot be considered substitutable or interchangeable for a lawful product
- If unlawfulness of the *off-label* use is not established, the competition authority is allowed to consider the two products as competing on the same market

# The decision of the CJEU in Jan 2018 (2)

- If two competitors arrange to disseminate **misleading information**, in a context of scientific uncertainty, related to the adverse reactions arising from the off-label use of one of their competing products, with the view of reducing the competitive pressure existing between the products
- That arrangement is an agreement ***restrictive of competition "by object"***
- It is for the national court to decide whether such information is misleading
- Misleading:
  - *Designed to confuse the regulators*
  - *Intended to heighten public perception*
  - *Indicia: pharmacovigilance duties lie solely with the MA holder of a given product. The involvement of another product is irrelevant.*

# Excessive prices for pharmaceuticals: the Aspen case

# The Aspen case

- In 2009 Aspen bought four old off-patent drugs (the Cosmos drugs) from GSK
- Aspen **requested a reclassification** from reimbursed products (A class) to non-reimbursed ones (C class), in order to "*align prices to those applied in other EU countries*"
- IMA **rejected** (life-saving and essential drugs) and agreed on a **renegotiation of reimbursement prices**
- **Price proposal** received was considered **unbearable**. Failure of negotiation
- Aspen again **requested reclassification** and **threatened the interruption of supplies**
- Finally IMA agreed on the following reimbursement prices:

| Product name | Active ingredient | % increase in price |
|---|---|---|
| Alkeran | melphalan | +1540% |
| Alkeran inj | melphalan | +257% |
| Leukeran | chlorambucile | +1166% |
| Purinethol | mercaptopurine | +465% |
| Tioguanina | tioguanina | +306% |

# The relevant markets

- Based on the **absence of therapeutic alternative t**he ICA defined **four relevant product markets at ATC5 level (molecule level)**: markets of drugs based on the active ingredients mercaptopurine, tioguanine, melphalan and chlorambucile.

- **Aspen considered dominant based** on:

  - *Lack of effective competition (*only Aspen was present in each of the relevant markets.

  - *Lack of potential competition* (small market)

  - *Inelastic demand for life saving drugs*

# The *United Brands* price-cost test

- **"Unfair" prices are not just "excessive" prices**
- **Two-step approach:**
  - ***First step: excessiveness***
    - *"whether the difference between the costs actually incurred and the price actually charged is excessive"*
    - Excessiveness must be significant and persistent in time
  - ***Second step: unfairness***
    - *"whether the price […] is either unfair in itself or when compared to competing products".*
    - two alternative prongs

# The "excessiveness" in *Aspen*

**FIRST METHOD: gross margin**

- Calculation of the difference between *ex ante* prices and direct costs
- The resulting gross margin in % of sales was compared to the total costs in % of sales
- This allowed to conclude that:
  - already before the increase prices applied granted a positive margin (btw 20-30% and 70-80%);
  - therefore, a price increase % ranging between 300% and 1500% of the initial prices conducted to an excess of prices on the economic value

# The "excessiveness" in *Aspen*

**SECOND METHOD: Cost Plus**

- Cost Plus = costs + a reasonable rate of return
- Costs = Costs actually incurred = *direct costs* of pruduction and supply + appropriate apportionment of the *indirect costs* reasonably attributable to the product
- *Reasonable rate of Return*
  - ROS = 13% (*average ROS of the two main generic companies' active worldwide*)
- The analysis allowed to conclude that:
  - excess in % over the Cost Plus ranged from round 100% to almost 400%;
  - these % are well above those considered «abusive» in previous CJEU cases.

# The "unfairness" in *Aspen*

- **No economic justification behind the price increase**
- **Absence of non-cost related factor:** no improvement of production/ distribution
- **Old off patent drugs**
- **No R&D efforts**: the Cosmos purchase appears as a speculative business model
- The **nature of the drugs** and the **absence of substitutes**
- Prices charged in other countries might be excessive > no comparison
- **No competitors' products were found**
- **Misuse of NHS limited resources**, in a context of budget restraint, for the only purpose of increasing company surplus
- **Aggressiveness** of the conduct

# The abuse

- Aspen adopted a **very aggressive negotiation strategy** towards the IMA to obtain the price increase:
  - **strategic request for drug reclassification** from A class to C class: Aspen awareness of AIFA's impossibility to accept (due to the essentiality of the medicines);
  - **threat of withdrawal** from the Italian market, had AIFA not promptly accepted the proposed prices;
  - **creation of an artificial shortage** through a misuse of the «oncology stock allocation mechanism».
- Aspen abused its dominant position by having charged unfair excessive prices through an instrumental and distorted use of the regulation (fine: over Euro 5 million in 2016)
- ICA's decision has been upheld by the 1st instance (2017) and 2nd judge (2020)

*Thank you for your kind attention!*
*Questions?*

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