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Excessive pricing: Takeaways from the Aspen and Leadiant investigations

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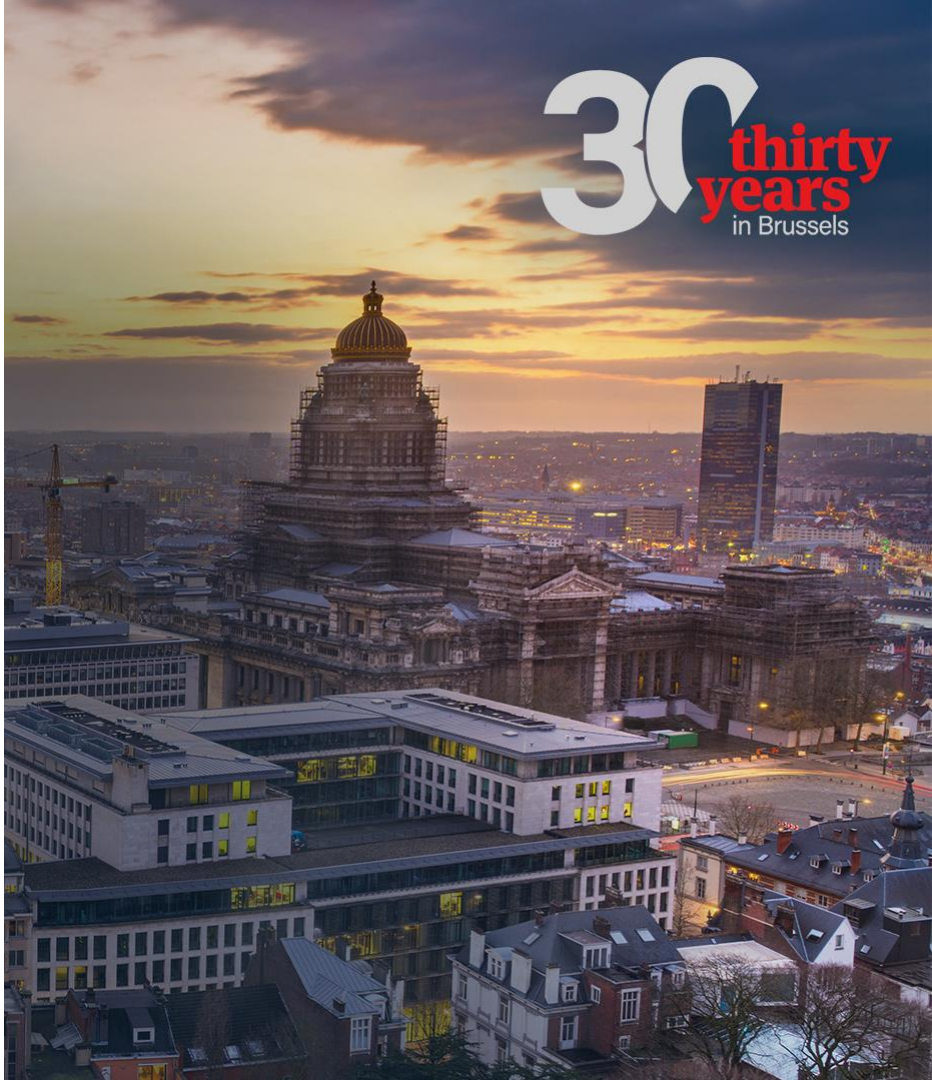


Pharma excessive pricing cases

- Aspen
- Pfizer/Flynn (Phenytoin Sodium)
- Auden McKenzie and Actavis (now Accord-UK) (Hydrocortisone)
- Advanz, HgCapital and Cinven (Liothyronine)
- CD Pharma (Syntocinon)
- Leadiant

Where did Aspen take us?

Aspen case - Timeline

Italian Aspen Case A480 – Measure No. 26185

Findings of fact

- The drugs at issue were developed in the 1950/60s.
- In 2009, Aspen bought the relevant trademark and marketing rights from the original producer, i.e. GlaxoSmithKline ("GSK"). Competitors did not enter the relevant markets because of their small scale.
  - IP protection had already expired, and so the drugs were off-patent.
  - Products were essential and non-substitutable.
- Products were included in the A and H repayment classes – prescribed at the Italian Health System's ("SSN") expense. Accordingly, an agreement was needed between AIFA and Aspen, subject to potential renegotiation every two years.

Italian Aspen Case A480 – Measure No. 26185 (cont'1)

- In 2013, Aspen started its negotiation with AIFA, claiming that Cosmos should have been included in class C and treated as "non-reimbursable". As such, they could have been susceptible of price increase.
  - Aspen took aggressive positions, including threatening to withdraw the products.
  - AIFA was forced to agree to price rises between 257% and 1540%.

Italian Aspen Case A480 – Measure No. 26185 (cont'2)

AGCM's conclusions

- Aspen held a stable dominant position on the relevant markets.
- Aspen abused its dominant position by imposing excessive prices. AGCM applied the two-step *United Brands* test:

AGCM assessed the (dis)proportion between the prices and costs of production, identifying the profit margin.

- AGCM applied multiple methods to assess whether the price was excessive, including (i) gross margin, (ii) profitability based on (a) gross contribution margin and (b) cost plus benchmark, and (iii) IRR.

AGCM evaluated whether the prices were unfair. The fact that Aspen had not innovated played a key role.

- Other factors considered included (i) lack of economic justification, (ii) lack of benefit to patients, (iii) harm to the SSN, (iv) nature of the products, and (v) prices for the products over time.

EU Aspen Case – Case AT.40394

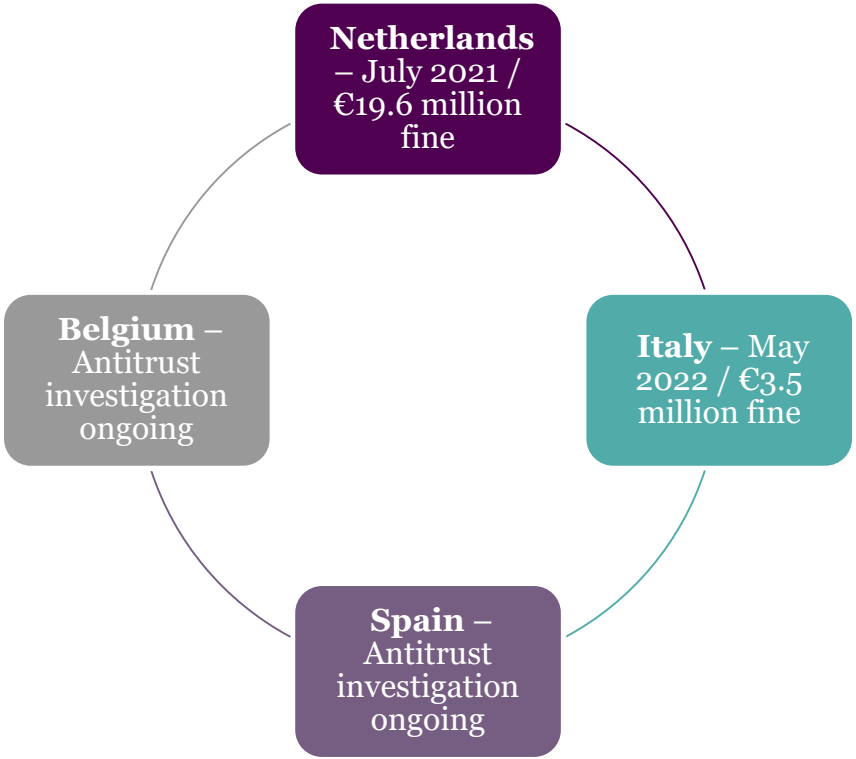
- 15 May 2017: the EC Commission opened an investigation of Aspen's pricing practices for off-patent niche medicines used to treat cancer, sold formulated in various ways and under multiple brands. It investigated price increases of up to several hundred percent, and it had information that Aspen threatened to withdraw the medicines in some Member States, and did so in certain cases.
- The EC found
  - Aspen's accounting data showed that, after the price increases, Aspen consistently earned very high profits (300% on average) from sales of the products in Europe, both in (i) absolute terms and (ii) when compared to the profit levels of comparators.
  - No legitimate reasons for Aspen's very high profits: Products off-patent for 50 years, i.e. R&D investment long been recouped.

EU Aspen Case – Case AT.40394 (cont‘1)

  - Lack of alternatives to these particular products, exacerbated by Aspen's (threats of) withdrawal.
  - Aspen's practices covered the entire EEA, although not every medicine is sold in each country.
- Aspen sought to address the EC's concerns with commitments. Following the market test, Aspen made adjustments revised commitments were considered to offer a fast, comprehensive and lasting solution.
- 10 February 2021: EC accepted Aspen’s commitments and closed the investigation. The commitments remain in force for ten years.

What has Leadiant added?

Leadiant – 4 Member States involved



Dutch Leadiant case - ACM/20/041239 (Facts)

2008

- Leadiant acquired a CDCA-based drug (Chenofalk) priced at EUR46 per 100 capsules. Leadiant rebranded the drug as Xenbilox, and increased the price to EUR885 in late 2009.

2014

- Leadiant applied for orphan drug designation and marketing authorization for its CDCA-based drug for the treatment of CTX; it raised the price of Xenbilox from EUR885 to EUR3,103 in July 2014.
- Product was granted orphan designation in late 2014 and the Marketing Authorization in April 2017 (conferring on Leadiant the exclusive right for ten years to treat CTX in the EEA).

June 2017

- Leadiant launched rebranded product (CDCA-Leadiant) on the Dutch market and stopped selling under the Xenbilox brand; ACM concluded that the two drugs were molecularly identical, and did not differ in efficacy, safety and form. Leadiant increased the price to EUR14,000
- ACM was concerned about the increase, taking the view that the July 2014 increase covered the costs associated with the orphan designation and related MA.

Dutch Leadiant case - ACM/20/041239 (ACM's conclusions)

Dominant position

- 100% market share (market for CDCA-based drugs for CTX treatment)
  - Kolban registered to treat CTX, but not prescribed in the Netherlands
  - Amsterdam UMC manufactured CDCA (compounding)
- Responsibility to negotiate actively and effectively with buyers to achieve a price that was not excessive

Abuse through Excessive prices

- ACM concluded that the price in combination with the low costs and the low risks resulted in an enormous return for Leadiant (*i.e.*, United Brands test)

Dutch Leadiant case - ACM/20/041239 (ACM's conclusions) (cont'1)

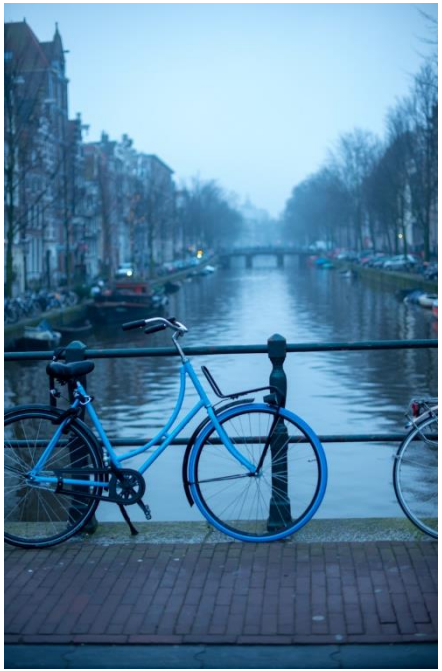
- Abused market exclusivity granted through the orphan drug designation
- Even the lower price that was envisaged by Leadiant was excessively high and unfair, and thus excessive

Unfairness of the prices

- Is the price exorbitantly high and unfair?
  - Can be the case with orphan drugs – issue is the way the exclusivity is used
  - High price can be justified if necessary to recoup high costs, the product offers many benefits or is innovative
  - The drug had already been on the market for years, under a different trade name, at a very much lower price (*i.e.*, 46 euros in 2008)

Dutch Leadiant case - ACM/20/041239 (ACM's conclusions) (cont'2)

- ACM looked at costs and revenues attributable to orphan designation (and MA)
  - Costs: investments since 2014, costs of manufacture and distribution, risk of project failure
  - Revenues: generated by Xenbilox (after 2014 increase) and CDCA-Leadiant
- Concluded the price was "unfair" because patients benefited little from orphan designation - rebranded product did not offer advantages over the product sold since 2008 and was not innovative
- Noted requirements for orphan drugs contribute to efficacy and safety; limited benefit for CDCA-Leadiant, since it had been safe and effective for prescription for CTX for decades
- Price was significantly higher than price for Chenofalk and Xenbilox (molecularly the same drug)



Italian Leadiant case - A524 – Measure No. 27940 (AGCM's conclusions)

- The AGCM found that:
  - Leadiant charged, since June 2017, the Italian health authority ("SSN") unfairly excessive prices for CDCA-Leadiant. It abused its dominant position on the Italian market for the production and sale of the drug. The price applied was €15,500 euros per pack.
  - Leadiant adopted dilatory and obstructive behaviour during price negotiations with the SSN.

Italian Leadiant case - A524 – Measure No. 27940 (AGCM's conclusions) (cont'1)

- Under the *United Brands* test, a price is unlawful when the undertaking has used its dominant position to gain commercial advantage that it would not have obtained if there was effective competition. The price did not have a reasonable relationship with the economic value of the product/service provided.
  - Leadiant never defined the price of CDCA-Leadiant based on costs; its formula reflected the maximum price that SSN was willing to pay
  - Quantification of the overall costs for the registration of the CDCA-Leadiant showed a level of costs below what would have justified such a high price.

Italian Leadiant case - A524 – Measure No. 27940 (AGCM's conclusions) (cont'2)

- AGCM used two methodologies to assess whether the price was excessive:
  - Financial methodology: based on internal rate of return (IRR). The authority concluded that the IRR was equal to at least [250-350%] of the cost of capital which was considered to be excessively disproportionate.
  - Accounting methodology: based on comparing sales revenues made in Italy and the cost (plus), *i.e.,* direct and indirect incurred by Leadiant. Measure of profitability quantified as a return on sales of 21%. Based on that, the excess for the period from the start of marketing CDCA-Leadiant in Italy up to the end of 2020 was equal to [60-70%].

Italian Leadiant case - A524 – Measure No. 27940 (AGCM's conclusions) (cont'3)

Unfairness of the price

AGCM concluded comparative criteria for analysis of unfairness inapplicable: no competing products that could be comparators for CDCA-Leadiant.

- AGCM concluded it was not appropriate to compare prices for CDCA-Leadiant in other member states, as its pan-European strategy was under scrutiny by various competition authorities.
- Unfairness of the price in itself:
  - CDCA-Leadiant was a repurposed drug – the molecule was already on the market, such that it could not be considered to be a newly introduced medicinal product. Changes meant that it remained equivalent to Xenbilox.

Italian Leadiant case - A524 – Measure No. 27940 (AGCM's conclusions) (cont'4)

- Low investment in research and development by Leadiant
- Investments made did not add therapeutic value compared to the therapies already on the Italian market:
  - Three drugs therapeutically identical
  - Leadiant was aware of the absence of added therapeutic value
  - Only difference was formal registration of CDCA-Leadiant for the treatment of CTX

Lessons learned

Lessons Learned

Start with a benchmark (in the first step of the United Brands test)

- In determining “excessiveness”, EC benchmarked profit margins of comparator companies
  - Aspen’s “comparators” generated majority of revenues from debranded medicines in the ATC-2 L1 category (i.e., active substances were similar)
  - Across Aspen’s comparators, 54% median gross profit margin and 23% median EBITDA margin. EC used 23% median EBITDA as proxy for “reasonable profit margin” (the “cost-plus level” for the Aspen products)
- Use reasonable profit margin proxy to determine whether profits are significantly above cost-plus level
  - Aspen’s were 280-300% in excess of cost-plus; on top of a reasonable return, Aspen’s profits were roughly three times cost-plus
  - Aspen’s EBITDA margin of 80-90% was higher than any of the comparators
  - EC used IQVIA data to build the comparator benchmark – enabling any company concerned about excessive pricing to identify a cohort of comparators with which to calculate a reasonable profit margin

Lessons Learned (cont'1)

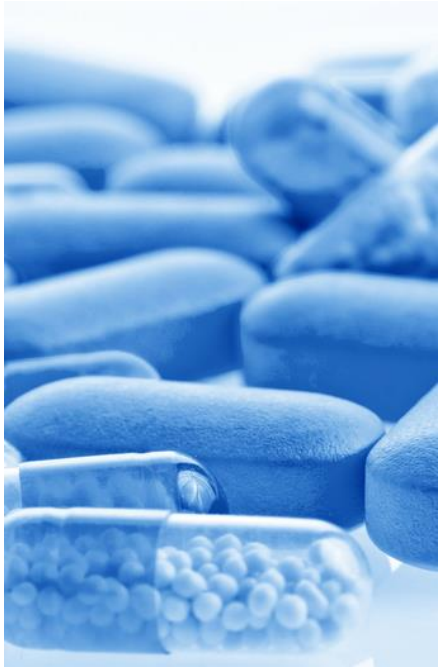
Check for materials suggesting "Intent" and "strategy" that could be used to support findings of exploitative abuse

- Whether the price is "unfair in itself" relevant in determining "unfairness"
- Consider whether internal materials could be construed as providing evidence that the products have not been improved through R&D, but that there is a strategy to "exploit national health systems" through disproportionate price increases without a legitimate reason
- Arbitrage between different pricing systems likely to be seen as being intended to "defeat the purpose and effectiveness of the external reference pricing systems and to avoid parallel trade"
  - Aspen made significant increases in Germany because the law allowed it to unilaterally set increased prices which it used to seek increases elsewhere
  - Aspen's unit cost for products had increased only 10-40%, while price increased 180-430%

Lessons Learned (cont'3)

Key role of the pricing regulatory regime

- Regulatory regimes allowing pharma companies to freely set the price
  - In UK, once drugs are off-patent (as discussed in *Pfizer/Flynn*)
  - In Italy, for class C drugs *i.e.,* non reimbursable drugs or in case of failure of the pricing negotiations with the authorities (as discussed in ASPEN)
    - Full discretion to set the price will be seen as a situation where the risk of "excessive pricing" is rather high
    - The risk will be even higher if the drug benefits from a legal or de facto dominant position (exclusivity resulting from orphan drug designation, absence of competitors, *etc.*)



Lessons Learned (cont'4)

Key role of the pricing regulatory regime (cont'd)

- Pricing regulatory regimes where price setting is heavily regulated, with multiple boundaries
  - In France / Spain:
    - No distinction between patent and off-patent drugs; No full discretion to set the price of reimbursable drugs
    - Pricing negotiations with authorities following legal criteria regularly updated; If the negotiations fail, authorities have the possibility to set the price unilaterally
  - In France, for specific reimbursable drugs (essential drugs representing a high financial burden for the health system): even if the price is set through tender proceedings, the pricing authority (CEPS) is still entitled to set a maximum price

Lessons Learned (cont'5)

Key role of the pricing regulatory regime (cont'd)

- In France, for orphan drugs whose annual cost per patient > 50k€ : the pricing authority may set an annual overall cap and requires that all patients are treated without any volume
  - the risk of "excessive pricing" is seen as lower, even in case of drugs benefitting from a legal or de facto dominant position. **However …**

    … this is not completely "waterproof"
- In France: the regulatory "boundaries" did not work in the ASPEN case (i.e., an increase of 1330% for Alkeran, from EUR 6,71 to EUR 96)
- It probably resulted from "pressure" (as was found to have been exerted in Italy and elsewhere) and a request for alignment with other EU reference countries

Lessons Learned (cont'6)

Conduct in Negotiations

- Undertone of conduct that could have a flavour of abuses of regulatory structure

Threats to withdraw products

Sequencing of price adjustments to use "reference" pricing model to increase prices in multiple jurisdictions

Higher prices in other jurisdictions do not justify increases in lower price jurisdictions

Not "actively engaging" with national health authorities/insurers to "effectively and seriously" negotiate prices

NRF

Lessons Learned (cont'7)

Allocating costs intra-group

- Determining rate of return requires identification of appropriate costs, costs of intangibles, and separation of costs of producing multiple products (where not all product prices alleged to be excessive)
- Direct costs calculated as a modified version of COGS (to ensure excessive costs can't be used to justify an excessive price). Where seller is manufacturer costs can include fixed overheads (excluding depreciation, impairment and amortisation)
- Indirect costs can include MA costs, operation/management costs of the entities involved in selling the products (where those costs are "spread" across the relevant products in the relevant counties)
- R&D costs are recoverable, if not already been recouped.
- Recovery of acquisition costs side stepped, with the EC noting
  - future anticipated profits do not justify excessive prices
  - Need to account for specific tangible or intangible assets when acquiring products, to enable return on cost of capital employed (ROCE) calculation

Lessons Learned (cont'9)

Pricing for off-patent drugs with regulatory exclusivity

- EC stresses need to preserve innovation incentives for new products (but does not rule out scrutiny of new products
- Assumption is that expiry of patent protection (and data exclusivity) triggers steep fall in prices as generics enter, but
  - Not necessarily the case in markets with limited demand
  - Not the case for orphan drugs, given the regulatory protection
  - Which brings us to Leadiant
    - First cases re pricing of product with valid regulatory exclusivity
    - Exercise of exclusivity conferred by orphan designation scrutinized
    - Dutch and Italian authorities emphasized limited innovation and investment in R&D (since molecularly equivalent products, been available for years) – confirming that authorities will look products with regulatory exclusivity where there are large price increases and limited innovation

Lessons Learned (cont'10)

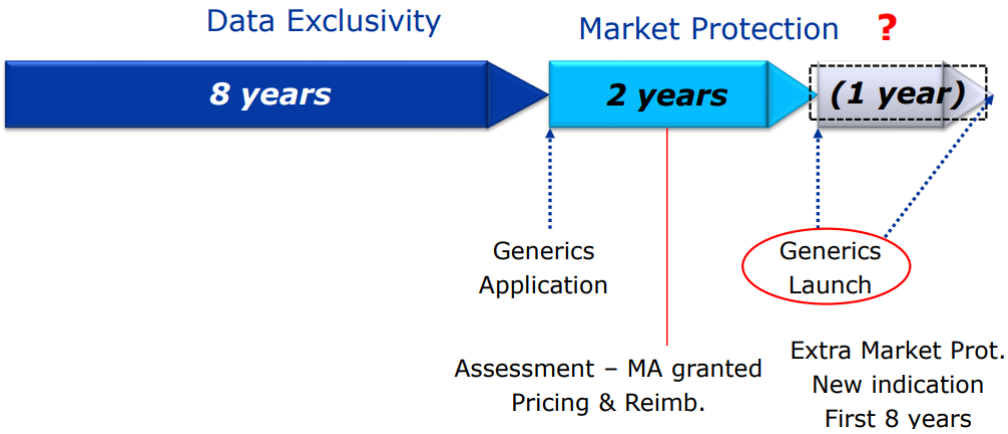
Scope of Regulatory exclusivities

Data exclusivity

New drugs benefit from an 8 years period of data exclusivtiy and a 10 years period of marketing protection

+ 1 years of data exclusivity in case of new indication for a well established substance

+ 1 year of market protection if the drug brings significant benefit in comparison with existing treatment or if MA for a new indication during the 8 years period



Lessons Learned (cont'10)

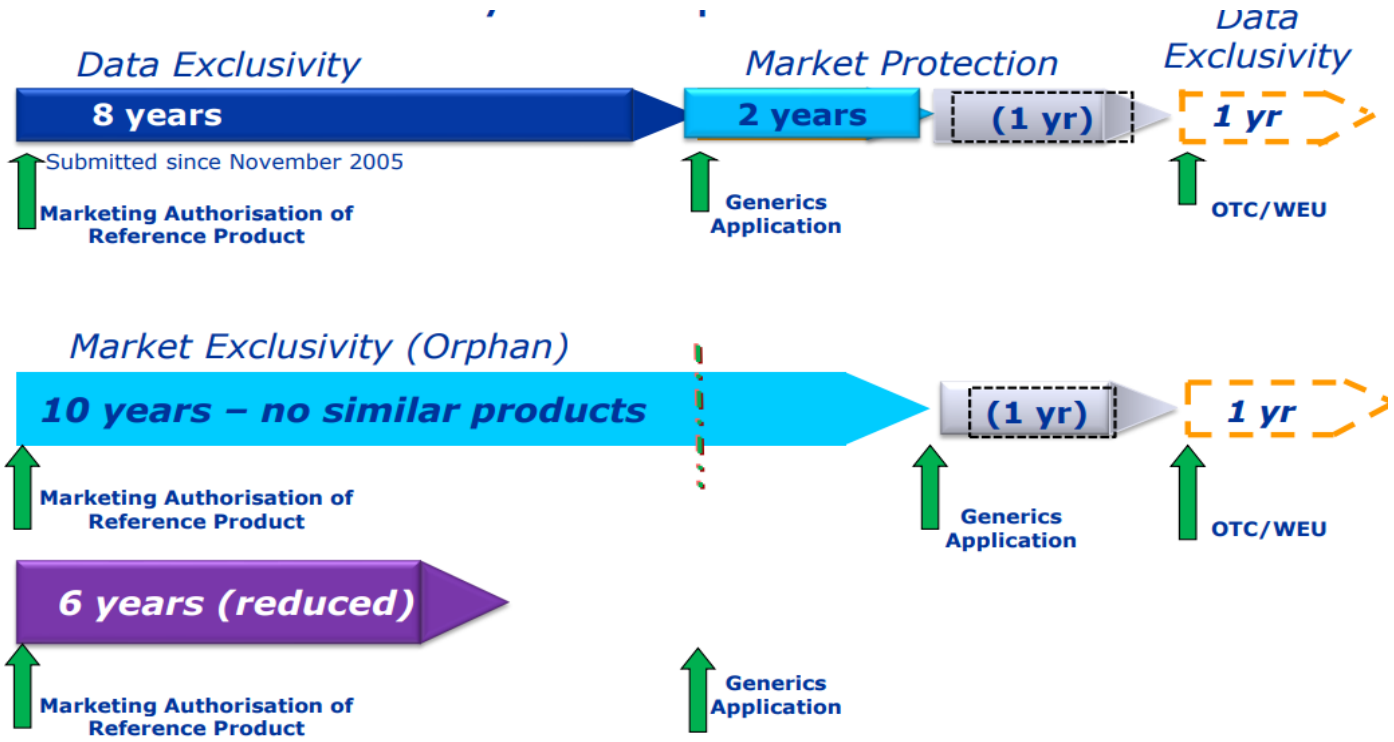
Orphan drug market exclusivity

- Market exclusivity of 10 years for each specific clinical indication with an orphan designation.
- A medicine that has mutiple orphan designations may benefit from separate market exclusivity periods.

Paediatric drug exclusivity

- Drugs authorized on the basis of a paediatric investigation plan (PIP) may benefit of a 6 months extension of their supplementary protection certificate (SPC).
- For orphan drugs, the market exclusivity is extended by 2 years (so 12 years).
- Medicines developed specifically for children that are already authorized but are not protected by a patent or SPC may be granted a paediatric-use marketing authorisation (PUMA) which give rise to a 10 years of market protection .

Lessons Learned (cont'10)



Lessons Learned (cont'11)

Compliance with regulatory framework

- Not an infringement to seek orphan designation (clearly), but also not a valid defense
  - Seeking orphan designation for a product long prescribed for the same orphan disease, knowing that there had been no molecular changes to the product, not unlawful
- Challenge to assumption that there is an "exclusivity" reward (from orphan designation) that confers unfettered discretion over pricing
- Price can increase to cover costs of obtaining orphan designation (and MA)
- Bear in mind *bpost*, *Deutsche Telekom et al* on the interaction of *ex ante* sector-specific regulation and competition law

Lessons Learned (cont'12)

Commitments structures

- "Transitory rebates" effectively used to reimburse payers (including patients making co-payments) for higher prices paid
- Question re what is appropriate level for post-commitment prices. In the Dutch Leadiant case, for example, the ACM only sanctioned 350% price increase in 2017; it did no address 1,800% increase in 2009 or 250% increase in 2014. Does that imply that reversion to the pre-orphan designation price is not excessive?
- UK CMA has negotiated repayments to the NHS (which may not have been possible to include in a formal infringement decision)
- EC officials have noted that purchasers seeking to recover potential "excessive payments" could pursue claims based on internal documents produced during investigation, and rely on the benchmark methodology used by the relevant authority as a start point for loss calculation.

Anything to add?

Debate around application to new patented products

Chair of the ACM and colleagues published re pricing of new patent protected pharmaceuticals (2018)

- Different threads in debate
  - Restrict excessive pricing to situations where investment and innovation play minor role, otherwise risk undermining essential objective of IP rights
  - Mechanism appropriate if endemic pricing problems (exploitative rather than exclusionary issue)
- Those in favour of excessive pricing being enforced in relation to patented products assert that incentives for innovation can be taken into account because
  - Ex ante probabilities of success and other metrics relevant for innovative products can be accounted for under the “excessive” limb (the first limb) of United Brands. How? Survival bias trap needs to be avoided.

Debate around application to new patented products (cont/1)

  - Market entry (which drives dynamic and allocative efficiency) would not be impaired? Argument is that entry would only be impaired where the relevant market does not include therapeutic alternatives (since competitive entry remains the most efficient solution otherwise). In the pharma world, there often aren't therapeutic alternatives, however…
- Some proponents point to regulatory measures (*e.g.*, maximum willingness to pay thresholds) as evidencing welfare justifications (although this rather suggests that competition law is not the appropriate instrument)

See

- "Excessive Pricing in Pharmaceutical Markets – Note by the Netherlands" (28 November 2018) in OECD (2018), *Excessive Prices in Pharmaceutical Markets* (http://www.oecd.org/daf/competition/excessive-pricing-in-pharmaceuticals.htm)
- "ACM Working Paper – Reconciling competition and IP law: the case of patented pharmaceuticals and dominance abuse", Fonteijn, Akker and Wauter, 2018. (ACM Working Paper: Reconciling competition and IP law: the case of patented pharmaceuticals and dominance abuse | ACM.nl)

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