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Excessive Pricing in Pharmaceutical Markets – Note by the Netherlands

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www.oecd.org/daf/competition/excessive-pricing-in-pharmaceuticals.htm

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1. Pharmaceutical pricing is increasingly a topic of public frustration and outrage, and some cases do seem self-evidently abusive.¹ Yet taking a policy perspective on possibly excessive pharmaceutical pricing inevitably involves not just looking at prices as such but addressing the tension between innovation and cost control.² Evidently the unmet need for new treatments requires incentives to innovate, not least to finance such innovation. The rewards for investment must therefore be sufficiently attractive. This may conflict with the societal need to control healthcare expenses inter alia given their apparent innate tendency to grow at rates exceeding GDP and the resulting displacement effect on other types of public expenditure – including the displacement of other health needs by increased expenditure on expensive drugs.

2. ACM is aware of how, in public policy, the balancing required by the inherent tension between these two objectives, is reflected both in the choice of instruments, regulation and competition policy, and in the manner in which they are deployed. The tension between innovation and cost control also arises in the relationship between intellectual property rights and competition law, and within competition law when looking at the issue of excessive pricing: when it may occur, whether the application of competition rules is justified, and how they could practically be applied.

3. In this paper, we will first briefly discuss and compare the instruments involved: excessive pricing under Article 102 TFEU and (very briefly and generally) EU pharmaceutical regulation. Second (and in greater detail) we will focus on the excessive pricing tool, addressing i. the compatibility of competition rules with intellectual property rights and related rights and ii. how to account for innovation under the legal test of excessiveness, specifically survival bias and cost of capital. In conclusion we will briefly recap the above while focusing on answering the question under what conditions pursuing excessive pricing cases under competition policy is a credible, desirable and practical approach in the pharmaceuticals sector.

4. We do not intend to fundamentally question the regulatory framework in this paper. Our working assumption is that the applicable EU and national pharmaceutical regulation is broadly in working order and that competition policy primarily serves to correct regulatory and/or market failures at the margins. However if we are wrong and there is a

¹ For two well-used examples see e.g. Zoe Thomas and Tim Swift, “Who is Martin Shkreli - 'the most hated man in America'?”, *BBC News*, Washington 4 August 2017, with regard to a 5000% overnight price increase of a life saving drug Daraprim (used to treat infections in babies and aids patients) at Turing Pharmaceuticals; and John LaMattina, “Gilead's CEO Admits To 'Failures' In Setting Price of \$1,000-A-Pill Breakthrough”, *Forbes*, 8 December 2016, with regard to Hepatitis C Drug Sovaldi.

² See e.g. Sarah Wheaton, “5 BIG reasons Europe sucks at curing cancer: Why does the US outperform the EU in drug research?” Global Policy Lab, Politico, 4 October 2018; <https://www.politico.eu/article/cancer-5-big-reasons-europe-sucks-at-curing/> In our view the article mainly shows that the US outperforms the EU financially, i.e. in raising public funding for research and subsequently monetising the results privately (we would add: again at a significant cost to the public purse), not in medical invention and innovation as such. However it also shows that time to market for cancer drugs (often based on research done in the EU) is shorter in the US with consequently better health outcomes.

structural problem with regard to high prices for pharmaceutical products, or a recurrent problem that the competition rules cannot address, the next question would obviously be whether there is a need to correct the regulatory regime, and if so, in what manner. We will not deal with this issue systematically here.

1. Instruments involved

5. First we will now briefly consider the instruments involved, first more abstractly, and then in relation to the actual regulatory regime.

1.1. Elements of a binary division

6. When looking at high prices for pharmaceutical products the question naturally arises whether this is properly a subject where policy based on the general competition rules should be applied, or whether it should be sectoral regulation in the form of legal rules specific to medicines. More generally, the debate of competition law versus regulation is a long and involved one that is certainly not new in the OECD framework.³

7. Broadly generalizing, from a practical perspective deciding on which instrument to use includes variables that coincide with key characteristics of these instruments such as:

- Pursuing individual more exceptional cases v general rules for standard situations
- Corrected by courts v elections and checks and balances of law making
- Legal rules applicable across sectors v sector specific rules
- Independent enforcement v democratic legitimized law
- Flexibility in approach v structural solutions
- Speed v scope and predictability⁴

8. In each case the competition law approach is found to the left and the sectoral regulation approach to the right side of the “v” sign. To some extent this binary distinction is obviously artificial and the probable outcome of any exercise in comparing these instruments is that they are in many instances complements more than alternatives. In actual fact we also see that pharmaceutical products are subject both to regulation, and to application of the competition rules. Consequently in this paper we will not focus on this issue. However we will use the dichotomy between competition and regulation as a

³ Niamh Dunne, *Competition law and regulation: making and managing markets* (Cambridge University Press, 2015); Martin Lodge, Robert Baldwin and Martin Cave, *The Oxford handbook of regulation* (Oxford University Press, 2010); <http://www.oecd.org/competition/reform/> For a discussion of Dutch healthcare pricing from a regulatory perspective in the context of a discussion of excessive prices see also the OECD submission by Misja Mikkers and Wolf Sauter, *Some background on excessive prices*, DAF/COMP(2011)18, 405-411.

⁴ Obviously we are talking about speed in relative terms here and not in any sense recognizable to the general public. Both can take years to complete, especially if judicial review is included on the competition side. However laws must also first be implemented and enforced, not just adopted, before the game begins. In addition competition procedures normally allow for settlements and exceptionally for expedited intervention such as interim measures. See e.g. Luis Ortiz Blanco (ed), *EU competition procedure*, 3rd edn (Oxford University Press, 2013).

backcloth to our discussion, in order to be able to say more on the balance between the two in our conclusion below.

1.2. The competition rules

9. Concerning the competition rules, we will limit ourselves to the EU. Here we have a prohibition on unfair pricing in Article 102a TFEU which concerns “directly or indirectly imposing unfair purchase or selling prices or other unfair trading conditions”. In the celebrated *United Brands* Case of 1978 (concerning bananas) a twostep test was introduced for excessive pricing: (i) a cost based determination of excessiveness – essentially based on comparing the actual margin with a normative framework; and (ii) a determination of whether the resulting margin is also unfair, either as such – for instance based on an unjustified price hike – or by means of a meaningful comparison across other products, countries or a combination of both.⁵

10. This cost-based test was then effectively sidestepped in the main subsequent case law on excessive pricing, that primarily regarded music rights.⁶ This is not surprising as in these cases the fixed costs are difficult to establish or irrelevant and the variable costs close to zero. In *AKKA/LAA*, a similar recent case, the Court therefore established price comparisons as a possible alternative for the excessiveness leg of the test, which if shown could be countered by a fairness defense by the undertaking, for instance based on costs and therefore the margins involved, but also on other justifications.⁷ Advocate General Wahl in particular in his Opinion in this case emphasized the role of benchmarks, which he equated with the competitive price that could be based, largely, on comparisons.⁸

11. What these approaches have in common with *United Brands* is that they seek to establish whether the price has a reasonable relation to the economic value of the product.⁹ In this context the role of demand has been especially difficult to accommodate. Of course the position of the Court has always been that multiple methods can be used (and increasingly: should be used) to establish excessive prices. Hence it should not come as a surprise there is currently no standard method.

12. Over the past two years various national competition authorities in the EU, notably the Italian AGCM and the CMA in the UK have taken up excessive pricing cases with regard to pharmaceuticals based on the classic *United Brands* approach set out above.¹⁰ The

⁵ Case 27/76, *United Brands Company and United Brands Continentaal BV v Commission*, Judgment of 14 Februari 1978, ECLI:EU:C:1978:22, paras 248-253.

⁶ Notably Joined cases 110/88, 241/88 and 242/88, *François Lucazeau et al. v SACEM et al.*, Judgment of 13 June 1989, ECLI:EU:C:1989:326; Case 395/87 *Criminal proceedings against Jean-Louis Tournier*, Judgment of 13 July 1989, EU:C:1989:319.

⁷ Case C-177/16 *Autortiesību un komunikēšanās konsultāciju aģentūra/ Latvijas Autoru apvienība v Konkurences padome (AKKA/LAA)*, Judgment of 14 September 2017, ECLI:EU:C:2017:689.

⁸ Case C-177/16 Opinion of AG Wahl, 6 April 2017, ECLI:EU:C:2017:286, paras 17ff and 38ff.

⁹ Case 27/76, *United Brands Company and United Brands Continentaal BV v Commission*, Judgment of 14 Februari 1978, ECLI:EU:C:1978:22, para 250.

¹⁰ Such as in Italy and the VK: Aspen Pharmaceuticals (Case A480) AGCM Decision of Besluit van 29 September 2016; Pfizer (Case CE/9742-13) CMA Decision of 7 December 2016. The Danish

CMA's Decision in *Pfizer/Flynn* was overturned recently by the Competition Appeals Tribunal, who arguably extended the line set out in *AKKA/LAA*. In particular it required more emphasis on the economic value of the product concerned, and on price benchmarking instead of the cost-plus approach adopted by the CMA.¹¹ Although it is clear that price comparisons have become a more important alternative to the cost based approach assumed in the past it is arguably a case by case decision which approach to take, based on the balance of the facts and the context of each case. It will be interesting to see what approach the European Commission will take, which launched a pan-EU investigation into the excessive pricing by pharmaceutical company Aspen in 2018.¹²

1.3. The regulatory regime¹³

13. Regarding excessive prices in pharmaceuticals, patent protection is especially important as a general device designed to protect innovation. Patents typically run for 20 years. However because of the lengthy time to market given the necessary regulatory approval the EU has introduced supplementary protection rights (SPCs) which effectively extend the exclusivity term (remaining patent plus SPC) following market authorization to 15 years, a pediatric extension, and a data protection regime. In addition the EU has created a special regime for orphan drugs, which provides for a monopoly on the disease instead of on the invention, in order to promote research and drug development for rare diseases.¹⁴ Orphan status lasts 10 years, and is based on the alternative criteria of prevalence (1:2000 persons) or demonstrable lack of potential profitability (a rarely used option). The complex

competition authority made a similar announcement: 'CD Pharma has abused its dominant position by a price increase of 2000 percent', Press release, 31 Januari 2018.

¹¹ *Pfizer Inc. and Pfizer Limited v Competition and Markets Authority*, Judgment of 7 June 2018 [2018] CAT 11.

¹² European Commission, 'Antitrust: Commission opens formal investigation into Aspen Pharma's pricing practices for cancer medicines'. IP/17/1323.

¹³ We do not intend to be complete in our description of the regulatory regime in this contribution, as this would merit a whole study in itself. The purpose of our description of regulation here is to position regulation as an instrument vis a vis applying competition law for balancing the tension between innovation and cost control. For a complete overview, we would like to refer to [M.I. Manley and M. Vickers \(eds\), Navigating European pharmaceutical law \(Oxford University Press, 2015\)](#), [S. Shorthose \(ed\), Guide to EU pharmaceutical regulatory law, 6th edn. \(Wolters Kluwer, Alphen aan den Rijn, 2015\)](#).

¹⁴ See Regulation (EC) 469/2009 of the European Parliament and of the Council of 6 May 2009 concerning the supplementary protection certificate for medicinal products [2009] OJ L152/1; Regulation (EC) 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products [2000] OJ L18/1; Regulation (EC) 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use [2006] OJ L378/1; Regulation (EC) 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorization and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency and Directive (EC) 2001/83 of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use [2001] OJ L311/67 as amended by Directive (EC) 2004/27 of the European Parliament and of the Council of 31 March 2004 [2004] OJ L136/34.

universe of EU pharmaceutical law thus provides a number of IP rights and related rights (henceforth: IP rights) awarding various types of exclusivity that are often cumulative.¹⁵

14. In addition the EU regulates market access: market authorization is centralized for various types of medicines such as cancer drugs, and for orphans. In this respect, as with regard to the patent and related rights mentioned above, an internal market is effectively in place. However the rules on financial reimbursement that typically seek to control costs are purely national in nature – and therefore both fragmented and characterized by a disconnect from the EU level IP and market access rights. Moreover regarding the effectiveness of the EU level rules there is conceptual divergence between EU Member States with a significant stake in the production of pharmaceuticals, and who are home to big pharmaceutical companies, and those who are primarily consumers and not producers.

15. Needless to say this raises the question whether the EU regulatory regime provides the right incentives. Several elements of the regulatory framework are presently being re-evaluated, notably the Orphan Drug and Paediatric Regulations (for rare diseases, and for children respectively).¹⁶ When recently looking at supplementary protection certificates however the EU Commission appears to have focused more on the investment climate for pharmaceutical companies.¹⁷ At EU level therefore there is a third variable, industrial policy, alongside innovation and cost control. Industrial policy however is outside the remit of this paper.¹⁸

1.4. Working assumption

16. As stated above, we do not intend to fundamentally question the regulatory framework in this paper. Our working assumption is that the applicable EU and national pharmaceutical regulation is broadly in working order and that competition policy primarily serves to correct regulatory and/or market failures at the margins.

2. IP and excessive pricing rules: conflict or compatibility?

17. It has sometimes been charged (especially perhaps by those benefitting either directly or indirectly from their monetisation) that the existence of IP rights and related rights effectively excludes the application of the competition rules. In EU competition law

¹⁵ See generally M. I. Manley And Marina Vickers (eds), *Navigating European pharmaceutical law* (Oxford University Press 2015) and S. Shorthose (ed), *Guide to EU pharmaceutical regulatory law*, (6th edn, Wolters Kluwer 2015).

¹⁶ Regulation (EC) No 141/2000, above n 15 and Regulation (EC) No 469/2009 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004, OJ 2006, L378/1; <https://ec.europa.eu/info/law/better-regulation/initiatives/ares-2017-6059807>.

¹⁷ European Commission, DG MARKT, Study on the economic impact of supplementary protection certificates, pharmaceutical incentives and rewards in Europe (carried out by Copenhagen Economics), Brussels 11 September 2018.

¹⁸ See however G. Permanand. *EU pharmaceutical regulation: The politics of policy-making* (Manchester University Press, 2006).

this is not so: the two types of law are not alternatives or mutually exclusive but apply in parallel. So legally, the existence of an IP right does not automatically mean that there is a dominant position in place, nor is obtaining or extending an IP right normally an infringement. And the existence of a dominant position in a particular relevant market, in addition to proof of an infringing behaviour, is required to establish an abuse in EU competition law. At the same time the existence of an IP right does not provide competition law immunity either. Hence from a legal perspective we submit that IP and competition law are not mutually exclusive but instead apply in parallel.

18. In an earlier paper with Chris Fonteijn (on which we also draw for the remainder of this section) we addressed this issue at length. Hence, here we will limit ourselves to the two main arguments against enforcing the prohibition on excessive pricing with regard to pharmaceuticals more on economic or policy (rather than strictly legal) grounds, while adding a new third element as yet not fully developed.¹⁹

2.1. Innovation and investment

19. A first objection against targeting high prices as excessive prices under the competition rules is that this may undermine innovation and the risky investment that is required to fund such innovation. (Although notably actual drug discovery is frequently funded publicly.) High prices may be considered a market based reward for risky investment. In this context special caution is required with respect to products covered by IP rights because here innovation is involved by definition and the misapplication of the excessive pricing prohibition might directly impede future innovation. A conceptual trap to avoid here is survival bias: capping profits on successful products without taking the ex-ante possibilities of failure into account could jeopardize the incentive to invest and thereby the possibilities to innovate.

20. However there is no necessary tension between the objectives of intellectual property law –and excessive pricing. This does presuppose that the enforcement of the prohibition on excessive pricing takes the incentives for innovation into account. Vice versa the existence of patent protection does not bar enforcement of the excessive pricing prohibition. One way to take innovation incentives into account when looking at prices and costs, and therefore margins, is to include ex-ante probabilities of success under the relevant test. This is a way out of the abovementioned conceptual trap. It would allow pharmaceutical companies to continue making significant but not unlimited profits based on successful innovation, protecting socially valuable investment. Conversely, where effectively no such innovation, or little of it, can be shown lower margins would already trigger excessive pricing review of pharmaceutical products.

2.2. Market entry and efficiency

21. The second objection is that by encouraging market entry high prices promote both dynamic and allocative efficiency. This means that from a perspective of economic efficiency, the preferred mechanism to reduce prices would not be regulation or competition policy intervention, but a competitive response in the market. If excessive

¹⁹ See Chris Fonteijn, Ilan Akker & Wolf Sauter, “Reconciling competition and IP law: the case of patented pharmaceuticals and dominance abuse”, in Marianna Tavassi and Gabriella Muscolo (eds.), *The Interplay between Competition Law and Intellectual Property - An international perspective* (Kluwer Law International, Deventer), forthcoming 2019, and the references quoted there.

pricing cases are pursued aggressively *where scope for effective entry exists*, the mechanism promoting entry would be eroded.

22. Here entry barriers are key: IP rights may constitute such barriers. This is also why the existence of IP rights reduces our concern about the effect of price as a signal for entry. They reduce the relevance of entry right up to the point where protecting entry may no longer be a significant consideration as regards the application of competition law. This may be the case especially for orphan drugs with their 10 year exclusivity on the specific disease that they treat.²⁰ However IP rights do not automatically create a monopoly that forms a dominant position because the scope of the IP right does not necessarily coincide with the definition of the relevant markets at hand. Orphan drugs usually excepted, there may well be therapeutic substitutes that compete with each other. This means that a relevant market must be defined, and dominance established there by looking inter alia at the existence of effective competitors, not merely at the existence of IP rights.

2.3. Fairness

23. To these two arguments that we already set out in our earlier paper we would like to add a third one. Arguably efficiency and innovation are not the primary concerns of Article 102 sub a TFEU in the first place.²¹ Literally this provision speaks of unfair pricing (*directly or indirectly imposing unfair purchase or selling prices or other unfair trading conditions*), and excessive pricing regards the exploitation of consumers. Although efficiency and combatting exclusion has long held sway in EU competition law it is not the only legitimate concern – alongside effective competition and market structure, including the creating and protection of the internal market. Rather fairness, as an element of the European Union’s goal to prevent discrimination and promote social justice (article 3 TEU), also referenced in the preable of the TFEU, may be developing into a substantively relevant dimension that expands the reach of at least Article 102 sub a TFEU beyond the traditional predominance of efficiency considerations.²²

24. Fairness is so far not a recognized standard in and of itself. However, in the context of excessive pricing for pharmaceuticals, eventually more emphasis may be placed on a fair distribution between producers and consumers. This is a matter of striking a balance. In the context of such a distribution, it is both already possible and justified to take different degrees of innovation into account. That is to say that a stricter cost based test can and should be applied to drugs that involve limited innovation than to those where a significant investment in developing new cures is involved. This will be examined below.

²⁰ Regulation (EC) 141/2000 (n4). There are some exceptions, notably for drugs that are safer or more effective. However investing in such drugs is discouraged as there can be no certainty of such superior performance in advance.

²¹ Competition Commissioner M. Vestager, Fairness and Competition, speech 25 januari 2018, https://ec.europa.eu/commission/commissioners/2014-2019/vestager/announcements/fairness-and-competition_en and DG COMP Director General J. Laitenberger, Fairness in EU competition law enforcement, speech 20 juni 2018, http://ec.europa.eu/competition/speeches/text/sp2018_10_en.pdf

²² For a critical view: M. Trebilcock and F. Ducci, : The multifaceted nature of fairness in competition policy”, *Competition Policy International Antitrust Chronicle*, October 2017, <https://www.competitionpolicyinternational.com/wp-content/uploads/2017/10/CPI-Trebilcock-Ducci.pdf>.

3. Accounting for innovation in cost research

25. Above, we have argued that there is no necessary conflict between IP rights and excessive pricing. The existence of IP rights are however relevant in the analysis of excessiveness and require a certain degree of caution, although not the kind of general caution that would lead us to regard such cases as off-limits. Rather we propose that in such cases the effects on the incentives to innovate should be taken into account. The two most important issues for cost research in this respect are (i) accounting for the costs of R&D efforts that did not lead to market introduction and (ii) calculating the cost of capital.

26. It is important to tackle the issues of R&D costs and capital costs separately and as different concepts – even though there is a relationship between them. A crucial distinction is that unsuccessful R&D is a technical risk that is in principle diversifiable from the perspective of the investor, whereas the cost of capital can only be calculated based on non-diversifiable risk.

- **R&D investment risk:** to give a simplified example: suppose R&D projects in new drugs have only two possible outcomes: (i) *Market Access* and (2) *Total Failure* and that the chance of a product obtaining market access is 10%. Suppose further that the costs for the successful are €100 million and the investments on the non-successful drugs are on average €50 million.²³ A single project with a 90% chance of failure seems like a high risk investment. However if we look at a larger portfolio, an investment in ten projects (on average an investment of €550 million) has a 65% chance of at least one successful market introduction. With investments in even more projects with independent risks this percentage will increase further. The so called probability of success (POS) should therefore be seen as a technical risk that can largely be diversified. A trap to be avoided here is punishing successful or lucky investment solely based on ex post outcomes. In order not to undermine investment incentives (and thereby innovation) we suggest that the ex ante POS should be taken into account.
- **Capital costs:** by contrast the cost of capital is only to a limited extent affected by technical risks. This effect exists where the risk is non diversifiable. For example lower success rates lead to higher fixed costs, which increases the cost of capital. At the same time the value of the weighted average cost of capital (WACC) can be of an enormous influence as IP competition cases would often require taking a longer period of time into account. This means that cost research in an IP-context generally requires taking longer periods of time into account (preferably a whole life cycle).

27. It is important to stress that the IP rights protecting different drugs create property rights that cover to various degrees of underlying innovation and originality. The importance of analyzing the effects on the incentives to innovate also depends on the extent of actual innovation that is involved.

28. For example orphan designations that essentially monopolize the medical condition involved rather than the effective ingredient are granted both to new innovative drugs as well as to long existing drugs. Even the latter may in some cases constitute a bona fide breakthrough if it concerns a new application. In other cases however registration merely formalizes already existing practice, for instance if the drugs was already used off label or

²³ For simplicity of the example we keep the costs of capital at 0.

as a magisterial preparation. An excessive pricing case in this instance is obviously less complicated regarding the balance between innovation and cost containment than a case concerning truly innovative products based on original research. Consequently, probabilities of success, capital costs and the life cycle approach are in such situations less (or not at all) relevant.

4. Accounting for survival bias

29. Here we will further develop how technical risk and specifically survival bias could be taken into account in an analysis of excessive pricing. By survival bias we mean the trap of only considering successful R&D investments when analyzing excessive pricing. If we disregard failures – either real or in terms of ex-ante scenario’s – we would not be able to distinguish between (i) excessive prices and (ii) high profits as a consequence of success or pure chance. If we then intervene solely based on ex post profits this would seriously interfere with incentives to invest ex ante.

30. It is useful to think of R&D in the pharmaceutical sector as a collection of related and conditional subprojects. Investments in pre-clinical trials either may lead to a phase 1 clinical research trial or to the abandonment of the project as a whole. The costs involved tend to increase in every phase closer to actual market access, although the same is true for the probability that the specific drug will receive market access: the odds improve.

31. Below we discuss two possible approaches to account for the ex-ante multitude of possible scenarios. These are (i) using the development costs of bringing one single drug to the market and (ii) using the average success rates of clinical research. After discussing those two approaches, we will go into a difficulty that is relevant for both approaches, namely the wide variety of commercial success of drugs.

4.1. Approach 1: using the development costs of bringing one single drug to the market

32. In the first approach the way to deal with possible survival bias is to complement cost research with the average costs of bringing a single drug to the market. This would mean that a company could have large profits in case of success, in terms of advancing from R&D to market access. Ideally, these costs benchmarks would be specific for the type of drug involved. There is relatively abundant literature that estimates the costs of bringing a single drug to market, accounting for failures. A serious problem is however that the different studies arrive at very different estimates. So far the highest estimate is made by DiMasi et al. (2016).²⁴ Their study arrives at an estimate of \$1395 million out of pocket.²⁵ With an average time period between the initial investment and sales of 7 years and 10,5% capital costs, the authors arrive at \$2870 million capitalized costs. Note that more than 50% of costs are capital costs: we will come back to this in our discussion of the costs of capital

²⁴ Joseph A. DiMasi, Henry G. Grabowski & Ronald W. Hansen, “Innovation in the pharmaceutical industry: New estimates of R&D costs”, *Journal of Health Economics*, volume 47, May 2016, p. 20-33.

²⁵ In terms of 2013 prices

below. The lowest estimate shows capitalized costs of \$161 million²⁶, which is almost 18 times lower than the estimate of Dimasi et al.

33. These enormous differences in estimates are not just a recent phenome. Morgen et al. (2011)²⁷ concluded in their review of articles on this issue that these studies are neither transparent nor replicable. They explain the variations in estimates by the different methodologies used. DiMasi et al (2016) is based on self-reported data of pharmaceutical companies with regard to a set of unknown drugs. Young et al (2001) aggregate R&D costs of pharmaceutical companies and divide them by the number of FDA-approvals in one year, resulting in much lower costs than the study of DiMasi et al.²⁸ Other examples of relevant methodological choices are (i) incorporation or exclusion of tax benefits and (ii) the choice to include or exclude registrations of already registered molecules.

34. Reliable and replicable studies on the costs of bringing a single drug to the market would be very valuable for competition authorities. The problems identified are however likely to persist in the short run. As a pragmatic solution and to err on the side of caution (or to avoid type 1 errors), the higher estimates would arguably be most suited as a cost benchmark. In the meantime, we would strongly recommend independent research in this area. Profits could then be calculated not just in relation to the actual costs, but also to the benchmark costs of bringing a medicine to the market. However one could argue that even this benchmark is not adequate, as market access is not the same as market success. We will address this problem after discussing the second approach to account for survival bias.

4.2. Approach 2: using average success rates of clinical research

35. A second way to avoid survival bias is to take ex-ante probabilities into account directly. There have been several studies that estimate the probability of success when moving from phase 1 clinical research to phase 2, to phase 3 and ultimately approval. Fortunately, the outcomes of these studies are much closer than the earlier described studies of costs to bring a single drug to the market. We want to mention especially two studies that are both based on databases of the relevant pipeline information of pharmaceutical companies. Those studies are (i) Wong et al. (2018)²⁹ and (ii) Hay et al (2014).³⁰ Wong et al. arrive at a total POS of 13,8% and Hay et al. at a POS of 10,4%. Both find higher POS of so called lead indications, namely 15,3% and 21,6%. Both studies also differentiate between indication types. An important conclusion is that oncology drugs have a remarkably lower POS – in Wong et al. of only 3,4% - than other indications.

²⁶ Steve Morgan, Paul Grootendorst, Joel Lexchin, Colleen Cunningham & Devon Greyson, “The cost of drug development: A systematic review”, *Health Policy*, volume 100, issue 1, April 2011, p. 9.

²⁷ Morgan, Grootendors, Lexchin, Cunningham & Greyson (2011), The cost of drug development: A systematic review, *Health Policy*; 100 (2011) 4-17

²⁸ Bob Young, Michael Surrusco, “Rx R&D myths: the case against the drug industry’s R&D ‘Scare Card’”, Public Citizen Congress Watch 2001, Washington D.C.

²⁹ Chi Heem Wong, Kien Wei Siah & Andrew W. Lo, “Estimation of clinical trial success rates and related parameters”, *Biostatistics* 2018, p. 1-14.

³⁰ Michael Hay, David W. Thomas, John L. Craighead, Celia Economides & Jesse Rosenthal, ‘Clinical development success rates for investigational drugs’, *Nature Biotechnology*, volume 32, no. 1, January 2014, p. 40-51.

36. Those numbers are in themselves already quite useful. Taking Hay et al. 10,4 % for all indications tells us that on average a pharmaceutical company would have to invest in roughly 10 indications in order to bring a single drug to the market. These studies do however also help us to estimate how much is invested in those drugs that made it to market approval. For example, whereas investment in roughly 10 indications is on average necessary to arrive at a single approved drug, only 6 phase-II study and 2 phase-III studies investments are necessary on average. Table 1 shows first the probabilities of advancing to the next (clinical) phase based on Hay et al (2014). The total probability of success of 10,4% is a multiplication of those percentages. Table 1 also shows the number of trials in every phase that is on average necessary to get one product to the market.

Table 1.

	Phase 1	Phase 2	Phase 3	Approval
Phase to phase POS	64%	32%	60%	83%
Amount of studies needed on average for 1 approval	9,6	6,2	2,0	1,2

Source: calculation based on results Hay et al 2014

37. This type of information provides us with an idea of how much failed R&D research should be taken into account when assessing costs of a patented drug. This is both relevant for determining which i. actual failures a company could reasonably bring in as failed R&D costs for a drug under investigation, as for ii. adjusting the cost basis of successful companies. The latter is more likely to be relevant for pharmaceutical companies with a limited number of marketed products and products in their pipeline.

4.3. The diversity of market success

38. Here we will delve into a complication that may arise in both approaches. As already mentioned, one could argue that the approaches described above do not take into account the fact that drugs may have very different degrees of commercial success. Even after a correction for the probabilities to receive market access, high profits may still be justified based on the commercial success. Importantly the number of ex-ante scenarios of commercial success are potentially unlimited and do not fit the simple world of failure and success. Some sources have estimated that between 70% and 80% of the products that reach market access, have sales that do not cover the capitalized costs.³¹ High profits may just be an ex-ante unlikely outcome that would not be excessive from this ex-ante perspective.

39. Hence, it could be argued that the commercially successful drugs do not only have to cover R&D that does not lead to market access, but also drugs with limited commercial success. This argument is however flawed in the sense that all investments projects are in principle independent. The decision to invest or not to invest depends on the prospects of the actual project, including all its possible scenarios and probabilities. It would therefore make more sense to argue that commercially successful drugs have to cover for the ex-ante probabilities of failure and limited success. Knowledge of the ex-ante scenario's would therefore be helpful to qualify such a claim in an individual case. It is questionable however that reliable information can be found in practice, especially given the time lack between

³¹ John A. Vernon, Joseph H. Golect & Joseph A. Dimasi, "Drug development costs when financial risk is measured using the Fama-French three-factor model", *Health Economics*, volume 19, issue 8, August 2010, p. 1002-1005

the actual investments and the competition case. At first glance alternative methods seem necessary to deal with the commercial success claim.

40. The use of benchmarks could be such an alternative. The distinction between commercial success and excessiveness also raises the issues of how to determine the value of a drug to society and possibly how this value should be distributed between the demand- and supply side. This is an area that is still much debated and in our view under-researched. What seems clear is that as a matter of the applicable EU law benchmarks are the most appropriate method in bridging this gap. At least this is in line with the recent case law in *AKKA/LAA* and the CAT³² judgment where benchmarks play a central role.

41. In the Dutch context, the price of €80 thousand per quality adjusted life year (Qaly) would be such a benchmark value. The Qaly allows the price of a drug to be compared with that paid for other drugs (and other medical treatments) in terms of relative health outcomes and thus value. Canoy & Tichem show in their working paper that higher prices are welfare decreasing and harm investment incentives.³³ Higher prices are consequently in themselves problematic and in itself an indication of excessiveness. In our view the Qaly approach is complementary to cost research, especially for its independence of ex-ante probabilities.

5. Cost of capital

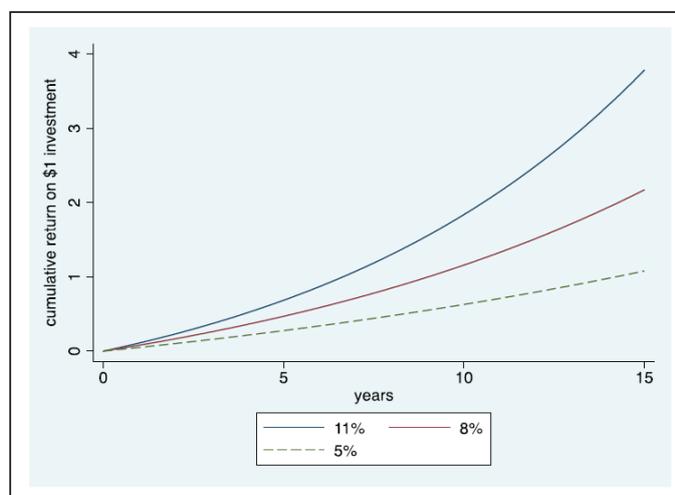
42. The cost of capital is the profit that an investor may expect for investing its capital. Alongside survival bias, the cost of capital is a crucial issue in excessive pricing cases where large up front R&D investments are required. This feature makes an assessment based on cost and sales based on one year less suitable. A life cycle approach in which several years of R&D investment and patent use is investigated is more appropriate. In such an approach, the costs and sales from different years have to be taken into account using the cost of capital as a discount factor (or alternatively calculating an internal rate of return that is compared with the cost of capital).

43. The actual chosen discount factor has an enormous impact on the assessment because of its impact on the margins that can be attained. Figure 1 gives an example on the impact of using capital costs of 5%, 8% and 11%. An investment of \$1 leads to a profit of \$1 in 15 years with capital of 5%, whereas the same investment with capital cost of 11% leads to a profit of \$4 in the same period. Hence the cost of capital has to be calculated with some confidence before conclusions can be drawn with regard to costs, prices and margins – and therefore excessiveness – as a whole.

³² Case 1276/1/12/17, *Pfizer Inc. and Pfizer Limited v Competition and Markets Authority*, CAT Judgment of 7 June 2018, [2018] CAT 11

³³ Canoy & Tichem (2018), Lower drug prices can improve innovation, *Working Paper ACM*

Figure 1.



Source: Bron: Chit, Chit, Papadimitropoulos, Krahn, Parker & Grootendorst (2015)³⁴

44. There are several issues that need to be resolved in order to determine the correct cost of capital. Most crucially are (i) method and (ii) level of analysis.

- **Methodology:** to start with the appropriate method: traditionally the Capital Asset Pricing Model (CAPM) is used to calculate the cost of capital. This method determines the riskiness of an investment by the volatility of the stock (or a group of stocks) compared to the volatility of all stocks. However, some authors argue that multi factor models, such as Fama & French' three-factor model would do a better job of capturing the actual costs of capital.³⁵ The Fama & French model also takes size related risk and book to market risk – risks associated with having a high stock value compared to accounting value - into account. Vernon et al. compared their calculation between the two methods, finding that the cost of capital would be more than 3%-point higher using the 3-factor model.³⁶ Given that the discount factor is applied for every year, such a difference would have an enormous influence. Several authors such as Trecartin (2000)³⁷ have however found that the predictive power of book-to market risk is rather limited. This is even more so for

34 Ayman Chit, Ahmad Chit, Manny Papadimitropoulos, Murray Krahn, Jayson Parker & Paul Grootendorst, "The opportunity cost of capital: Development of new Pharmaceuticals", *The Journal of Health Care Organization, Provision and Financing*, volume 52, May 2015.

35 E.g. John A. Vernon, Joseph H. Golect & Joseph A. Dimasi, "Drug development costs when financial risk is measured using the Fama-French three-factor model", *Health Economics*, volume 19, issue 8, August 2010, p. 1002-1005.

36 E.g. John A. Vernon, Joseph H. Golect & Joseph A. Dimasi, "Drug development costs when financial risk is measured using the Fama-French three-factor model", *Health Economics*, volume 19, issue 8, August 2010, p. 1002-1005.

37 Trecartin (2000), The reliability of the book to market risk as a risk proxy in financial service review 9 361-373

size. Combined with the fact that the CAPM model is still widely used by investors suggests competition authorities can still rely on this model.

- **Level of analysis:** the lowest possible level of analysis is based on a company's beta which is a measure for the relation between the company's market risk and the market risk of the economy as a whole. However, using company level cost of capital may turn out impractical, for instance if the stock of a company is not sufficiently traded to calculate the cost of capital. Company level cost of capital calculation may also show strong year to year variation. An alternative is using industry averages. Currently, the industry average of the cost of capital for the pharmaceutical sector is around 8% to 9%.³⁸ While this figure may seem low at first glance, it is as a consequence of both lower inflation and lower risk free interest rates that industry averages have decreased significantly. Di Masi et al. show that the cost of capital for the pharmaceutical industry decreased from 14,2% in 1994 to 11,4% in 2010.³⁹ Timing of the investment therefore matters for determining the appropriate cost of capital. If relying on industry data a relevant question is to what extent the risk profile of the company matches the industry average, which could possibly lead to some adjustments.

6. Conclusion

45. ACM's research shows that within the limits of the present regulatory system excessively high prices for pharmaceutical products undermine the financing of healthcare systems even while the underlying drugs provide benefits to individual patients. They thus erode solidarity. This means it may be necessary to apply competition law and – although we have not examined this in detail here – possibly more restrictive new regulation, including price regulation. At the same time there is considerable social value in the fact that new drugs are developed to meet previously unmet needs. In this paper we have examined the question how best to deal with the tension between innovation and cost control that arises in the relationship between intellectual property rights and competition law in general, and in particular within competition law when applying the prohibition against excessive pricing to pharmaceutical products. We have discussed when the application of competition rules is justified, and some practical suggestions for tackling the question of how to do this.

46. On the legal side this has rendered the following: firstly, we have restated our conclusions in a previous paper that as a matter of EU law IP rights by definition do not stand in the way of applying the competition rules. This does not mean that the presence IP right in itself demonstrates the existence of a dominant position, let alone an abuse. Second we have discussed the recent development in competition policy embracing fairness as an appropriate objective alongside efficiency – with special salience for excessive pricing which is after all a subspecies of unfair pricing. Third we have recapped the recent case

³⁸ http://people.stern.nyu.edu/adamodar/New_Home_Page/datafile/wacc.htm Damodoran calculates two different costs of capital for i. drugs (pharmaceutical): 8,13% and drugs (biotechnology): 9,24%.

³⁹ Joseph A. DiMasi, Henry G. Grabowski & Ronald W. Hansen, "Innovation in the pharmaceutical industry: New estimates of R&D costs", *Journal of Health Economics*, volume 47, May 2016, p. 20-33

law that emphasizes the use of benchmarks (as an expression of a fair price) alongside more traditional cost measures.

47. On the economic side we have done the following: firstly, we have identified survival bias and the cost of capital as two crucial issues in applying excessive pricing in an IP-context. Getting those two issues right is of great importance in order not to let competition enforcement impede incentives to innovate. Second, on the issue of survival bias we have suggested the approaches of i. using benchmark data on the cost of bringing one drug to the market and ii. using success rates. Third, we have in broad strokes discussed two important elements in getting the cost of capital right.

48. Finally, although regulation and competition law are in principle complementary the balance between the two may require fixing certain regulatory gaps or realigning incentives in the regulation. It is worthwhile to examine whether steps in this direction could be taken without overhauling the existing structures as a whole. Therefore, a further, multidisciplinary assessment of the interactions between the EU regulatory system, supplementary protection mechanisms and the need for cost-control and their impact on access, innovation and affordability within the EU pharmaceutical system is required. The ongoing evaluation of the European Commission into the pediatric extension and orphan medicines regulation may benefit from insights from a competition law perspective. Other recent studies into supplementary protection mechanisms published by the Commission and the Netherlands may provide further food for thought for a further debate on the functioning of EU pharmaceutical regulation and competition-law.

49. In conclusion, it probably goes too far to state that there is a complete absence of effective selfcorrecting mechanisms with regard to pharmaceutical prices. However because apparently self-correction fails frequently it appears that effective competition law remedies – including enforcing the prohibition excessive prices – are necessary. More stringent regulation may also be needed due to the inherent limitations, duration and costs of ex post competition law based interventions. Meanwhile we believe that balancing cost control and innovation within the application of the excessive pricing instrument does not always involve a strict contradiction. There is not so much a correlation between high levels of innovation and high costs as between high margins and a lack of outside options. Hence we think that if the relevant social value can be determined with some confidence, prices can be safely capped, including by means of competition law in individual cases, with minimal loss to innovation.