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A Cure for All Ills? The Effectiveness of Therapeutic and Biosimilar Pharmaceutical Competition in the Netherlands

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I. Introduction

The scope for effective competition in those drug markets where alternative treatments or different brands are in principle available is directly relevant for both innovation and cost control in the pharmaceutical sector. It also affects ongoing and possible future antitrust enforcement regarding pharmaceuticals in dimensions ranging from market definition to establishing dominance abuse and remedies. As such it is relevant for the degree to which the competitive process and competition policy may be expected to help control health care costs. The cost of pharmaceuticals has become a public issue in our home EU member state, the Netherlands. In general terms, by the late 2010s price increases of inpatient drugs (at some 8% annually over around 10% of hospital costs) were structurally consuming the entire budgetary room for growth (in the area of <1%) in the Dutch hospital sector. If this continues new and more expensive drugs will displace other hospital expenditures as the room for budget growth is declining to zero and will as a result effectively be negative for those other expenditures.

Unsurprisingly, this trend has concentrated the minds among public authorities as well as hospitals and health insurers. It is in this context that the Netherlands' Authority for Consumers and Markets (ACM) has focused on the pharmaceutical sector by publishing guidance on collective purchasing (2016) that was recently evaluated and launching a sector inquiry on TNF-alpha inhibitors (2019) to understand and influence the mechanisms involved, while also investigating excessive prices of prescription drugs that may indicate abuse of market power, including a formal complaint on excessive pricing (2018).[1]

In this article we will primarily discuss competition both within and between active pharmaceutical substances – i.e. therapeutic and biosimilar competition – based on the recent sector inquiry on TNF-alpha inhibitors, drugs that are widely used to treat several diseases, primarily rheumatoid arthritis. Before their gradual patent expiry starting with infliximab (Remicade) in 2015, TNF-alpha inhibitors were the category of drugs (in the Netherlands as well as worldwide) with the highest total costs, and remarkably so given the early existence of various therapeutic alternatives. When discussing possible remedies we will also refer to the abovementioned Dutch experience with antitrust guidance regarding the scope for collective purchasing of pharmaceuticals as a form of compensating buyer power. We will not discuss the alleged excessive pricing case as no public conclusions are available yet.

After briefly setting out the Dutch context, the three main questions that we will seek to address are: what is the scope for (i) therapeutic respectively (ii) bio-similar competition, and (iii) which levers can be used to promote each of them?

II. The Context of Dutch Hospital-Insurer Relations

To set the scene we must touch on the role of health insurers and hospitals in the Dutch inpatient setting. Unlike most EU member states, in the Netherlands both health care provision and funding are carried out exclusively by private parties. Hospitals are directly responsible for buying the drugs they need for inpatient treatments and for negotiating their purchasing prices with pharmaceutical companies. Many hospitals participate in joint purchasing col-

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1 See complainants' press release of 7 September 2018: 'The Pharmaceutical Accountability Foundation requests the Authority for Consumers and Markets to take action against medicines manufacturer Leadiant for abuse of its dominant market position.' <https://www.farmaterverantwoording.nl/information-in-english/> (English text of complaint available there.) See also <https://www.acm.nl/en/publications/acm-sees-opportunities-lower-prices-expensive-prescription-drugs>

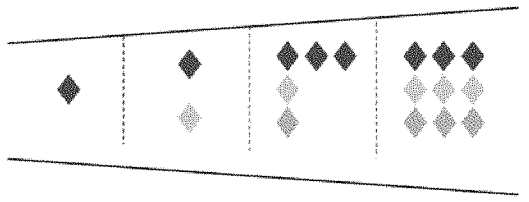

Figure 1: Four phases of competition

lectives – hospital buying groups. Health insurers either simply provide reimbursement for the hospital treatment involved as a whole, or provide separate reimbursement from the treatment itself for so-called add-on drugs that are listed by the Dutch Healthcare Authority (NZa). Add-on drugs were previously those above a cost threshold of more than 10.000 Euros per patient/year, but more recently this category has not been based on a fixed threshold but on joint application by at least one insurer and a hospital.

Insurers in turn may decide not to reimburse the listed prices of a drug fully, anticipating savings based on discounts that the hospitals may be able to negotiate. At the same time hospitals try to retain the savings achieved by negotiating lower drug purchasing prices (that are normally considered business secrets and subject to non-disclosure agreements). The difference between the reimbursement price paid by the health insurer and the price negotiated with the pharmaceutical company could be either a profit or a loss for the hospital. Hence both reimbursement levels and the way in which any savings are shared determine the incentives for hospitals to negotiate price reductions, and form a perennial bone of contention between hospitals and health insurers.

III. Competition Before and After Patent Expiry for Small Molecule and Biological Drugs

In the EU (and as we would expect elsewhere), the competition and intellectual property rules apply in parallel.[2] As mentioned in the introduction, in pharmaceutical markets competition is central both to stimulating innovation and to controlling prices. The availability of intellectual property rights protection promotes *competition for new markets* (innovation) while at the same time limiting entry and thereby the scope for *competition in existing markets* that could keep down prices. It should be clear that holding a patent as such (although it constitutes a temporary exclusivity), does not necessarily imply dominance in a particular relevant market in the competition law sense (although it may in some cases lead to such dominance), let alone the further step of finding an antitrust abuse.[3] Where intellectual property rights and related regulatory exclusivities exist (drugs that are protected by the orphan regime excepted), competition is in principle still possible from therapeutic alternatives, that is to say drugs with other active ingredients. At the same time restrictions of competition and patents may co-exist, as in the pay for delay cases,[4] and generic or bio-similar competition – between different brands with the same active ingredients – only begins after the relevant patents have expired.

The Dutch Ministry of Health has identified four different prototypes of pharmaceutical markets based on the degree of market power involved – in other words the ability to charge high prices – of the supplier.[6] This funnel (in FIFA World Cup 2010 terms: *Vuvuzela*) shaped figure shows[5] on its left side the situation in which a drug does not face any kind of competition. As the sole drug to treat the main indication(s), this is called a 'monopoly' drug.

2 See Case T-472/13 *H. Lundbeck A/S and Lundbeck Ltd v European Commission*, Judgment of 8 September 2016, ECLI:EU:T:2016:449; Case C-170/13 *Huawei Technologies Co. Ltd v ZTE Corp. and ZTE Deutschland GmbH*, Judgment of 16 July 2015, ECLI:EU:C:2015:477; Case C-457 *AstraZeneca AB and AstraZeneca plc v European Commission*, Judgment of 6 December 2012, ECLI:EU:C:2012:770.

3 Chris Fonteijn, Ilan Akker and Wolf Sauter, 'Reconciling competition and IP law: the case of patented pharmaceuticals and dominance abuse', Chapter 24 In: Gabriella Muscolo and Marina Tavassi (eds), *The interplay between competition law and intellectual property: An international perspective* (Kluwer Law International, Alphen a/d Rijn 2019) 411-425.

4 Case AT.39685 – Fentanyl, Decision of the European Commission of 10 December 2013 based on Article 7 of Regulation 1/2003, <https://ec.europa.eu/competition/antitrust/cases/dec_docs/39685/39685_1976_7.pdf> ; Case T-472/13 above note 2; Case T-691/14 *Servier SAS a.o. v Commission*, Judgment of Uitspraak van 12 December 2018, ECLI:EU:T:2018:922. See Eugène Buttigieg, 'The Servier judgment - the GC's evolving case law on 'pay-for-delay' patent settlement agreements' (2019) Journal of Antitrust Enforcement 7, 279–289.

6 See also the report for the ACM the consultancy Strategies in Regulated Markets (SiRM), Maarten Cozijnsen, Saskia van der Erf and Jan-Peter Heida, *Clarification is helpful, but not a panacea: evaluation of the ACM guideline collective procurement of drugs*, October 2019, 6. <https://www.acm.nl/sites/default/files/documents/evaluation-acm-guidelines-collective-procurement-of-prescription-drugs-new.pdf>

5 Phases of competition: 1. Monopoly 2. Oligopoly 3. Generic entry and 4. Full competition

The second square to the left illustrates the situation where a few (but at least two) drugs with different active ingredients are interchangeable from a therapeutic perspective for most of the indications for which they are used. This market is characterized by oligopoly – or a market with only therapeutic competitors. In the third square, at least one of the active ingredients is already out of patent and the original brand medicine concerned faces generic competitors. (In the picture, a new competitor representing another active substance is also added in this phase.) In the right square, all the active ingredients are out of patent and face generic competitors. The latter situation is called a market with 'complete competition' and represents the holy grail of antitrust authorities and purchasers alike.

The ACM sector enquiry on TNF-alpha inhibitors focused on the (transition between the) oligopoly and generic competition phases.[7] For the collective purchasing guidelines however, monopoly and oligopoly are the two most relevant phases.

1. Market developments before patent expiry

a. Three Explanations for Weak Therapeutic Competition

The sector inquiry focused on competition before and after patent expiry. Both the sector inquiry and the evaluation of the collective purchasing guidelines confirmed the intuition at the outset: that competition between drugs with different active ingredients has generated only weak competitive pressures in the Netherlands. Three distinct explanations seem to play a role.

- First, the *segment of patients that is contestable* is generally limited to 'new' patients. This is a result of the well-established practice of not switching patients that are using a certain drug to another active ingredient without good medical reasons.[8] Especially for chronic (life-long) diseases this means that most patients are locked in. In the case of TNF-alpha inhibitors, in any given year more than 80% of the patients are likely to use the same drug that they did in the previous year.
- Second, as far as *effective substitution* is concerned, for hospitals to be able to buy a higher volume of a better priced drug (or less from a comparably expensive drug) the concurrence of medical opinion on which drugs are equipotent is crucial. After all doctors want to prescribe their patients the best available treatments and tend to prefer drugs that they have had good experiences with. Hence, unlike many non-medical goods, in hospital care a less effective drug cannot compete with more effective drugs by charging a lower price. If prescribers find drug A is better than drug B for patient population X price competition for those patients is excluded. Marketing efforts by pharmaceutical companies in turn are aimed at creating and fostering such beliefs of clinical superiority. Moreover the various indications for which two different drugs are registered may only partly overlap – for instance for one or more of the main indications, while diverging for smaller indications. In the case of TNF-alpha inhibitors, they are all registered for rheumatic arthritis, but for other indications only one of them is available. Whether drugs are seen as substitutes is also codetermined by the mode of administration: in the case of TNF-alpha inhibitors subcutaneous use is generally preferred above intravenous use.
- Third, *financial incentives* often do not direct hospital purchasing towards the most cost-effective drug. In the Dutch health care system these incentives result from the contractual agreements between health insurers and hospitals. For drugs such as TNF-alpha inhibitors, the individual health insurers and hospitals agree on the price of a drug as part of a larger contract that determines the reimbursement rates for all types of health care products offered by the hospital. Contracts generally include caps (contractual ceilings akin to a budget) on the total cost across all treatments that a hospital can claim from an insurer over a year. However in many cases expensive drugs are not included under such general caps, making hospitals less susceptible to any negotiating pressure that the insurers would otherwise exert on them. To resolve this problem prior agreements on transparency of hospital purchasing prices and on how to share any savings would have to be made, possibly in

7 ACM, Sector inquiry into TNF alpha inhibitors, September 2019 <https://www.acm.nl/sites/default/files/documents/2019-09/sectoronderzoek-tnf-alfaremmers.pdf>

8 ACM, Sector inquiry into TNF alpha inhibitors, September 2019, Chapter 2, 14.

exchange for insurers agreeing to continue separate reimbursement of each drug.

b. Margin Competition Versus Appropriate Drug Use

The financial incentives that result from the relevant agreements between the hospitals and insurers are usually not suitable for inducing reductions in drug spending for other reasons too. There may well be a positive margin for the hospital between the price reimbursed by the health insurer for a drug and the price that the hospital itself paid. This has the undesirable effect of generating margin competition – financially incentivizing hospitals to buy the drug that offers the highest margin, instead of the most cost effective drug from a broader societal perspective: a form of moral hazard. The ACM sector inquiry in fact clearly showed that margins for hospitals were higher for the more expensive drugs.[9] Some health insurers have countered this mechanism by using alternative reimbursement models, for example by determining the price based on the drug's working mechanism and setting a single price level for all different TNF-alpha inhibitors.

Apart from influencing the relative choice of drug, margin competition may also tempt hospitals to increase volume by using more of the high margin drugs. These perverse incentives run counter to the nationwide policy in the Netherlands that aims to achieve 'appropriate drug use'. This serves to limit drug use to necessary levels and quantities, which can result in smaller doses and on occasion different treatments than originally recommended by the pharmaceutical companies. An example is the drug eculizumab where a university hospital found out the recommended dosages were seven times higher than medically necessary.[10]

Health insurers tend to counter financial incentives for using more drugs by adding conditions to their agreements with hospitals such as transparency obligations and participation in benchmarking. It should be noted, in spite of the above, that generally hospitals and their medical staff are driven by other factors than mere private financial incentives. The importance of controlling national health care spending is widely recognized and supported across the board. From a more macro perspective, framework agreements between hospitals, health insurers and the government limit health care spending nationwide.[11] This means that 'earnings' on expensive drugs may result in cuts for other types of spending on hospital care.

c. Recent Trends Found in the Sector Inquiry

Even though therapeutic competition is in many cases expected to remain a weaker form of competition, there is scope for increasing its potential. A promising development is that Dutch hospitals have in recent years become more professional in their purchasing practices. All hospitals now have expert groups in which medical specialists and pharmacists discuss the interchangeability of different drugs and possible switching strategies. This clearly has the potential of improving therapeutic competition.

Another way to stimulate therapeutic competition is at the level of incentives. The findings in the sector enquiry and the evaluation of the guidelines for collective purchasing are consistent. It follows from the evaluation that setting the incentives right for buying hospitals turns out to be a more crucial objective of collective purchasing than increasing buying power by increasing volume. Successful collaboration on collective purchasing would shift the focus of the negations between health insurers and hospitals to the results of collective efforts vis-à-vis the pharmaceutical companies. So far however the question of how to share any savings achieved most effectively remains a difficult hurdle to overcome.

2. Market Developments After patent expiry

a. What Can We Expect from Bio-Similar Competition?

The second main (and in practice most important) subject of the sector inquiry was biosimilar compe-

9 ACM, Sector inquiry into TNF alpha inhibitors, September 2019 <https://www.acm.nl/sites/default/files/documents/2019-09/sectoronderzoek-tnf-alfaremmers.pdf>

10 Kioa Wijnsma et al, 'Safety and effectiveness of restrictive eculizumab treatmen in atypical haemolytic uremic syndrome' (2018) Nephrology Dialisys Transplantation, 33, 635-645.

11 The framework agreement for specialist medical care sets among others thing goals for total growth of spending in hospital care. It also includes mechanisms for cost control in case the commitments of the parties involved turn out not to be sufficient.

tition. Over the last 10 years, generic competition for drugs in outpatient (non-hospital) markets has been reasonably successful in keeping drugs affordable in the Netherlands. Thus the increase in spending on expensive drugs was counterbalanced by lower prices in generic markets. For the coming years however, total spending on drugs will certainly go up because generic markets can hardly become more successful in terms of cost control than they already are and both the number and prices of expensive drugs keep going up.

A further challenge for generic markets is the increasing share of biological drugs. Generic markets for biologicals – in other words biosimilar markets – will certainly not be as successful in controlling prices as traditional generic markets. Biologicals are 'alive', far more complex in structure, much larger in size and therefore less stable than synthetic drugs. The production process itself is complex, generally takes more than six months and the number of companies able to develop and produce biosimilars is much smaller than for synthetic drugs.

For generic markets, a crucial difference is that a biosimilar cannot be an identical exact copy of the originator drug. It should be emphasized however that even different batches of the originator are not exact copies. This fact directly impacts the regulatory requirements for registering a biosimilar. Registering a synthetic generic drug is relatively straight forward. Registering a biosimilar on the other hand requires clinical studies to prove clinical equivalency. Switching to biosimilars, especially for TNF-Alpha inhibitors, has on the other hand been helped significantly by the 2017 Norswitch study,[12] which concluded this practice was medically sound.[13]

All the differences mentioned so far have consequences for how we should look at biosimilar markets and what we should expect from them. A first observation is that investment incentives clearly matter to biosimilar producers. Developing and bringing a biosimilar to the market is costly and risky. Therefore strategies to delay entry are even more harmful in biosimilar markets. They do not only impact (short and long term) prices for the specific drugs involved, but also impacts incentives for biosimilar markets more broadly. Biosimilar markets therefore deserve close scrutiny from competition authorities. A second observation is that over all fewer companies can be expected to be active in biosimilar markets than in generic markets. This follows both from the expertise required and the financial risks involved. Third, in terms of the size of the effect of biosimilar competition, we would expect smaller price reductions than for traditional synthetic drugs as the cost of entry for biosimilars is higher.

b. Findings in the Sector Enquiry

Based on data collection of net prices from 30 Dutch hospitals,[14] the ACM observed in its sector enquiry stable prices before generic entry. The price level of a drug can best be explained by the year of registration of the drug. Figure 2 shows that the price of adalimumab and etanercept has long moved around €35 per daily dosage[15]. Events such as the entrance of a competing molecule did not affect net buying prices or sold quantities. Moreover, price decreases of a competing molecule as a consequence of biosimilar entry affected the price of drugs that were still under patent only modestly, and did not affect quantities at all. While the net buying price for etanercept had gone down with 60% after biosimilar entry, Humira's (adalimumab) price dropped only by 10% to 15%, and the quantities of Humira even increased in this period.

Figure 2 also shows prices going down as a consequence of biosimilar entry: overall, after biosimilar entry prices ultimately dropped by more than 50%. The first originator facing biosimilar competition was MSD, the producer of Remicade (infliximab), in 2015. Etanercept and rituximab followed in 2016 and 2017 respectively. Adalimumab faced biosimilar en-

12 Kristin K Jørgensen et al, 'Switching from originator infliximab to biosimilar CT-P13 compared with maintained treatment with originator infliximab (NOR-SWITCH): a 52-week, randomised, double-blind, non-inferiority trial' (2017) The Lancet 389, 2304-2316.

13 Similar outcomes resulted in several studies such as in the managed switching programme in the University Hospital Southampton (UHS). See: Razanskaite et al, 'Biosimilar Infliximab in Inflammatory Bowel Disease: Outcomes of a Managed Switching Programme' (2017) Journal of Chron's and Colitis 11 (2017) 690-696

14 The 30 hospitals included the 20 largest hospitals that made up just over 50% of total use of TNF-alfa inhibitors. 10 other hospitals were selected randomly.

15 The Defined Daily Dosis (DDD) is a measure developed by the WHO to compare the price of different drugs with one another, based on the average dose to be taken for its main indications. See <https://www.who.int/medicines/regulation/medicines-safety/toolkit_ddd/en/>

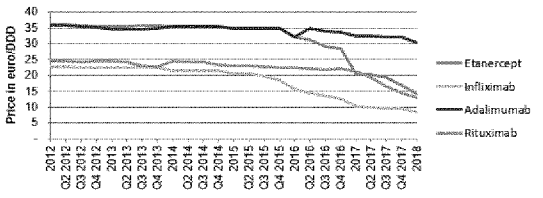

Figure 2 Net price developments

try in the end of 2018 (for which the sector inquiry has not collected data). Price developments after biosimilar entry follow by and large the same trend, although price reductions seem to have speeded up. In terms of market share however, the ACM has observed diverging trends, which differ according to the strategies employed by the various originators. Both the market share of the originators Remicade (infliximab) and Mabthera (rituximab) went down quickly after entry of biosimilars. The loss of market share of Enbrel (etanercept) followed a much more gradual trajectory and seemed to have stabilized around 80% in 2018.[16] Also Humira (adalimumab) kept a majority of market share one year after biosimilar entrance.

Two related factors may explain these diverging patterns. First, the originators of infliximab and rituximab have only reduced their prices after already having lost significant market share. The prices of Enbrel (etanercept) and Humira (adalimumab) were reduced at a much earlier stage. Second, the originators of subcutaneously self-administered drugs (such as etanercept and adalimumab) have a much stronger first mover advantage vis-à-vis biosimilar producers than the originators of intravenously administered drugs. The reason for this is that switching costs are much higher for drugs that patients have to self-administer with a device, as patients tend to resist switching devices. Additionally, in any event not all patients are able to switch to a biosimilar (hence within the same active substance), leaving a population that is locked in of 5% to 20% of the total volume.

Such advantages can be exploited both by originators and buyers, again in two ways. Everything else being equal, in the first place on the side of the buyers (the hospitals) switching costs predicate a preference not to switch. This causes a risk that hospitals merely use biosimilar offers as a benchmark to reduce the prices of the originator drugs, without the biosimilars actually gaining market share. Unpredictable and non-transparent tenders facilitate such outcomes. This has the potential to weaken the market structure and competition in the long run. Second, the originator may deliberately attempt to use the locked in population to weaken competition for the patient population as a whole by means of conditional rebates. This is to say discounts are given that include historic volumes, which are difficult or impossible to match for new entrants who cannot compete for the delivery of the same total volume.

c. Remedies

To allow biosimilar producers a clear shot at establishing themselves as alternative providers, and ultimately to promote a competitive market structure, the tender procedures established by the purchasing hospitals must provide a level playing field. In practice, if hospitals have a non-price preference for not switching, originators are sometimes favoured by allowing them to submit a second (informal) bid to beat the entrants. Given that the first mover advantage is in any event considerable, fair and transparent contracting practices – which as a matter of common sense should be applied in any event – are all the more important here. This may be complemented by health insurers promoting biosimilar entry and thereby long term competition. A potentially effective way in which health insurers can do this, is by reimbursing hospitals at a premium for using biosimilar drugs, and some health insurers in the Netherlands have in fact done so. An application for interim measures by Pfizer that attempted to stop this preferential practice failed in December 2019.[17] This outcome provides legal backing for initiatives that aim to encourage biosimilar entry, and we also expect increased scrutiny of potentially anticompetitive originator behaviors aiming to delay such entry.

16 See for comparison eg Sweden where biosimilar market shares for etanercept was between 40% and 82% at the end of 2017 depending on the county. Moorkets et al, 'Different Policy Measures and Practices between Swedish Counties Influence Market Dynamics: Part 2- Biosimilar and Originator Etanercept in the Outpatient setting' (2019) Bio Drug 33, 299-306.

17 Case C-09-583793-KG ZA 19-1135, *Pfizer v Achmea and others*, The Hague District Court, Judgment of 24 December 2019, ECLI:NL:RBDHA:2019:14242, <https://uitspraken.rechtspraak.nl/inziendocument?id=ECLI:NL:RBDHA:2019:14242>

IV. Collective Purchasing

1. Background and Principles of the Guidelines

From the perspective of the ACM five years ago, facilitating the organisation of countervailing market power in response to questions by especially health insurers about the legal possibilities for such initiatives in view of the antitrust regime appeared both a possible alternative and complement to direct intervention against possibly excessive prices. Hence in 2016 the ACM adopted collective purchasing guidelines for inpatient (medical specialist care) drugs.[18] Both health insurers and hospitals in the Netherlands are (private) undertakings – as are pharmaceutical companies. As such the competition rules apply to all of them, and the ACM enforces these rules in the healthcare sector as a whole. Although generally less harmful than a sales cartel, collaboration in purchasing markets may sometimes exploit sellers, and remove important competition parameters between the participants in their own sales markets based on shared costs and coordination. In fact the EU guidance on horizontal cooperation suggests that joint purchasing only benefits from a presumption of legality below joint market shares of 15% on the purchasing as well as the selling side.[19] More intensive cooperation would require an individual assessment.

Aside from the question how the parties concerned could confidently define markets in order to determine their own market shares, this meant that in most cases achieving significant collective purchasing power is likely to fall outside the safe harbour under the general standard for EU competition law.

Following a dialogue with the European Commission's directorate general for competition (DG COMP) and a public consultation among stakeholders in the Netherlands, in June 2016 the ACM set out a tailor-made safe harbour under the competition rules in relation to joint purchasing of inpatient drugs by hospitals and/or health insurers in a set of guidelines. These guidelines,

identified shared cost thresholds as the key to any competition concerns, instead of market share.[20] Focusing on possible restrictive effects on competition on the selling market, the market for hospital care, the ACM formulated three conditions: (a) only a limited share of the *costs* involved could be harmonized (as a rule of thumb of 15% for hospitals and 5% for health insurers); (b) admission to the joint purchasing organization would be possible on the basis of objective and nondiscriminatory criteria that are known in advance; and (c) the joint purchasing organization should not impose unnecessary constraints on participants in terms of the contract period, purchase obligations, and withdrawal from the collaboration. Collaboration that did not meet these conditions would have to be assessed individually, and might be prohibited. This opened the door to new purchasing initiatives.

The functioning of the guidelines was evaluated in 2019. The evaluation, which was carried out by an external consultancy, suggested that although the uptake in terms of new initiatives was limited, and joint purchasing was in any event no panacea, parties were positive about the nature and impact of the guidelines.[21]

2. Findings of the Evaluation

The most noteworthy findings were that the health insurers and hospitals were leaving the full potential of the Guidelines untapped for the following three reasons:

- First, the ability to organize effective switching by patients and prescribing doctors even within the same hospital or a limited group of hospitals was more significant in terms of the ability to obtain results than organizing large volumes to obtain discounts (P x Q) by uniting more hospitals and health insurers. It is also much more difficult to

18 ACM, Guidelines on collective procurement of prescription drugs for medical specialist care, June 2016 <https://www.acm.nl/sites/default/files/old_publication/publicaties/16341_guidelines-on-collective-procurement-of-prescription-drugs-for-medical-specialist-care.pdf>

19 Communication from the Commission — Guidelines on the applicability of Article 101 of the Treaty on the Functioning of the European Union to horizontal co-operation agreements, OJ 2011, C11/1, Chapter 5, pp 44-47, <https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52011XC0114(04)&from=EN>

20 Wolf Sauter and Susan van Velzen, 'Joint purchasing of pharmaceuticals under competition law: the case of the Netherlands', *European Competition Law Review* 37 (2016) 458-464. Using costs instead of market share has the additional advantage that it is quite straightforward for each organisation involved individually to calculate their own costs in order to determine whether they remain below the threshold.

21 <https://www.acm.nl/en/publications/health-insurers-and-hospitals-leave-full-potential-collective-procurement-prescription-drugs-untapped> See also the SiRM report, above note 4.

so, and it is telling that the most effective collaborations (between top clinical hospitals and academic hospitals respectively) have already been dovetailing their efforts for decades. Consequently, it appears that in some cases collective purchasing – if the ability to switch effectively is compromised as a result – may even be less effective than the results for a single well organized hospital that can credibly deploy switching.
- Second, counterintuitively, bargaining with monopolists was frequently found to be more effective than with oligopolists. This is because joint purchasing organizations could reduce friction for monopolies in return for a modest reward, but were internally much less effective where there were more choices available – and hence a greater risk of divergent views resulted in the agency problem set out above.
- Third, the main benefit of the participation of health insurers was that at least in theory their participation made it possible to provide hospitals with incentives to economise on expensive drugs by offering them shared savings. However a handicap here was that in practice it turned out to be difficult to agree on how to apply shared savings.

The parties interviewed as part of the evaluation requested additional guidance primarily on three topics: shared savings (within hospitals and between hospitals and insurers), the legal scope for information exchange and for admissible conditions that could be imposed on membership of a joint purchasing organisation. The latter was raised especially given the need to obtain credible commitments for effective switching. In addition, parties claimed that bringing joint purchasing of medical devices within the scope of the guidelines should be examined. There was less interest in looking at possibilities for joint purchasing across borders under the umbrella of the ACM guidance – say between Dutch hospitals and German private hospitals.

The ACM is presently reviewing its guidance on collective purchasing in light of the above.

3. Product Market Definition

The above findings lead us to several observations that are relevant to market definition. Market definition is a perennial bugbear of antitrust enforcement, and as the 2018 *Servier* ruling of the General Court (where the Commission's market definition and thereby dominance argument was annulled) has shown,[22] pharmaceutical markets are certainly no exception. At the same time there are a number of specific features that emerge from our analysis above that can place the recent case law in context. In the first place we should distinguish between weak price competition between therapeutic substitutes on the one hand, versus strong price competition where biosimilars are concerned on the other. If therapeutic substitutes are nevertheless included in the same relevant market – such as when it is defined on the basis of the indication for which drugs are authorized (leaving to one side issues of pharmaceutical compounding and off-label use[23]), this raises the risk that the definition is diluted to the point where anticompetitive behaviours cannot be countered effectively as dominance has been defined away.

In its 2014 *Servier* decision the Commission had defined the relevant market as limited to a single molecule (perindopril, a cardiovascular drug developed by French pharmaceutical undertaking Servier to combat chronic hypertension as well as heart failure) within the ACE inhibitor class, in its original and generic form. In December 2018 the General Court held that the market should instead have been defined more broadly to include therapeutic alternatives, based on non-price factors.

Its reasoning was that doctors prescribe drugs and are not sensitive to price but may be susceptible to advertising.

The ACM sector inquiry findings cast doubt on the General Court's reasoning as regards the price insensitivity of doctors, as we have seen that doctors are ready to switch to biosimilars to obtain a better

22 Case T-691/14 *Servier SAS and Others v Commission*, Judgment of 12 December 2018, ECLI:EU:T:2018:922. See the (somewhat unusual for a case pending appeal before the CJEU) comment by General Court Judge Eugène Buttigieg, 'The EU General Court's Servier Judgment', *Journal of Antitrust Enforcement* 7 (2019) 279–302; Flip van der Kraan and Wolf Sauter, 'A spoonful of sugar makes the medicine go down: pay for delay and market definition in the Servier judgment', *European Pharmaceutical Law Review* 2 (2019) 1-9.

23 See Joined Cases C-544/13 and C-545/13 *Abcur AB v Apoteket Farmaci AB and Apoteket AB*, Judgment of 16 July 2015, ECLI:EU:C:2015:481; Case C-179/16 *F. Hoffmann-La Roche Ltd and Others v Autorità Garante della Concorrenza e del Mercato*, Judgment of 23 January 2018, ECLI:EU:C:2018:25. Tamara Klimenta and Wolf Sauter, 'An eye for an eye? Off-label use and misleading information: *Hoffmann-La Roche v AGCM*', *European Pharmaceutical Law Review* 1 (2018) 100-107.

deal for the hospital, provided that this is defensible from a medical point of view, such as was proven to be the case for TNF-alpha inhibitors by the Norswitch study. Moreover, as we have seen in the sector inquiry, first mover advantages are significant because they effectively lead to a captive group of patients that is not susceptible to advertising or branded competition for therapeutic alternatives. Effectively competition from second and third available therapeutic alternatives only occurs for new patients, and is therefore limited – especially if volume based discounts are applied that take the captive population into account. This casts doubt on the validity of General Court's reasoning in *Servier* as regards the plausibility of therapeutic competition.

The General Court in *Servier* also pointed to the fact that advertising outlay of various drugs was considerable (and not necessarily less significant than the relevant R&D budgets). This raises the question of the role of advertising and brands: what value is there in this type of competition and how important is it? Advertising and branding is likely to affect prescription by less expert doctors more than that of specialists for instance in academic hospitals. The latter can be more confident of their own knowledge and that of their practice groups, are more likely to be member of expert groups and networks that establish treatment protocols, and more likely to align their prescriptions on that basis rather than switch (or retain) based on pharmaceutical ads. In any event, the sector inquiry outcome shows that the competitive strategies of pharmaceutical companies in this respect are very different before and after generic entry: at generic entry, the focus shifts from marketing to price competition. This appears to be because marketing efforts make less sense after generic entry as any benefits of convincing doctors of the superiority of your products are largely shared with the generic competitors.

Finally, the CJEU recently handed down its ruling in the *Paroxetine* pay-for-delay Case,[24] where it answered questions submitted by the UK's Competition Appeal Tribunal (CAT) inter alia on market definition. This concerned the issue whether the Consumer and Markets Authority (CMA) had appropriately taken generic producers of the active substance paroxetine into account when defining the relevant market, which arose because the legality of the generic products was in doubt in the pending patent dispute.[25] The Court ruled that the definition of a specific relevant market limited to the originator product and those of generics is possible if from a medical perspective only these are held to be interchangeable. The existence of an intellectual property right cannot lead to a different finding, provided generic producers 'are in a position to present themselves within a short period in the market concerned with sufficient strength to constitute a serious counterbalance'.[26] Although the outcome of such an analysis revolves around the facts of the individual case (in this case to be interpreted at national level) the notion of a relevant market consisting of an originator product and its generic competitors only is consistent with the findings in the ACM sector inquiry. The same applies for the Court's finding that the interchangeability (or substitutability) of products is naturally dynamic.[27]

v. Future / Regulatory Issues

Given the importance of investment incentives, a relatively new problem has arisen. For certain biological drugs, especially those with relatively few patients (often orphans), biosimilars do not even enter the market after the relevant patents have expired. An example is the drug Myzyme (alglucisidase alfa) for Pompe disease. With just over 100 patients, total spending on this drug was €56 million in 2016, ranking in the top 10 of drugs with the highest total spending in The Netherlands.[28] Price regulation based on some cost plus model might be a more reliable mechanism for controlling prices than hoping for biosimilar markets to develop.

A second issue is the pricing of new drugs that have only incremental benefits compared to already

24 [2018] CAT 4, *Generics (UK) Limited, Glaxosmithkline Plc, Xellia Pharmaceuticals Aps, Alpharma Llc, Actavis UK Limited and Merck Kgaa v Competition and Markets Authority*, 18 March 2018. <https://www.catribunal.org.uk/sites/default/files/1.1251-1255_Paroxetine_Judgment_CAT_4_080318.pdf>

25 Case C-307/18 *Generics et al v CMA*, judgment of 30 January 2020, ECLI:EU:C:2020:52, para 140.

26 Factors to take into account are whether there is a prior effective strategy for market entry, and having taken the steps necessary to achieve it which may include having registered for a marketing authorisation or having obtained one or having concluded supply contracts with third party distributors. ibid para 134.

27 ibid para 130.

28 NZa, *Monitor geneesmiddelen in de medisch specialistische zorg januari 2019* <https://puc.overheid.nl/nza/doc/PUC_264248_22/1/>.

existing drugs. One possible example are the new JAK-inhibitors that may partly replace the currently out of patent TNF-alfa inhibitors. The benefit of these drugs mainly seems to be that JAK-inhibitors are ingested as pills instead of applied as subcutaneous injections. Relying on hospitals' ability to negotiate prices may turn out to be tricky and lead to overspending on these drugs. If patients or prescribers turn out to prefer JAK-inhibitors, the price of TNF-alfa inhibitors is unlikely to play a significant role in negotiating the price of a JAK-inhibitor. Different JAK-inhibitors may face some mutual price pressure amongst each other, but based on past experience with the TNF-Alpha inhibitors we expect this therapeutic competition to be weak. In this context competition does not seem to be a reliable mechanism to control additional health care costs.

Current price regulation by means of external reference pricing also falls short as this is based on list prices – not actual prices – abroad. In the decision on the maximum price at which a new drug may be included into the Dutch health insurer package its price is evaluated against the list prices of the already existing alternatives. However these list prices are artificial and inflated compared to the prices actually paid after biosimilar entry. This is because pharmaceutical companies do not have any incentive to post lower list prices at any stage. In the sector inquiry, the ACM found that even biosimilars tend to set list prices that are comparable to (or even steeper than) those of the originator drugs. In such cases the actual 'discounted' price that is paid by hospitals is almost wholly unrelated to the publicly listed prices. To prevent paying too much for drugs that offer only incremental improvements, it would be preferable to take average actual prices into account, when determining the maximum price for the new drug.

VI. Conclusion

We believe that skipping any of the four phases of pharmaceutical competition that range from monopoly to full competition set out in figure 1 above would neither be a realistic ambition nor in most cases desirable from the point of view of protecting incentives for innovation/dynamic competition. At the same time, in the interest of access and cost control it is harmful to remain stuck halfway. Therefore we see the main role of antitrust with regard to pharmaceuticals as speeding up the flow and transition between the four phases of competition. This leaves us with those sources of friction that do not qualify as antitrust infringements but are nevertheless harmful. These should be addressed by regulatory means with the objective not of subverting the competitive process, but facilitating it.

Furthermore, we have seen that effective entry is not only key for first mover originators (who tend to establish an edge that is difficult to contest by therapeutic alternatives given switching costs and lock in), but also in the subsequent phase for biosimilars if they are to contest markets successfully. An example is when they are faced by originators' strategic discounting. Hence, entry should be a key concern for competition authorities and purchasers, including hospitals and purchasing authorities or health insurers) alike. For purchasers this means taking account of the market structure and balancing short and long term interests. This may for instance mean contributing to a healthy market structure by building a sustainable competitive position for biosimilars once they become available, and possibly paying an initial premium for this privilege. At a minimum any procurement processes should be effective and transparently designed not to handicap entrants any further.

A further lesson from the Dutch experience is that just like promoting a competitive market structure on the supply side, organizing countervailing market power on the demand side is both more complex and time consuming than anticipated. (There is evidently a reason that 'pay for delay' strategies have been found in this sector.) In fact achieving effectiveness in directing prescribing practices that would allow selective purchasing tends to be at cross-purposes with achieving scale and volume. Here too, short term purchaser opportunism with long term negative effects on market structure is an issue. Nevertheless we have found some benefits to collective purchasing even in monopoly markets, and further clarifying the competition rules with respect to shared savings, information exchange and access conditions for purchasing groups may help. In the meantime however we find that biosimilar markets deserve more intense antitrust scrutiny to try and forge a competitive market structure while the iron is hot.