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Excessive pharmaceutical pricing and repercussions on paediatric health services

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Context: *Paediatric pharmaceutics have a significant share in expensive drugs. Recent years have seen significant calls for intervention against high prices for pharmaceutical products. The prohibition of prices that are excessive as a form of abuse of dominance is considered as Competition law violation in the European Union Law and national legal orders of its Member States. Majority of the Organization for Economic Cooperation and Development (OECD) member countries have similar prohibitions in their respective Competition laws with important exemption of United States (US) Antirust Law, although there is some indication of change in US exactly in the area of pharmaceutical sector. Regulation of excessive prices also exists in Competition laws of all BRICS (Brazil, Russian Federation, India, China, and South Africa) countries. The problem of excessive prices in pharmaceutics is one of the emerging themes in Competition law literature and case law development. This is the area where intellectual property rights, usually patent protection, collide with competition rules. Costs of research and development for such pharmaceutics are often very high emphasizing the need for balance between colliding legitimate interests: access to health and research development.*

Aim: *To present regulatory and case law development of application of excessive prices as form of abuse of dominance in pharmaceutical sector with emphasis on paediatric health services.*

Data source: *OECD, PubMed, Google Scholar, Scopus.*

Conclusion: *Balance between competition rules on excessive prices as form of abuse of dominance and intellectual property rights in the area of expensive paediatric pharmaceutics can be regarded as suboptimal. Thus, there is a need for further regulatory development and application of rules on excessive prices in that field.*

Keywords: LEGAL ASPECTS; COURT DECISIONS; PEDIATRICS; DRUG AND NARCOTIC CONTROL

INTRODUCTION

Recent years have seen significant calls for intervention against high prices for pharmaceutical products, and there have been a number of competition enforcement cases regarding exploitative excessive pricing in this sector (1). Excessive pharmaceutical pricing represents one of the most contentious issues in legal and political discourse and has recently gained renewed attention by courts, competition authorities and political forces on both sides of the Atlantic (2). The British Medical Journal dedicated a special issue in 2020 to achieving fair pricing (3). One study from 2020 demonstrated that global expenditure on pharmaceuticals increased 56% between 2007 and 2017 (4). Paediatric pharmaceutics have a significant share in expensive drugs including the most expensive drugs in world, as we will demonstrate further in this paper.

In the European Union Competition Law excessive pricing by dominant undertaking/undertakings or association of undertakings is considered to be a violation Article 102 of

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The Treaty on the Functioning of the European Union (TFEU). Thus, abusive conduct of dominant undertaking that consist in directly or indirectly imposing unfair purchase or selling prices or other unfair trading conditions, as stipulated in TFEU (5), can emerge in a form of excessive prices. Similar provision is contained in Article 54 of the European Economic Area (EEA) Agreement (6). Member States of EU have harmonized their competition laws with EU Competition Law so regulation of excessive prices is the correspondent.

The European Court of Justice has in 1975 in *General Motors Continental NV v. Comm'n* (7) case introduced that this prohibition of unfair prices and trading conditions can relate to excessive prices. It held that dominant undertaking service price is unfair if it is excessive in relation to the economic value of the service provided. In far better known case that was adjudicated several years later - *United Brands* case (8) - the Court established approach for determination of excessive prices. In that case Commission held that *United Brands* (UBC), big producer and exporter of bananas, charged the price of bananas to its customers in Germany, Denmark, the Netherlands that are considerably higher, sometimes by as much as 100%, than the prices charged to customers in Ireland and therefore produce for it a substantial and excessive profit in relation to the economic value of the product supplied (6). Court held that excess in prices could be determined objectively if it were possible for it to be calculated by making a comparison between the selling price of the product in question and its cost of production, which would disclose the amount of the profit margin. The Court held that excess in price is therefore to be determined in answering the question whether the difference between the costs actually incurred and the price actually charged is excessive, and, if the answer to this question is in the affirmative, whether a price has been imposed which is either unfair in itself or when compared to competing products (8). Conclusion of the Court concluded that Commission did not succeeded to prove excess in prices. Failure on the Commission part to provide analysis of UBC cost structure analysis was paramount to such judicial decision (UBC was found to be in abuse of dominance in other aspects but execs in prices was not sufficiently proven).

In *Bodson v. Pompes Funèbres* case (9) from 1988 the Court of Justice held that the excess in price can be determined by comparing what the dominant undertaking had charged in other markets in which it is subject to more intense competition (6). Method of comparison with other markets was further elaborated a year later in *Tournier* case (10), in which the Court required objective justification for price difference from the similar/comparable markets. In some cases, the Court held that prices exceeding the competitive benchmark in other markets between 25% to 40% were excessive, while other decisions concerned larger differences. In more recent case law, the Court in *AKKA/LAA* case from 2017 (11) held that there is no minimal threshold in price difference, it only required difference is significant and persistent. After the judgment in *United Brands* case two-limb test is frequently used in the assessment of the excess in price.

Particular problem are markets that are naturally monopolistic. Good example for this is Commission decision in *Port of Helsingborg* case from 2004 (12). In that case Commission held that that there is no sufficient evidence to conclude that the port charges have no reasonable relation to the economic value of the services provided by the port to the ferry-operators. The problem of the assessment by using comparative markets method in this kind of situation is locational monopoly. Port of Helsingborg is located in the southwest of Sweden, at the narrowest point of Øresund between Sweden and Denmark. Thus, there is literally no sufficiently comparable market or ferry route in whole of the EU method (6). Similarly, naturally monopolistic markets frequently occur in markets of pharmaceutical products.

Specific expanding area of case-law in EU Competition law is exactly in the field of pharmaceuticals. Leading case here is the Commission decision in *Aspen* case from 2020 (13). Case relates to excessive pricing of six cancer medicines in the European Economic Area (excepting Italy which adjudicated the matter in national proceedings also revoking excessive prices as abuse of dominance) by Aspen, an international pharmaceutical company headquartered in South Africa. The patent protection for the aforementioned medicines expired more than 50 years ago. Aspen imposed price increases by threatening to de-list or to withdraw the medicines. After having imposed the increased prices, often by several hundred percent, Aspen maintained the high prices (with profit margins over 80% and higher). Aspen also did not carry out any research and development or add any improvements or enhancements to commercialisation or distribution. Medicines in question did not have generic substitutes in Europe so the dependency of patients and health systems on Aspen's products made demand highly inelastic and customers vulnerable to exploitation. Case ended with Aspen commitment to reduce net prices for each of the medicines in all of the EEA Member States where price levels might raise concerns. The price reduction would be on average around 73% for the medicines across the EEA. The reduced net prices would apply for a period of 10 years.

Regulation of excessive pricing exists in all of the Organization for Economic Co-operation and Development Member countries except US, Canada, Mexico, Australia and New Zealand (14). US Antitrust Law under the influence of the Chicago School of Economics is still lead by the idea of self-

correcting markets that is estranged to excessive pricing as a concept. However, such practices can sometimes be categorised under general provisions of Sherman Act that addresses monopolization and attempts to monopolize not relating to excessive pricing. Furthermore, such views on excessive prices have been questioned from doctrinal point of view (15). Signs of possible acceptance in US Antitrust Law can be detected exactly in the area of pharmaceutical pricing practices (6). Example form US case law is *In re Nexium (esomeprazole)* case from 2014 that involves pay-for-delay agreements of AstraZeneca and their impact on competition and consumer prices (16). Regulation of excessive prices exists in competition laws of all BRICS countries (6).

PATENT PROTECTION EXPIRED VS PATENT PROTECTED PHARMACEUTICALS

Majority of developing case law in various jurisdictions relating to excessive prices of pharmaceuticals concerns situation where patent protection, as most common intellectual property right, expired. This was the situation in EU *Aspen* case, as we have seen form the introduction (as well in the Italian national proceedings in the same case). Described regulatory emphasis on pharmaceutics where patent protection expired has been clearly demonstrated in one study from 2023 (17). Usual preferred remedy for excess in prices of such pharmaceuticals (where patent protection expired) would be in lowering the barriers for entry on the relevant market for substitutes product/products. Especially preferred by the medical drug regulators are generic medicines. However, this is not always possible, as we have seen in the *Aspen* case - simply there were no substitute generics available at that time in Europe. Among crucial contributing factors for the existence of entry barriers, along with the costs of research and development, is time. Reason for time as limiting factor is that pharmaceutics standardly, weather original or generic, both in the EU and globally, may only be placed on particular relevant market after they have obtained a marketing authorisation. A marketing authorisation can be obtained through national authorisation or through a centralised procedure in EU, before the European Medicines Agency. Irrespective of the procedure, obtaining a marketing authorisation even for generic medicines is a resource-intensive and long process that, in principle, can take between 12 and 18 months for generic medicines and even longer for originator medicines. Competition Law regulators (either national regulators or DG Competition of the European Commission) can step-in in such situations when surge in prices occurs and are there are no available market substitutes with application of excessive prices as abuse of dominance.

Regulatory application of excessive prices as a form of abuse of dominance in patent protected pharmaceuticals is much less frequent, practically non-existent. Standard doctrinal explanation for this state is the intrinsic collision between intellectual property rights, that are exclusive in nature (patent protection in particular), and Competition law that promotes competition and non-exclusivity. However, there has been a very substantial application of Competition law on patent protection rights in other area outside excessive prices, including for example rules on agreements between undertakings and merger control. Real reason for rarity of application of excessive process as form of abuse of dominance in patent protected pharmaceuticals is reluctance on the part of regulators to initiate such proceedings. Excessive prices are viewed as controversial (not accepted in some jurisdictions like US) part of Competition law. Furthermore, excessive prices are considered as exploitative abuse and not as exclusionary abuse and thus not an enforcement priority. This reasons influenced on the small number of cases in which excessive pricing was determined within the EU Competition Law in general (18).

CASE STUDY IN PEADIATRICS: EXCESSIVE PRICES AND SPINRAZA®

Despite the rarity there is no legal reasoning that would exclude application of the legal institute of excessive prices (in jurisdiction where they are stipulated) on the patent protected pharmaceuticals. Recorded lack of Competition law enforcement in patent protected pharmaceuticals is therefore suboptimal. Good example for that is exactly in the area of paediatric pharmaceutics in the case of Spinraza®.

Spinraza® (nusinersen) is a medication used in treating spinal muscular atrophy (SMA) associated with a mutation in the SMN1 gene. Since the condition it treats is so rare Spinraza® entered in the realm of pharmaceuticals unofficially named 'orphan drugs'. Biogen, multinational biotechnology company, since 2015 holds patent rights on Spinraza®. Spinraza's® pricing is largely a 'black box' because of confidentiality clauses in pricing agreements with health authorities or insurers (19). Following their own investigations, the civil society groups estimate that the drug has a price of €210,000–280,000 per year per patient in Italy and of €529,800 per patient in the first year and €264,900 per year per patient thereafter in Belgium (17). The worldwide annual revenue for the product was around US$2 billion through 2018–2021. If 11,000 patients receive the medicine in one year, this puts the average worldwide price per patient per year at US$181,818 (17). Biogen says it bases its pricing on 'clinical benefit' and the 'prices of other orphan drugs' (19). However, consumer protection associations and civil society groups object in Italy and Belgium that Biogen invested US$648 million in the development of the medi-

TABLE 1. The list of the most expensive pharmaceuticals in the United States for paediatric use (source: www.drugs.com, April 1, 2024)

Generic name	Brand name	Diagnosis
Atidarsagene autotemcel	Lenmedly® (Libmedly®)	Metachromatic leukodystrophy
Delandistrogene moxeparvovec-rokl	Elevidys®	Duchenne Muscular Dystrophy
Elivaldogene autotemcel or eli-cel	Skysona®	Cerebral Adrenoleukodystrophy
Betibeglogene autotemcel or beti-cel	Zyteglo®	Beta-thalassemia
Onasemnogene abeparvovec-xioi	Zolgensma®	Spinal Muscular Atrophy
Metreleptin	Myalept®	Lipodystrophy/Leptin deficincy
Naxitamab-gqgk	Danyelza®	Neuroblastoma
Lonafarnib	Zokinvy®	Progeria and Progeroid Laminopathies

cine (20). If this is correct, then (based on the aforementioned average worldwide price per patient per year) Biogen would have recouped its direct R&D costs after treating 3,564 patients in one year (17).

It should be noted that generics to Spinraza® have been developed so application of excessive prices is not only applicable remedy to deal with high prices of this pharmaceutics. Biogen has faced scrutiny and investigation regarding the pricing of Spinraza®. Main reason is of course its high cost, which in some patients was up to $750,000 for the first year and around $375,000 for subsequent years. However, formal publicly available proceedings against Biogen for excessive prices of Spinraza® have not yet been publicized in any of the major jurisdictions (consumer protection associations have reported Biogen to Competition authorities in Italy and Belgium). If any national competition authority or DG Competition initiate proceedings usual steps in application of Competition law will be applied: determination of relevant market and assessment whether Biogen is in the position of dominance on that market prior to the determination of possible price excess in Spinraza®.

REPERCUSSIONS IN PAEDIATRIC HEALTH CARE SERVICES

Eight out of ten pharmaceuticals listed as the most expensive in the US in April 2024 have indication for use in paediatric population – Table 1 represents a list of most expensive pharmaceuticals for paediatric use. Similar situation is in the EU (with addition of exagamglogene autotemcel). Interestingly, only four pharmaceutics from the list can be found in the pharmaceuticals base in Croatia in 2024. Moreover, only two (Zolgensma®, Myalept®), are included in the medication list by the Croatian Health Insurance Fund (HZZO).

The most expensive medicine in the world currently is also a 'orphan drug' - atidarsagene autotemcel produced by Orchard Pharmaceutics, approved in US in March 2024 under the name Lenmeldy® (branded as Libmeldy® in Europe) with price per treatment exceeding four million US dollars. Its' efficacy in preventing disease symptoms or stabilizing progression was proven also in the clinical setting (21), however, the cost, as with many orphan drugs, raises concerns.

High prices of pharmaceuticals contribute to unequal healthcare accessibility worldwide. Variety of prices within and between the companies and generic drugs that are not necessarily cheaper are some of the reasons many countries, especially low-income, still face great challenges providing care for children with cancer (22). Even greater discrepancies in access to medicines and more unmet needs face paediatric patients with rare diseases as orphan drug developments are concentrated in only few therapeutic areas, as also shown in the Table 1 (23). The excessive cost has profound implications not only for oncology patients and children with metabolic diseases, but across the paediatric healthcare services, especially for children with neurological disorders, but also, for, example, for patients treated by the paediatric nephrology teams (24, 25). High price of previously described Spiranza influenced late broadening of indications of the drug in Croatia on the medication list of the Croatian Health Insurance Fund in 2019 after public outcry and treatments of patients abroad.

Stringer and more activist (by the Competition regulators) application of rules on excessive prices as form of abuse of dominance, especially in patent protected pharmaceuticals (in jurisdictions where they are applicable), could therefore be one of the effective tools in combating such inequality and access to health as fundamental right.

CONCLUSION

The main conclusion of this paper is that balance between competition rules on excessive prices as form of abuse of dominance and intellectual property rights in the area of expensive patent protected paediatric pharmaceutics can be regarded as suboptimal and there is a need for further regulatory development and activism on the side competition regulators. Even in those jurisdictions that do not have excessive prices, like US, possible regulatory change if it is to

come it will be most likely in the area pharmaceutical sector. Specially influenced is paediatric health care since majority of most expensive pharmaceuticals have indication for use in paediatric population. Stringer and more activist application of excessive prices as form of abuse of dominance can be an effective tool in combating inequality of healthcare accessibility and access to health as fundamental human right.

Abbreviations:

OECD – Organization for Economic Cooperation and Development
US – United States of America
BRICS – Brazil, Russian Federation, India, China, and South Africa
TFEU – Treaty on the Functioning of the European Union
EEA – European Economic Area
UBC – United Brands
EU – European Union
SMA – Spinal muscular atrophy

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SAŽETAK

Prekomjerno visoke cijene lijekova i njihov utjecaj na pružanje zdravstvenih usluga u pedijatriji

Dominik Vuletić

Kontekst: *Pedijatrijski lijekovi imaju značajan udio u skupim lijekovima. Posljednjih godina zabilježeni su značajni zahtjevi za intervencijom prema visokim cijenama farmakoloških proizvoda. Zabrana prekomjerno visokih cijena kao oblika zlouporabe vladajućeg položaja smatra se kršenjem prava tržišnog natjecanja u pravu Europske unije i nacionalnim pravnim porecima njezinih država članica. Većina zemalja članica Organizacije za ekonomsku suradnju i razvoj (OECD) ima slične zabrane u svojim propisima o tržišnom natjecanju uz važan izuzetak Sjedinjenih Američkih Država (SAD), iako i tamo postoje neke naznake promjena upravo u području farmaceutskog sektora. Regulacija prekomjerno visokih cijena kao povrede prava tržišnog natjecanja također postoji u propisima svih država članica BRICS-a (Brazil, Ruska Federacija, Kina, Indija, Južna Afrika). Problem prekomjerno visokih cijena u farmaceutskom sektoru jedna je od razvijajućih tema u literaturi prava tržišnog natjecanja i razvoju sudske prakse. Ovo je područje u kojem se pravo intelektualnog vlasništva, tipično patentna zaštita, sukobljava s pravilima tržišnog natjecanja. Troškovi istraživanja i razvoja takvih lijekova često su vrlo visoki, naglašavajući potrebu za ravnotežom između sukobljenih legitimnih interesa: pristupa zdravlju i razvoja istraživanja.*

Cilj: *Predstaviti razvoj zakonodavstva i sudske prakse u primjeni pravnog instituta prekomjerno visokih cijena kao oblika zlouporabe vladajućeg položaja u farmaceutskom sektoru s naglaskom na pedijatrijske zdravstvene usluge.*

Izvor podataka: *OECD, PubMed, Google Scholar, Scopus*

Zaključak: *Ravnoteža između pravila tržišnog natjecanja o prekomjerno visokim cijenama kao obliku zlouporabe vladajućeg položaja i prava intelektualnog vlasništva u području skupih pedijatrijskih lijekova može se smatrati sub-optimalnom. Stoga postoji potreba za daljnjim regulatornim razvojem i primjenom instituta prekomjerno visokih cijena u tom području.*

Ključne riječi: PRAVNI ASPEKTI; SUDSKE ODLUKE; PEDIJATRIJA; KONTROLA LIJEKOVA I NARKOTIKA