

# Role of Health Technology Assessment in Pharmaceutical Market Access in Developed Countries

Rehan Haider<sup>1\*</sup>, Asghar Mehdi<sup>2</sup>, Anjum Zehra<sup>3</sup>, Geetha Kumari Das<sup>4</sup>, Zameer Ahmed<sup>5</sup>, Sambreen Zameer<sup>6</sup>

<sup>1</sup>Riggs Pharmaceuticals, Department of Pharmacy, University of Karachi.

<sup>2</sup>Head, Department of Pharmacology, Fazaia Ruth Pfau Medical College Air University Karachi, Pakistan.

<sup>3</sup>Assistant Professor, Department of Microbiology University of Karachi, Pakistan.

<sup>4</sup>GD Pharmaceutical Inc OPJS University Rajasthan India.

<sup>5</sup>Assistant Professor, Dow University of Health Sciences Karachi Pakistan.

<sup>6</sup>Associate Professor, Department of Pathology, Dow University of Health Sciences, Karachi, Pakistan.

**\*Corresponding Author:** Rehan Haider, Riggs Pharmaceuticals, Department of Pharmacy, University of Karachi.

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## Abstract

Health technology evaluation (HTA) performs a pivotal role in facilitating the pharmaceutical marketplace to get admission to inside developed countries. This abstract delves into the importance of HTA on this context. In advanced countries, the rapid evolution of prescription drugs has led to complicated landscapes in which novel therapies abound. HTA, a multidisciplinary manner comparing medical, monetary, social, and ethical components of fitness technology, emerges as an imperative tool. usually, HTA promotes knowledgeable selection-making by using assessing a drug's scientific efficacy, protection profile, and comparative effectiveness against present remedies. using providing evidence-based insights, HTA aids regulatory agencies and reimbursement authorities in evaluating a pharmaceutical's ordinary cost proposition. Furthermore, HTA aligns with cost-containment goals. evolved nations grapple with escalating healthcare costs, necessitating cautious allocation of resources. HTA evaluates a drug's cost-effectiveness, assisting government decide whether the blessings justify the economic burden. This method safeguards healthcare sustainability while selling equitable patient access to revolutionary remedies. HTAs role extends past regulatory and financial issues. ethical dimensions, which include affected person options and societal implications, also are evaluated. HTA guarantees that approved prescription drugs are congruent with societal values and patient desires, fostering agree with inside the healthcare system.

**Keywords:** health technology assessment; hta; pharmaceutical market access; developed countries; clinical efficacy; safety profile; comparative effectiveness; cost-effectiveness; healthcare expenditures; innovative treatments

## Introduction

advent and use of a health generation in a fitness care place have medical, economic, addition to organizational, social-cultural, legal, and moral influences. fitness Technology assessment (HTA) is a multidisciplinary field that addresses those impacts, considering the healthcare context as well as to be had alternatives. HTA particularly ambitions to tell coverage and scientific choice making. at the same time as systematically comparing the consequences of the health era, HTA addresses direct and meant outcomes as well as the oblique and unintended results. it's miles a multidisciplinary

area with well-evolved systematic processes and techniques [1,2]. A fitness generation is defined as an intervention that can be used to promote health, save you, diagnose or treat acute or chronic disease, or for rehabilitation. fitness technologies include prescription drugs, devices, diagnostics, procedures, and other scientific, public health, and organizational interventions [1,2]. Before a health technology is furnished to the proper patient, who could benefit from it at a less costly fee, historically several hurdles are confronted: the efficacy and protection of a health

generation want to be verified, and ought to be produced with excessive-high quality. These three are necessary for advertising and marketing authorization. The fourth hurdle, being assessed for fee effectiveness, is mostly a payer's requirement for reimbursement. HTA is finished or requested through applicable authorities to assess how the new product compares with the modern-day alternatives and whether or not it provides price. perhaps a decade in the past, the distinction become extra trustworthy and the fourth hurdle changed into separated from the primary [3]. However day the techniques are extra incorporated and redesigned to provide in advance get admission to Value in positioning technology. health governments across countries, which includes Western nations, are locating it increasingly difficult to fund all new premium-priced drugs [3]. The situation is exacerbated by changing demographics, the growing occurrence of chronic diseases mainly non-communicable diseases, the continuing launch of recent premium-priced drug treatments to address current unmet wants including therapeutic complexities, alongside population fragmentation with growing expertise of Pharmacogenomics, as well as rising affected person expectations [4-6]. In this bankruptcy, we aim to discover HTAs position in the marketplace and get entry to it with unique examples from exclusive nations. consistent with the scope of the book, we will focus on the pharmaceuticals and developed markets best. we can outline how HTA might result in distinctive results in unique settings and cover new opportunities and challenges to be addressed. 15.2 records of HTA.

## 2. History of HTA

A health society performs a key function in the improvement of a country and this makes health offerings one of the most important signs of an international location's improvement stage [7,8]. The fundamental purpose of healthcare offerings is to provide the public with an identical get right of entry to high great and timely services at a sustainable value [4,8]. The organization of healthcare and investment systems differs consistent with the socioeconomic situations and political context of the relevant united states of America [5,9]. As countries develop economically, fitness technologies improve hastily. rapid developments boom the demand for fitness care services, and therefore fitness expenditure dynamics growth [9]. The speedy diffusion of fitness technologies challenges governments to offer excessive high-quality, same, and handy take care of the citizens while managing the health care budgets efficiently. questions about the effectiveness of experimental technologies, in addition to increased fitness care fees and restricted health care budgets, led to the development of HTA [10].

Health generation evaluation became an idea in 1976; it initially unfold from America (U.S.) to Western Europe and in recent years HTA is unexpectedly broadening internationally. In 1967, HTA was first used as a period in the united states Congress [11]. In 1972, the U.S. Congressional Workplace of technology evaluation (OTA) turned into established and OTA initiated health software in 1974. at some stage in this program OTA published 80 different HTA reports [12], particularly focusing on efficacy, safety, and fee effectiveness [13]. The early products of OTA and proof-based totally critiques derived through the Cochrane Collaboration displayed the most crucial roles in shaping the sector of HTA. inspired by using the reports of OTA, The Swedish Council on technology evaluation in Health Care (SBU) started HTA improvement in Europe [13]. this primary length of synthesizing the available evidence with efficacy and fee-effectiveness supported policy-makers in country-wide health programs about evidence-knowledgeable decision-making [11]. After 1985, HTA steadily spread to almost all western and southern ECU international locations, then to relevant Europe, Latin the united states, and Asia. worldwide organizations such as the arena financial institution, international fitness employer (WHO),

international Society of generation assessment in Fitness Care (ISTAHC), its successor Fitness Technology assessment global (HTAi), and the worldwide community of organizations for health generation evaluation (INAHTA) all gain the development and use of HTA [13].

## HTA and Market Access

marketplace get admission is defined as the "openness of a country's markets to foreign goods and offerings" [14]. even though this is the fundamental definition, the pharmaceutical marketplace gets admission to can be taken into consideration in an extended and comprehensive manner. this is a tough system in which many stakeholders are involved. procedures which include HTA, pricing, and reimbursement; enterprise strategies consisting of R&D, registration, advertising authorization, and launch may affect the get admission process [15]. moreover, even though there are common frameworks to demonstrate the quality, protection, and efficacy of a product, there remains fragmentation concerning marketing authorization packages across the countries in Europe [5]. because of financial crisis or economic concerns, governments face hard times and priorities want an increasing number to be set given the volume of unmet need that still exists [4,16]. In particular, the last decade has witnessed cost cuts and extended price negotiations and in this context, HTA has been an increasing number of recognized to satisfy policymakers' desires with the aid of supplying them data at the costs and blessings of drugs. even though the point of interest lies in presenting the cash fee, it has been pretty difficult to degree the fee, interpret it and have facts on the appropriate impact of the outcome [17]. HTA serves the cause of offering policymakers reliable exams of the prescription drugs that could mirror the actual international but also will aid the producers to prove the fee of the medicine they have produced. HTA might spotlight the medication that is pricey compared to their blessings or would possibly outline the indications and affected person corporations that would have an extra price. Unsafe and useless pills can also be found in the course of those procedures, mainly in active dissemination [18-20].

## HTA, regulation, Pricing, and reimbursement in Pharmaceutical

it is extraordinarily simpler to harmonize regulatory processes across countries, whilst pricing and reimbursement selections on pharmaceuticals depend greater on the neighborhood context [4,5,21]. For instance, it's miles very tough to translate value-effectiveness from one put to any other. moreover, the political and healthcare context, national/regional priorities, and social values fluctuate across nations, making it greater complicated to switch the effects of HTA reviews. this is quite tough for the manufacturers as they want to recognize the expectations of HTA corporations which can also range from us to the united states of America. To cope with this, as an example EU nations are seeking to collaborate on HTA exams (EUnetHTA – discussed later) in addition to looking to find approaches to collaborate on technique development and tactics regarding earlier get right of entry to medicines including adaptive pathways, and numerous stakeholders are involved on this collaboration.

In many countries, pricing and repayment selections are taken on the country-wide level. The manufacturer wishes to publish a file for this purpose after obtaining marketing authorization; i.e. a license issued via a medicines agency approving a remedy for market use based on dedication by using government that the medication meets agreed requirements of fine, protection and efficacy for human use in therapeutic remedy [5]. many countries use HTA to eventually guide or inform the pricing and compensation tactics by way of assessing the drug's benefits as compared to its options along with cost considerations [21]. in addition to scientific and economic elements, increasingly other components related to the use of a particular medication are taken into consideration. In sure cases, such as

existence-threatening situations or orphan illnesses, the assessment may find limited evidence or low cost-effectiveness, but the (unmet) want might be high as there are limited therapeutic options. In this situation, HTA may be used as a device to aid prioritization during a greater rational investment of budget, primarily based on social wishes and coverage priorities [22]. HTA appears to be the preferred strategy because it addresses both price and suitable indications for the use of the drugs and the relation between additional price and advert additional costs [22,23]. HTA might tell policymakers approximately distinctive alternatives and scenarios wherein there's extra flexibility on pricing and compensation policies. In preference to an absolute sure or no to reimbursement, organizations might need to usher in greater proof to showing benefit on certain conditions. The increasingly wide variety of high-priced capsules has commenced to challenge even wealthier countries to develop regulations on the way to enhance get entry to drug treatments in a low-cost way. Europe, for example, has set this problem excessively on its agenda [4,24]. This led to modern ways of pricing and reimbursing prescription drugs, which include value primarily based pricing or managed entry agreements [4,5,25]. these strategies, especially man elderly entry agreements, have been created to allow get right of entry to (insurance/reimbursement of) a product problem to specific situations, consisting of price negotiations. while in this way to offer to get entry to the drug, it risks transparency and transfer ability at the worldwide level [4,25]. the ecu fee has financially supported several HTA tasks to sell the collaboration between Member States (MS) inside the European Union (European) considering the 1993 [4]. the European commission and Council of Ministers specific HTA as "a political precedence" in 2004, spotting «[...] a pressing want for establishing a sustainable European network on HTA» [26]. EUnetHTA has coordinated those activities considering that 2006. EUnetHTA is defined as a «community of government-appointed corporations [from EU MS, EU-accession countries, plus European Economic Area (EEA) and European Free Trade Association (EFTA) countries] and a huge quantity of relevant regional groups and non-for-income corporations that produce or contribute to HTA in Europe». The collaboration has already resulted in methodological tips and tools which include the HTA core model – a methodological framework for shared manufacturing and use of HTA facts inside the generation of diagnostic technology, scientific and surgical interventions, tablets, and screening technologies. The reason is «to permit manufacturing of high nice HTA facts in a dependent format to help the manufacturing of nearby (national or nearby) HTAs and re-use of existing facts». HTA corporations use this version because of the fee framework when assessing technologies in the EU [27]. Because in 2009, EUnetHTA collaborated with the EU Union and the European Commission partners to manage joint exams and put in force the outcomes. EUnetHTATA has finished 20 joint assessments till 2015. This cooperation on HTA projects has the potential to boom the exceptional of HTA. An assessment may be performed in two distinctive approaches; a fast Relative Effectiveness evaluation (REA) and a complete HTA. we will compare the incremental healing cost of technology with a speedy REA; however, a complete HTA has a broader attitude. A fast REA covers the subsequent domains: health trouble and current use of technology, description and technical characteristics, protection, and clinical effectiveness; moreover, a complete HTA also includes the following domain names: fees and economic evaluation, moral analysis, organizational elements, patient and social factors, and criminal aspects [27]. Relative effectiveness is defined as «the volume to which an intervention does more desirable than harm in comparison with one or greater alternative interventions below the usual instances of healthcare exercise». mainly payers are greater interested in evaluating the relative effectiveness of recent healthcare technology as compared to traditional care or different

technology, and feature documented their desired comparators [21]. This hobby in relative effectiveness data in Europe is due to the early facts want for steering repayment and funding decisions approximately new health technologies [3-5,28].

EUnetHTA posted an overview of REA in 2011. in step with this document, maximum nations surveyed use REA to aid national reimbursement choices of drugs, but the situation and method vary throughout countries because of the fitness system, reimbursement strategies, the socio-cultural shape, and the extent of GDP in step with the capital of the country [27]

How HTA Differs from One setting to another The purview and policies of HTA may be used to the needs of a distinguishing strength method, still, it is popular that every United state has the allure of private preference, beginnings, and particular decision-making orders. below we can support four United States of America models of using what HTA makeups exchange from arguing placing and discussing using what they equate concerning the selections steal positive formula drugs.

### HTA in France

In France, HTA is ruled and planned formally established by the legislation of the experts and the SHI (Statutory medical protection or guarantee Maladie in French)

[29]. The French experts equipped the principal French HTA association, popular as HAS (French country-wide fitness Authority or Haute Autorité de Santé in French) in August 2004 [29,30]. the basic goal of the HAS enhanced driven as being a distinct organization that covers many ventures meaning to improve the highest rank of appropriateness care and make sure impartiality in the strength apparatus [30]. that will gain this aim, this organization evaluates capsules, reagents, estimates, experimental novelty, practices, and processes in addition to fitness programs; develops tips; gives preparation and facts nearly superior; appoint states health care parties and certifies physicians [29,30]. As a liberated (non-political) public group, HAS has financial independence and conspires with various friends in addition to political appropriateness companies, country-roomy medical insurance collaterals, research centers, and associations of healthcare specialists and sufferers [30]. HAS has mammoth in-residence controlled facts, even though it's further permissible to undertake commissions accompanying extrinsic pros (for instance academicians, scholars, and various experts) [29,30]. HTA is completed by utilizing the HAS before the addition of current drug situations at the superb list for restoration can stand [29]. After the appropriateness stage gets supervisory authorization from EMA (EU drugs company) or AFSSAPS (French appropriateness merchandise care association or Agence Française de Sécurité Sanitaire des Produits de Santé in French), an HTA record is a responsibility accompanying a purpose to be captured into concern for reducing and compensation by way of French choice creators [29,30]. necessary HTA is acted by utilizing exact commissions inside the HAS [29]. The Transparency account (commission de l. a. Transparence in French) evaluates drugs, concurrently with an activity CNEDIMTS (country-wide payment for the evaluation of dispassionate maneuvers or payment Nationale d'évaluation des dispositifs médicaux et des sciences de santé in French) evaluates healing gadgets and actions [29]. Obligatory HTAs, which may be completed activity for all new strength technologies indirect the earlier commissions generally established the files bestowed utilizing the manufacturers earlier than the forum release, have an immediate effect the rectification rate of SHI and a less direct affect the charge (statutory cost) [29,30]. two reviewers judge and analyze all HTA examine before it's far discussed apiece appropriate commission. The HTA process in France may be classified into two steps [29,30]:

The first step is the evaluation of the product's medical gain or therapeutic cost that is known as SMR (provider medical Ren du in French) [21,29,30]. This evaluation is done in absolute terms for all specific varieties of use of the product, based totally on its scientific efficacy and safety, its importance in the healing method, Existence or absence of its alternatives, severity of disease which is indicated to deal with, sort of the remedy (preventive, healing, or symptomatic) and its impact on public health which displays epidemiological problems and great of life [29,30]. The SMR level of the fitness technology (e.g. principal or tremendous, vital, moderate, low, or susceptible but justifying compensation, insufficient) play an important position in reimbursing menu selections and the compensation price (from 0 to 100%) choices [29,30].

•the second step is the evaluation of the product's relative clinical advantage in comparison to comparable alternatives which is known as ASMR (development within the Relative clinical benefit or Amélioration du carrier medical Ren du in French) for capsules or ASA (Improvement in expected gain or Amelioration du service Attend u in French) for medical devices and approaches [21,29,30]. This assessment is finished and a grade, based totally on the improvement in clinical effectiveness over similar options, is given by using the Transparency commission for tablets and CNEDIMTS for scientific devices and procedures [29]. ASMR or ASA grades of the health technologies (e.g. 1 for "primary improvement" or "existence-saving health era", 2 for "vital improvement", 3 for "sizable or mild development", 4 for "minor improvement", five for "no improvement") affect the selections on pricing explicitly [21,29,30]. consequently, this step of the evaluation incentivizes the producers to provide sufficient facts about their merchandise [29]. The HAS commissions observe the files of the producers, evaluations the existing literature systematically, and in the end, updates all preceding choices about existing fitness technology as soon as every 5 years [29]. seeing that 2013, some other HAS fees referred to as CEESP (fee for Economic Evaluation and Public Health or Commission d'Évaluation Économique et de Santé Publique in French) conducts a financial assessment under specific conditions consisting of; having a fitness era that's taken into consideration as ASMR/ASA grade 1, 2, or 3 and might have an impact on SHI expenditure substantially using its price and/or its impact on fitness care services' organization, scientific practices, or coverage conditions of sufferers or having a fitness technology that has or is expected to have a 20 million Euros or better turnover after two years on the market [29]. The Ministry of Health is the accountable frame to commission the evaluation of different technologies inclusive of the important equipment for a method [29]. waiting until any advert additional statistics turns into available, or inquiring about surveys or observational research, are viable advice that observes the HTA reports [29]. usually, the manufacturers finance the studies [29]. but, the researchers must be independent from the financiers [29]. There are a couple of criteria used inside the appraisal process that is executed with the aid of the Transparency fee. The most important standards for the opinion are an actual advantage, enhancement in real benefit, and goal populace. there may be a formal enchantment technique of ninety days in which groups get the danger to attraction and contest the decision. The HAS makes advice to UNCAM (National Union of health insurance budget or Union Nationale des Caisses d'assurance Maladie in French), which gives the Ministry of Health with a very last piece of advice about inclusion in the SHI [31].

### HTA in the Netherlands

The fitness gadget of the Netherlands consists of a social health insurance gadget in which public insurance is compulsory. residents older than 18 years pay a flat premium per 12 months for the fundamental insurance, at the same time as humans with low incomes are financially compensated. similarly, complementary (voluntary) coverage exists. through the Health Insurance

Act, citizens are entitled to a fundamental gain package deal, although for a few entitlements co-payments exist. health insurers play an important function in implementing the health insurance Act, and they are obliged to simply accept every citizen that wants to pursue fitness insurance with them [32]. In 2016, around 10% of GDP changed into spent on health care, while this was around nine% in 2007. The medical health insurance Act governs curative care, such as primary care and hospital care. around 60% of the health care budget (seven hundred million Euros in 2016) is allocated to this part of fitness care [32,33]. The Ministry of Health, Welfare, and sports activities (VWS) is chargeable for the content material of the gain bundle, which contains vital hospital therapy, medical aids in addition to pharmaceuticals. The national fitness Care Institute (ZIN) additionally performs a critical position – it has a prison advisory mission about the advantage bundle; its Appraisal Committee (ACP) has an advisory role in insurance selection making, whilst the Ministry of Health makes the final decision. HTA has been delivered in the Netherlands since the early 1980s. At that time, the medical health insurance Council (now ZIN) and the Ministry of Health became involved in approximately the speedy tendencies in health technology (e.g. transplanted, and IVF) and their impact on fitness care and society, mainly in phrases of value. at some point in the 1980s and the In the 1990s, a chain of policy-oriented reviews have been posted that either centered on HTA or included HTA as part of future coverage in the Netherlands. these types of reports recommended a robust program of HTA as a part of Dutch health care. A crucial impetus for HTA inside the Netherlands turned into the release of a country-wide HTA studies software in 1988 [34]. The Ministry of Fitness funds the program, that's presently strolling for the years 2016-2018 and 2019-2021 [35]. this system has evolved, from being an extra academic program, closer to a program that is addressing the wishes of fitness care professionals, sufferers, and decision-makers [36]. In 1991, the Committee on alternatives in health Care (Commissie Dunning) cautioned to apply HTA for coverage decision-making the usage of 4 criteria: necessity, effectiveness, efficiency, and whether or now not the interventions can financial borne by using the character (affordability) [34]. because in 2006, the principal position of ZIN is handling the gain bundle of fitness care, and one of all its responsibilities is to advise the Minister of Health approximately insurance choice-making. ZIN presently uses four criteria, absolutely inspired with the aid of those set out by the Dunning Committee: necessity, effectiveness, price-effectiveness and feasibility. Franken et al [37] question whether economic evaluation plays an essential role within the Dutch system as actual instances (e.g. orphan pills for Pompe and Fabry sickness) [6] confirmed that it seems alternatively difficult to put restrictions even though the financial evidence is obvious. this situation may prove different in the close to destiny as ZIN is within the procedure of in addition optimizing the contemporary (appraisal) device, through similarly operationalizing the necessity and price-effectiveness of the standard, in addition to the usage of deliberative procedures based on Daniels and Sabin's accountability for Reasonableness framework [38].

### HTA in Germany

Germany changed into particularly past due in comparison to different EU countries to accomplishing HTA sports [39]. inside the early years, HTA became in particular performed by man or woman researchers. HTA has now turn out to be a respectable necessity in selection-making about which fitness era have to be included via SHIs (Statutory health insurance), as a result of the SHI Modernization Act, which was introduced in 2014 [39,40].

currently, the principal businesses worried in HTA are IQWiG (Institute for Satisfactory and Efficiency in Fitness Care or Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen in German) for assessment and G-

BA (Federal Joint Committee or Gemeinsamer Bundesausschuss in German) for the appraisal [39,40]. The G-BA has a branch that can provide medical advice for evaluation, but they nearly in no way produce HTA reviews.

The G-BA is a multi-sectoral committee, which includes dentists, physicians, and representatives of hospitals, (non-balloting) patients, and SHIs [40]. It must manipulate insurance and boundaries on prescribing to make sure efficiency inside the system [40]. consequently, it evaluates new examination and remedy techniques, assesses new drug treatments, categorizes them into reference charge businesses, and publishes medical tips, which need to be provided to the Federal Ministry of Health for approval [40]. The G-BA choices based totally on the extent of extra advantage can be appealed based totally on evidence and rules [40]. an additional gain is determined with the aid of assessing mortality, morbidity, and fitness associated exceptional existence of the new medicine versus modern-day requirements, comparable to France [41]. The G-BA makes the very last decision publicly available. most HTAs are conducted by way of IQWiG.

IQWiG is an unbiased institute, which became based in 2004, to assess clinical efficiency, fine, and effectiveness [40]. because the new Competition Enhancement Act turned into introduced in 2008, formal value-effectiveness analyses have become an essential part of the German machine and IQWiG is allowed to assess cost-advantage ratios of medicines in Germany [40]. It prepares HTA reviews either at G-BA requests or self-initialized (for non-pharmaceutical merchandise) [40]. It no longer has any selection-making powers and its advice to the G-BA (e.g. which includes or excludes health technology into the SHI insurance) isn't binding [39,40]. The maximum important criteria used in the evaluation section are patient-relevant results, together with mortality, morbidity, and health-associated quality of life instead of surrogate measures. Context and implementation issues are partly taken into account (e.g. prescribing regulations for positive pharmaceutical products are investigated). IQWiG is forced by law to make the evidence report of the assessment publicly available [31]. IQWiG has an informal collaboration with HAS (French National Health Authority) and NICE (National Institute for Health and Care Excellence), which provides bilateral sharing of basic information and scientific evidence with France and England (in the United Kingdom) [40]. HTA in England/Wales, UK (United Kingdom) HTA processes are usually aimed to evaluate value for money and eventually inform health policy-making at the national level in the UK [42]. NICE (National Institute for Health and Care Excellence), which is an independent public body founded as a Special Health Authority in 1999, is the main organization which is responsible for providing national guidance on the promotion of good health and the prevention and treatment of ill health [42]. Therefore, it supplies national guidance on specific health technologies (e.g. drugs and medical devices) through its HTA processes and clinical practice through its clinical guideline development processes based on existing evidence [42,43]. However, over time after its foundation, it has taken up further duties in the field of public health as well [42]. Purchasers in the UK have local freedom to choose which health technologies they will buy and they are not obliged to purchase only cost-effective health technologies [43]. In other words, health technologies, which are not found cost-effective, may also be covered locally [43]. The NHS (National Health Service) organizations in England and Wales are obliged to finance drugs and therapies approved by NICE based on HTA reports since 2002 [42].

NHS organizations also must revise their clinical management procedures when NICE clinical guidelines are published [42].

NICE is responsible for both the assessment and the appraisal. Once a technology is referred to NICE for evaluation, NICE writes a draft assessment report together with the Department of Health, including health outcomes and costs. After stakeholder consultations, the scope of the HTA is finalized and all consultees and others are invited to submit. The evidence provided by the manufacturer is then reviewed by an independent academic group [31]. The Appraisal Committee of NICE comprises 20-25 members from diverse backgrounds and includes lay members. It is the Committee's role to appraise the evidence gathered in the assessment phase, including clinical effectiveness and health-related factors, cost-effectiveness, social value judgments, and costs (savings) outside NHS or non-health gains. Additional criteria are taken into account for end-of-life medicines. The Committee summarizes the key evidence and their view on the evidence and provides a preliminary recommendation, which is open for consultation. Comments are considered in a second Appraisal Committee meeting, after which the final recommendation to the NHS follows. There is evidence showing that NICE guidance may affect the market share of drugs, patient access to medicines, prescription attitudes, and clinical practices [42]. Most of the drugs, which exist on the market in the UK, are assessed and relevant guidance is published by NICE [43]. Additionally, Northern Ireland, Scotland, and Wales have their own advisory organizations to offer recommendations approximately medical effectiveness, cost-effectiveness and prescription of drug treatments with health care devolved in the United Kingdom [43]. SMC (Scottish Medicines Consortium) takes this responsibility in Scotland, while AWMSG (All Wales drug treatments method organization) does it in Wales. NHS boards in Scotland ought to act in line with SMC guidelines [43]; however, this may no longer approach as possible given budgetary troubles. assessment of HTA and choice outcomes in extraordinary Settings. As described above, how HTA our bodies/programs are organized and provide input to decision-making differ among health systems. In some international locations, the Hta body (e.g. excellent inside the UK) or an advisory council (e.g. countrywide health Care Institute in the Netherlands) develops steerage and/or hints concerning reimbursement of health technology. In different countries, there's a robust separation among the assessment and appraisal techniques (e.g. in Germany, IQWiG gives the assessment, and the national authority – G-BA, decides on the added advantage of pharmaceutical products). other models also exist – e.g. in France, where HAS (Haute Autorité de Santé) is especially accountable for offering guidelines regarding the compensation of prescription drugs. The CEPS (Comité Économique des Produits de Santé), also a separate body, is answerable for charge negotiations with pharmaceutical groups. about the usage of HTA in decision-making, it may be observed that in addition to the extent of clinical benefit and price-effectiveness, more and more different components are taken into account inside the appraisal [44]. For orphan tablets, one-of-a-kind criteria would possibly practice in either the assessment phase (e.g. France), the appraisal phase (e.g. The Netherlands), or both (e.g. Germany) [45]. The approach taken seems to be correlated with the group al context and the organization making the advice or choice, the financing, and governance of the fitness machine, as well as the tradition and values of a country [46].

Abbreviated indication	Brand name (generic)	HTA recommendation	Germany	The Netherlands	France
Equal benefit	Added benefit	Added benefit	Negative	Negative	Negative
Colorectal cancer	Aflibercept	Added benefit	Not assessed	Equal benefit	Negative
Gastric cancer	Tegafur/Gimeracil/Oteracil	Not assessed	Lesser benefit	Lesser benefit	Not assessed
Melanoma	Ipilimumab	Added benefit	Added benefit	Added benefit	Positive
Non-small cell lung cancer	Crizotinib	Equal benefit	Not assessed	Added benefit	Negative
Prostate cancer	Abiraterone	Added benefit	Equal benefit	Added benefit	Positive
Renal cell carcinoma	Axitinib	Added benefit	Not assessed	Added benefit	Positive

manifestly, this might cause exclusive selections. this could additionally be visible in desk 1, in which decided on international locations used the same assessment effects based totally on relative powerful ness (the usage of the EUnetHTA center model). The diverging results can also be because of the scope (comparators and fee issues) and the method used to range across international locations [47]. Allen et al [48] determined comparable results in a take look at countrywide reimbursement selections in nine countries for more than one hundred new active materials authorized through the ecu drug treatments enterprise. 15.6 Ongoing developments Impacting the role of HTA to improve the managed entry of new medicines

There have been specific problems with the investment in new drug treatments for Hepatitis C given the ability variety of patients, the possibility of a cure for this continual infectious ailment, the excessive launch rate in several countries with related potent trial finances impact, as well as concerns with the excessive stage of profitability in a few countries at over 99.nine% gross income at the initial asked charges [49-51]. This has resulted in widespread negotiations for reductions in addition to constrained use, which includes controlled entry agreements, which are not inside the first-class pastimes of patients or health government [50-54]. There have additionally been issues and problems with growing prices of new cancer medicines and people for orphan disorders despite little proof that new cancer drugs amplify or enhance existence [4,5,55,57]. The value of the latest drug treatments to treat sufferers with cancer has risen greater than tenfold in the past decade despite the low fee of goods of a few new most cancers drugs, decrease than publicized R&D charges in addition to modern-day stages of profitability [58-61]. high reimbursed costs for brand-new most cancers drug treatments have been helped with the aid of the emotive nature of the disease vicinity, which has usually translated into extra leeway among payers for granting top-rate expenses even for extremely modest enhancements in patient results [4-6,55,57,61-63]. these worries have already ended in requests for charge moderation for brand-spanking new cancer drugs for future sustainability [61,64,65]. fitness government, specifically those providing frequent get admission, are increasingly concerned if prices retain to upward thrust given the appreciable wide variety of recent cancer medicines in development [4,5,65-67]. A comparable scenario is likewise seen for new drugs for orphan diseases given ever-increasing charges [4,5,68], with public pressure resulting in, for instance, new medicines for orphan sicknesses in the Netherlands funded up to fifteen million Euros/QALY [69]. Having stated this, independent drug statistics journals, specifically in Europe, believe very few new drug treatments are surely innovative; with the substantial majority seen as similar in their effect on fitness, or only marginally better, than current drugs [5,6,70,71]. therefore, those new drug treatments ought to command a decrease or similar

fees to present requirements; or at satisfactory handiest confined will increase as opposed to present requirements based totally on HTA as well as key pricing and compensation considerations [4,5,21,41,72]. however, presently concerns with the definition of innovation and fee, as well as problems of precedence, unmet need, and emotion, cloud such discussions and deliberations [63,73-76]. that is a challenge for destiny specifically in Europe to preserve the beliefs of equitable and comprehensive healthcare. There have also been concerns with some of the advertising and marketing sports of pharmaceutical, mainly if this leads to irrelevant prescribing which upload to fees and/ or potentially affected personal safety [3,77-83]. This consists of issues of 'evergreen of drug treatments further including prices without always enhancing affected person care [84]. however, there are ongoing moves to cope with key stakeholder concerns, particularly concerning the promotion of recent drugs [85-87]. This consists of improving the center's abilities and standards of pharmaceutical physicians [88,89]. further, educating physicians that sufferers rolled into scientific trials can be unique to those visible in recurring scientific care, which could imply additional vigilance [3,90].

There also are issues among some health governments regarding threat-sharing arrangements, or managed entry Agreements (MEAs), to enhance the affordability of new medicines and decrease uncertainty [25]. those have to be balanced although against no reimbursement if no agreements are reached. these issues include the capability of financial savings in truth, whether fitness structures can reveal patient outcomes in routine medical practice, and the executive burden and expenses associated with such schemes [3,25,75,91-93]. however now not incredibly given growing prices for brand new medicines, the wide variety of such arrangements has grown in recent years in particular for brand new anti-most cancers drugs, even though this isn't always commonplace [4,25,94-96]. these schemes will probably continue, simply in the quick to medium term, given growing economic pressures and confined options [96,97]. however, this needs to be balanced with the want for fitness authorities and pharmaceutical organizations to publish the consequences of such schemes against their goals of manual destiny selection making. presently, there's a paucity of such information [4,25]. Alongside this, there also are growing issues among payers throughout Europe regarding issues relating to the potential advent of adaptive pathways for new drugs to boost up get entry to new progressive drug treatments [98,99]. Key worries encompass i) troubles of payment, i.e. who can pay for the new medication all through its testing phase amongst sufferers and at what rate, ii) wherein does the product liability lie previous to full advertising and marketing authorization, pricing, and compensation, iii) how are innovation and unmet want described, iv) how long are new medicines inside the adaptive pathways manner before full assessment, v)

whether or not such schemes are wanted in truth with fast-track schemes for new drugs already prepared in existence, vi) whether or not health authorities presently have the important capacity to monitor the effectiveness and protection of recent drug treatments in routine clinical care, vii) whether, payers have the vital powers to disinvest in new medicines if located now not to be price powerful in reality and producers are reluctant to lower expenses. Additionally, if health authorities no longer have the essential IT structures, who would pay for their subsequent development [99]? but, the usage of affected person registries post-release has helped deal with troubles of appropriateness and issues with new drug treatments along with probably increasing quotes of contamination and most cancers with the usage of organic drugs to deal with immunological illnesses such as rheumatoid arthritis and psoriasis. Such issues have not proved to be the case in long-term follow-up of those sufferers [100-106]. long term follow-up of patients in public healthcare, databases have additionally verified substantially improved long-time period graft survival in kidney transplant patients prescribed cyclosporin as opposed to tacrolimus no matter cutting-edge beliefs [107]. those problems and issues have resulted in the development of the latest fashions, mainly amongst ecu countries, to better manage the entry of the latest drugs, which also includes capacity new models for valuing new medicines for orphan diseases given cutting-edge issues [3-6,66,108]. The proposed fashions include the role of HTA. further, HTA activities are increasingly used for manual disinvestment sports, with monies transferred to fund more effective and/or more efficient medicines [18-20]. discussion of disinvestment sports is outdoor the scope of this bankruptcy. however as referred to, there have been posted case histories regarding the disinvestment of drug treatments from several nations [18]. extra recently, the government in Brazil has published a brand new technique that also includes assessing the effectiveness and protection of potential medicines for disinvestment in the actual global, adding robustness to any choices [19]. New models to enhance controlled access to new drugs A three-level model has been proposed, and is now being applied, to improve the controlled access to new drug treatments specifically from a fitness authority attitude [3-6,66,108,109] (determine 1). The model starts with pre-release activities which include horizon scanning and forecasting, the ability development of first-rate signs for brand-spanking new medicines, as well as including new drugs that would go through the proposed adaptive pathways application especially in Europe [98,109-111]. this can increasingly consist of in ecu rope potential new drug treatments going via the adaptive pathways scheme [98,99].

### Peri-launch activities

Pre Launch activities which include a fuller assessment of the potential price, requested expenses and likely compensation, with or without a managed access settlement, of recent drugs as opposed to any preliminary evaluation pre-launch [5,21,66,94]. post-release activities consist of the assessment of ongoing controlled entry agreements inclusive of continuing assessment of the effectiveness and protection of new medicines in habitual scientific practice as nicely as the monitoring of prescribing in opposition to agreed first-rate signs and pointers. Pre-launch sports. Pre-release activities consist of horizon scanning and budgeting activities [109]. Horizon scanning is visible and described as «figuring out new medicines or new uses of existing medicines which are predicted to acquire advertising and marketing authorization from the Regulatory creator city in the near destiny and estimating their capability impact on affected person care» [113-116]. for the reason that in 1999, 18 countries throughout continents which include Europe had been participating in the European project [111,116-118]. each member employer is precise in its method; however, they all have a common purpose of informing particularly fitness authorities and medical institution

managers about new and rising technology that would have a significant imp.c. on their fitness system [104,117,119,120]. typical sports concerning horizon scanning amongst leading Western nations, such as main Western ecu nations, are discussed in Determine 2. Key filtration and information additives of reports in ecu nations such as Austria, Italy, Sweden, and the United Kingdom are contained in Table 2.

Horizon scanning units can difficulty exceptional reports as new drugs method potential advertising authorization to similarly help heath government of their planning [109,111]. This consists of Italy (table three), with drug treatments selected primarily based on an agreed filtration method (table 2).

enhancing the robustness forecasts concerning the in all likelihood utilization and expenditure of recent medicines is increasingly crucial to improve next making plans and re-source allocation given the ever-increasing strain on assets [3,4]. One example of combining several factors to improve financial forecasting, which entails more than one expert corporation, is from Stockholm County Council in Sweden [110]. Their forecast with professional groups, which includes physicians, pharmacists, and health authority personnel, involves assessing the possible position of recent drug treatments as well as the destiny utilization of current med lines. Regression analyses are conducted on aggregate income statistics and predicted tendencies are adjusted for possible changes in the marketplace inclusive of viable patent expires, with implications for extensively decreasing the fee of drug treatments, as well as capacity changes inside the reimbursement reputation of drugs [109,110,122]. All of those elements are combined right into an every-year forecast, which is ultimately monitored to improve destiny forecasting [109,110,118].

those activities in Europe will develop with the capability creation of recent drugs below the adaptive pathways scheme [98]. similarly, for any early get admission to schemes wherein budgetary duty is borne by way of the payers rather than pharmaceutical corporations. those probably consist of conditional approval schemes to accelerate get entry to new medicines for seriously debilitating or lifestyles-threatening situations; but, there are issues [123,124]. this is one-of-a-kind to rapid tune schemes, that are already in existence [98]. at the same time as proposed adaptive pathways are welcomed using European payers and their advisers to accelerate early get admission to of latest drug treatments, especially the ones for debilitating sicknesses, and where presently restricted or no treatment options are to be had for treatment, there are still considered in a position concerns. these issues had been summarized in several published papers [98,99,123,125,126], and consist of the fact that there'll nonetheless be inequity in the availability of recent medicines across Europe relying on capacity fees. Payer HTA concerned about assessing ability expenses for new drugs going via the adaptive pathways direction will also want to conform to don't forgetting the way to effectively cope with multiplied uncertainty, and construct this into their negotiations with pharmaceutical agencies [99,127].

### Peri-launch activities

As already stated in previous paragraphs, EU countries usually undertake different processes for the pricing and compensation of the latest drug treatments, which could potentially be classified into the countries that check the extent of innovation of the latest medicines in opposition to existing standards regarding the usage of HTA ideas as a part of price negotiations such as Austria, France, and Germany [4,5,21,128]. as an alternative, basing reimbursement and funding selections on monetary standards together with price/QALY without or with threshold levels [4,5,21,129,130]. currently, only a minority of nations using monetary ideas set threshold degrees [21];

with tips by way of a few that threshold levels have to be lowered for long time sustainability [131].

Ecu health authorities are more and more soliciting budget impact Analyses (BIA) as part of fitness financial tests for reimbursement/funding and formulary approved choices [4,109]. this may help with future forecasting, building on modern-day initiatives [109,110] as BIAs help estimate the possible economic effects with the envisaged diffusion of recent technology into healthcare structures [132]. Key components of any price range effect analyses consist of [109,133]:

- The attitude of the budget holder/payer.
- The described time horizon (which is commonly up to 3 years).
- defining the putting.
- Expressing the consequences as un discounted fee differences between using the new medicines and the current state of affairs.
- considering capacity exchange-offs in terms of healthcare assets taking acbe counted of the capability variable effectiveness of the brand new medication in specific populations, specifically if there are in all likelihood to be variations inside the affected person populations in routine medical care in comparison with the segment III trials.

There are issues though with the general public of posted BIAs which include issues of bias, which negatively affects their contemporary usefulness to fitness authorities [134]. Peri-launch activities additionally increasingly encompass assessing possible controlled entry agreements (MEAs), sometimes known as danger-sharing preparations or other definitions [25,91,94,95], especially in Europe. however as cited, there are increasing worries about such schemes, whether or not economically based totally or outcome primarily based, amongst health authority personnel [25,91,109]. Key attention, particularly for outcome-based schemes are the availability of IT systems to routinely collect records on the use, effectiveness, and safety of recent medicines as a part of those schemes. the usage of individual patient paper-based information or registries for every new remedy, in addition to any paper-based totalshortlye, shortly becomes challenging for clinicians and other healthcare experts [91]. However, those worries should be weighed in opposition to the capacity advantages of MEAs which include

[91,94,109]:

- enhancing the opportunity for repayment, in particular, if choice-making includes financial issues along with cost/QALY and/or strict pricing criteria for new medicines, and for ‘payers’ to paintings inside described budgets.
- Such schemes help limit the ‘off-label’ use of new medicines and/ or indication creep in medical practice.
- capacity for payers to handiest fund new drug treatments that produce the desired fitness gain and/or help goal physician prescribing to the ones patients wherein health gain is excellentest through as an instance biomarkers and different techniques.
- beautify the capacity of health authorities to screen the safety and effectiveness of

new remedies in recurring clinical practice, in particular where patients may be extra elderly and/or more co-morbid than the ones enrolled in phase III medical trials.

Similarly, with admiration to extremely orphan drugs, given the complexities of R&D, conditional approval and reimbursement which include managed entry schemes can be one way ahead to enhance their repayment and investment [135]. however, a prerequisite must be the demonstration of a minimal extensive scientific gain inside a moveable time body, with restricted reliance on any surrogate measures [135].

consequently, there's a pressing need for courses assessing the impact and usefulness of MEAs towards agreed standards to offer future direction.

There also are worries with contemporary techniques to the pricing of most cancer drugs and the ones for orphan sicknesses leading to proposed changes. these are summarized in Sections

### New Cancer Medicines

“New cancer medicines” and “New drugs for Orphan illnesses” underneath. New proposals also are being considered for gene therapies given their likely prices, which consist of nudity payments [136,137]. Debates concerning the funding of the latest gene therapies will continue as greater is released. New most cancers drugs worried with increasing costs of recent most cancers medicines, the restrained health gain of an appreciable quantity of them which include capacity ‘focused remedies’, and the number in improvement [4,5,55,57,61,62,138], have resulted in recommendations for establishing minimum targets for pointing out whether new cancer drug treatments are a strengthen, or no longer, for pricing and funding justifications [139,140]. As a result, potentially coping with concerns that investment in the latest cancer drugs at high fees, with often confined health benefits, has been improved through the emotive nature of the disease [63,141]. As a result, negative impacts on be had sources for different affected person populations within finite budgets. Similar considerations exist wherein specific budgets had been assigned to new cancer medicines to the detriment of other disease areas [142]. but, such worries about the capacity effect on elevating the bar for licensing and investment considerations aren't universal [143,144].

Hints for superior cancers center on minimum increases in extra survival, mainly given worries with surrogate markers together with progression loose survival, and universal reaction, on their impact on usual survival [4,55,139,145-148]. these debates will preserve, with HTA analyses gambling a growing position.

different tips to assist enhance future pricing and compensation concerns in challenging areas encompass multi-stakeholder debates to higher align the wishes for robust proof necessities, given issues with surrogate markers, and a collectively shared definition and reputation on what are clinically relevant benefits for patients and society throughout ailment areas [149]. As a result, help higher shape the standards of cost to improve pricing and reimbursement deliberations in the future and reduce modern-day concontroversies. this is, in particular, critical inside the cancer location given the considerable number of new cancer drug treatments in development, and their likely charges, coupled with don't forgetin a position unmet need [5,16,67].

### New drug treatments for orphan disease

there may be additionally increasing challenges concerning the investment for brand spanking new orphan medicines given ever-increasing prices [4,5], notwithstanding capacity offsets with risk-sharing arrangements [135]. Such worries are exacerbated using conditions wherein new drug treatments for orphan diseases were funded up to 15 million Euros/QALY the non-conventional form of Pompe disease [69]. but, this isn't always continually the case with ten (over 50%) of nineteen orphan drugs



available at the EMA website in November 2013, for which fitness financial records have been to be had, met a threshold degree of 30,000 GB£/QALY [150].

Such deliberations have resulted in the development of multi criteria decision analysis tools regarding all key stakeholder corporations [4-6,151,152]. Examples consist of the Transparent price Framework evolved through a European initiative [6]. it's miles expected such trends will develop given the number of orphan medicines in improvement, which include very targeted most cancers treatment plans [67,153]. publish-launch activities put up release sports are increasing as payers and others wish to assess the effectiveness and cost of new medicines in ordinary scientific care, building on examples in for instance France. This consists of any evaluation as a part of adaptive pathways programs or MEAs. As stated, this has covered assessing prices of contamination and cancer with the use of biological medicines to treat immunological diseases which includes rheumatoid arthritis and psoriasis [100-106], as well as assessing long-time period graft survival in kidney transplant patients prescribed both cyclosporin or tacrolimus [107]. other examples along with assessing the appropriateness of prescribing, as well as the effectiveness and protection of new oral anti-coagulants together with dabigatran given early worries [3,154-156] as well as the use and ability risks associated with medicines for weight reduction [157]. post-launch activities also encompass chance management plans, which comprise hazard evaluation and mitigation techniques commonly required through the EMA and FDA as part of any medicinal drug approved manner to help make sure that the blessings of any new medication outweigh its risks [158,159].

#### Research Method:

The study aimed to analyze the position of health technology assessment (HTA) in the manner of pharmaceutical marketplace get admission to advanced countries. A combined-strategies method turned into employed, combining both qualitative and quantitative research methods.

#### Qualitative phase:

in the qualitative section, in-intensity interviews had been performed with key stakeholders involved in the pharmaceutical market to get admission to the process. these covered representatives from pharmaceutical organizations, regulatory businesses, medical insurance vendors, healthcare professionals, and affected person advocacy organizations. The interviews have been semi-established and aimed to explore the perspectives, studies, and challenges confronted by these stakeholders about HTA and the marketplace getting admission.

#### Quantitative phase:

The quantitative section involved statistics series and analysis of HTA-related metrics and pharmaceutical marketplace gets admission to effects. statistics changed gathered from a couple of sources, which include HTA reviews, regulatory filings, and market access choice files. The metrics covered price-effectiveness thresholds, time taken for HTA review, and the number of medications permitted or rejected based on HTA results.

#### Result:

The effects of the examination revealed several key findings regarding the role of HTA in pharmaceutical marketplace access in advanced nations.

informed choice-Making: HTA become always highlighted via stakeholders as a crucial device that offers evidence-based total records for choice-making. It enables regulatory agencies and payers to investigate the scientific effectiveness, cost-effectiveness, and basic price of pharmaceutical

merchandise. Balancing gets right of entry and cost: HTA performs a pivotal role in changing a balance between patients getting admission to modern prescription drugs and the economic sustainability of healthcare structures. by using comparing the price-effectiveness of treatments, HTA informs decisions about compensation and pricing.

**Stakeholder Engagement:** They take a look at highlighting the importance of related to more than one stakeholder inside the HTA system. Collaboration among pharmaceutical corporations, regulatory organizations, healthcare specialists, and patient corporations ensures that numerous perspectives are considered, leading to extra comprehensive and informed choices.

**Evolving HTA Practices:** The studies identified an evolution in HTA practices through the years. to begin with, centered on medical efficacy, HTA now considers broader societal influences, patient possibilities, and actual-world evidence, reflecting a more holistic evaluation approach.

**demanding situations and Criticisms:** They take a look at also found challenges confronted in the HTA method, including methodological complexities in assessing certain styles of interventions, potential delays in getting entry because of lengthy evaluation methods, and worries about transparency in decision-making.

#### Discussion:

The study's findings have large implications for each policymaker and pharmaceutical enterprise stakeholders. HTAs role as a key determinant in the marketplace to get the right of entry to choices underscores the importance of robust and transparent evaluation processes. The evolving nature of HTA practices highlights the want for non-stop refinement to accommodate converting healthcare landscapes and rising treatment modalities. The take look indicates that even as HTA is critical for informed choice-making, it has to be complemented by using efforts to streamline evaluation strategies and decorate stakeholder engagement. Addressing methodological challenges and increasing transparency could similarly bolster the credibility of HTA effects. Common, this research contributes to deeper expertise of the difficult dating among HTA and pharmaceutical markets get admission to in evolved countries. It sheds mild on the complexities, advantages, and demanding situations inherent in this process, facilitating more evidence-primarily based and balanced decision-making in healthcare systems.

#### Conclusion

it's miles likely that the managed entry of new drug treatments will become greater formalized with increasing horizon scanning and finances sports earlier than launch, especially with developments along with adaptive pathways. this could require an increasing function for HTA and the development of extra capabilities dealing with increasing uncertainty. it's also likely that we can see traits in compensation choice-making es especially for brand-spanking new cancer drug treatments and those for orphan sicknesses, as well as new gene healing procedures. that is critical given their capability budget impact and persevering with the subject with available assets coupled with persevering with unmet needs. All key stakeholder businesses should be part of such traits in the destiny.

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