Mednarodno inovativno poslovanje
Journal of Innovative Business and Management

A proposed conceptual model for orphan drug market entry

Nataša Jalen*, Tina Vukasović**

***Abstract*:** The right to health is closely linked to the physical in mental well-being of all individuals in is a necessary condition for the realization of additional human rights, including the realization of an adequate standard of living. Rare diseases are diseases that affect a very small proportion of the population in have a special place because of their rarity. They are often chronic, progressive, life-threatening health conditions. Some of them can be treated with medicines called orphan drugs. Orphan drugs are developed by the pharmaceutical industry not for economic reasons, but to meet public health needs. New treatments need to be evaluated before they reach the market. This is done using health technology assessment, which assesses the relative effectiveness of new medicines, medical devices in other health technologies. The market entry of orphan drugs requires the active involvement of all stakeholders: marketing authorisation holders, competent authorities, the medical profession in patient organisations. Model of market entry for orphan drugs was developed using the qualitative methodology of constructivist grounded theory, tailored to the niche market in considers all key categories.

Keywords: marketing model, marketing strategy, rare disease, health technology assessment, orphan drug, grounded theory
JEL: O15, M12

Predlog konceptualnega modela za vstop zdravil sirot na trg

Povzetek: Pravica do zdravja je tesno povezana s telesnim in duševnim blagostanjem vseh posameznikov ter je nujen pogoj za uresničevanje dodatnih človekovih pravic, vključno z uresničevanjem ustreznega življenjskega standarda. Redke bolezni so bolezni, ki prizadenejo zelo majhen del prebivalstva in imajo zaradi redkosti njihovega pojavljanja posebno mesto. Pogosto gre za kronična, napredujoča ali življenjsko nevarna zdravstvena stanja. Nekatera od njih se lahko zdravijo z zdravili, ki jih imenujemo zdravila sirote. Farmacevtska industrija zdravila sirote ne razvije zaradi ekonomskih razlogov, temveč da zadosti potrebam javnega zdravja. Pred prihodom na trg je treba ovrednotiti novo zdravljenje, za kar uporabljamo vrednotenje zdravstvenih tehnologij, s katerim ocenimo relativno učinkovitost novih zdravil, medicinskih pripomočkov in drugih zdravstvenih tehnologij. Vstop zdravila sirote na trg zahteva aktivno (so)delovanje vseh deležnikov: imetnikov dovoljenja za promet z zdravilom, pristojnih organov, medicinske stroke in organizacij bolnikov. Z uporabo kvalitativne metodologije in konstruktivistične utemeljene teorije smo razvili model vstopa zdravil sirot na trg, ki je prilagojen nišnemu trgu in upošteva ključne kategorije.

Ključne besede: trženjski model, tržna strategija, redke bolezni, zdravilo, vrednotenje zdravstvenih tehnologij, zdravilo sirota, utemeljena teorija

**assist., mag. Marketing and sales, Univerza na Primorskem, Fakulteta za management, Koper; Salvea d.o.o., Ljubljana, natasa@jalen-sp.com*

***prof. dr., University of Primorska, Faculty of Management Koper; International School for Social and Business Studies Celje; DOBA Business School Maribor; tina.vukasovic@upr.si*

DOI 10.32015/JIBM.2024.16.2.1

Mednarodno inovativno poslovanje = Journal of Innovative Business and Management

ISSN 1855-6175

INTRODUCTION

Health is a fundamental human value, and it is considered priceless. The right to health is closely related to the physical and mental wellness of all individuals and is crucial for the fulfilment of other human rights, such as a decent standard of living (Kehayov, 2016). Inherent in the right to health is the right to health care, which often represents only a desired norm that cannot be decided by a court (den Exter, 2017). Access to healthcare and treatment should be available to all individuals, regardless of their financial situation (Kehayov, 2016).

Rare diseases are illnesses that impact only a small portion of the population and present unique challenges due to their infrequency. Developing medications for rare diseases is complex and uncertain because of the limited number of patients with a specific diagnosis (Abozaid et al., 2022). Orphan medicines are defined by Orphanet (2020) as medicines that are developed by the pharmaceutical industry not for economic reasons but to meet public health needs. Health technology assessment (HTA) is pre-market evaluation that aims to evaluate the relative effectiveness of new medicinal products, medical devices and other health technologies (JAZMP, 2021).

Marketing of medicinal products is a crucial strategic function of pharmaceutical companies (Anamul, 2011). Vukasović (2012) explains fundamental marketing strategies as methods to achieve basic marketing objectives using the organization's available resources, with the target being the market, product-market combination, or the entire company's assortment. Marketing models are used in the design of marketing strategies. Aaker and Weinberg (1975) proposed that the model is designed to explore behaviour in a real system. Boulden and Buffa (1970) believe that modelling is a process where specific organizational connections are identified and symbolically translated into a logical model; from this, it can be concluded that marketing models are tools that aid in decision-making (Montgomery and Weinberg, 1973; McIntyre, 1982). McIntyre (1982) emphasizes that marketing models are widely used and have proven satisfactory when the problem is properly structured, and the necessary data is available.

Marketing strategy is the market logic which requires a clear understanding of how marketing works in order to create value for customers (Kotler and Keller, 2016). Various marketing/strategic planning models are available in marketing literature that can be used in decision-making and marketing design. The marketing mix is designed to influence a doctor's decision-making. Marketing medicines involves complex and ethically sensitive relationships between customers (doctors) and pharmaceutical product manufacturers (pharmaceutical companies) (Brody, 2007). Marketing strategy is a powerful tool that must be used responsibly as it contributes to the development and transfer of knowledge and experience (Brody and Light, 2011).

Upon introduction of the new medicinal product to the market, the marketing authorization holder has the right to inform about and advertise the medicine. For prescription medicines, it is allowed to inform the professional public; for over-the-counter medicines, the medicine can be advertised to the general public (and, at the discretion of the marketing authorization holder, also to the professional public). Advertising and promotion of medicines involve products used to treat various diseases, making the way the product is presented very important. In Slovenia, the advertising of medicines is regulated by the Medicines Act (Official Gazette of the Republic of Slovenia, No. 57/2014) and the Regulation on the Advertising of Medicines (Official Gazette of the Republic of Slovenia, No. 105/08, 98/09, hereinafter referred to as the Regulation).

The article presents the development of a conceptual marketing model for the market entry of orphan drugs. Borden (1964) introduced the concept of marketing mix and designs

in the 1950s. McCarthy (1960) further developed the model and named it the 4P marketing, still widely used today. The 4P model represents the marketing mix of four elements: product, price, place, and promotion. Kesič (2004) mentions that in the pharmaceutical industry, the 11P model is increasingly coming to the forefront: product, patent, price, promotion, place, payers, providers, physicians, pharmacists, pharmaceutical industry, patients, which is significantly more complex compared to the 4P model. However, it is believed that the 11P model is not sufficient for the field of orphan drugs, as it does not consider the evaluation of health technologies, and some elements of this model are not relevant in the marketing of orphan drugs.

1 Methods

1.1 Research methodology

The research utilized a qualitative research paradigm. It is based on the constructivist grounded theory (GT) principles, which involve identifying common elements in all collected data using qualitative data sources (Glaser and Strauss, 1967; Strauss and Corbin, 1998). The decision to use a constructivist conceptual framework is rooted in Denzin and Lincoln's (2005) belief that the researcher's own perspectives should be considered when selecting a research methodology.
The theoretical part of the research focuses on creating new theories, identifying concepts, and revising existing ideas. The empirical part follows constructivist GT principles. Methodological design of the research is presented in Table 1.

Table 1: Methodological design of the research

Theoretical part	
Category	Developing the theoretical basis
General conceptual objective	Imagining
Specific conceptual objective	Recognition and revision
Research methodology	Qualitative research
Research methods	Method of analysis Descriptive method Compilation method Comparison method
Empirical part	
Category	GT development
Research process	Cyclical model
Conceptual position	Constructivism
Research methodology	GT
Research methods	Grounded analysis
Methods of data creation	Semi-structured interviews Group interview Content analysis
Sampling	Purposeful sampling Theoretical sampling
Analysing methods	Coding according to grounded theory Statistical data processing
Software	NVivo 1.7.2 (1560)

The diagram illustrating the constructivist grounded theory process, which is based and adapted from Charmaz (2014,), is presented in Figure 1.

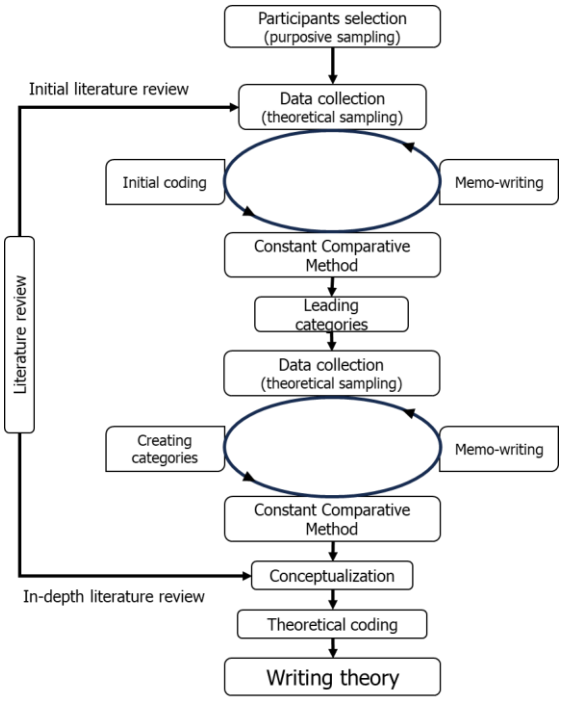

Figure 1: Diagram of the process of constructivist GT
Source: adapted from Charmaz 2014, str 11.

1.2 Selection of participants and sample

Participants in the research who meet the required criteria, which means they are professionally or personally connected to rare diseases and orphan drugs, are chosen through purposive sampling. Participants are chosen from various fields; specialists who work in the identification, diagnosis, and treatment of rare diseases at the tertiary level, general practitioners (GP's), representatives of innovative pharmaceutical companies (EFPIA), representatives of the Association for Rare Diseases Slovenia (ZRBS) and rare disease rare disease societies, as well as patients. The sample consisted of 11 participants, including 6 experts and 5 individuals diagnosed with a rare disease.

1.3 Research questions

The purpose of the research is to propose a conceptual marketing model for orphan drugs that is currently lacking in a specific area of drug marketing. The model is developed based on established marketing approaches and insights gained from qualitative research. The research questions (RQ) formulated are as follows:

> *RQ1: What is the marketing environment in Slovenia for the providers of orphan drugs?*

To understand the macro marketing environment faced by orphan drugs, an analysis of the market situation over a five-year period (2015–2020) was conducted, using publicly available sources. Additionally, a review of legislation related to drug marketing (advertising, pricing, and classification on lists) was carried out.

> *RQ2: How is awareness of rare diseases ensured/organised for patients and the professional public in the Slovenian market?*

Raising awareness of rare diseases is a crucial aspect of marketing orphan drugs. To understand the attitudes and information needs of patients and the professional public,

group interviews (patients) and semi-structured interviews (professional public) were conducted.

> *RQ3: What criteria does the Health Insurance Institute of Slovenia (ZZZS) use to allow or restrict access to orphan drugs for treating rare diseases on the Slovenian market?*

The ZZZS is the main decision-maker for drug market entry in Slovenia, ensuring optimal allocation of healthcare funds. Advances in the development of high-cost medicines for a small number of patients (biologics, gene and cell therapies) over the last decade have introduced a high price element into the financing scheme, alongside new effective medicines

> *RQ4: What role does strategic marketing planning play in the introduction of orphan drugs to the market?*

Marketing of drugs is subject to strict regulations regarding advertising, so strategic marketing planning in compliance with legislation is crucial. Clear communication of the benefits of orphan drugs is essential when introducing them to the market.

> *RQ5: How do participants in the research perceive the current marketing practices for introducing orphan drugs to the market?*

Based on findings on how participants perceive orphan drug market entry, a marketing model was proposed to determine the appropriate strategic marketing approach for introducing new orphan drugs to the Slovenian market.

1.4 Data creation and analysis

Qualitative research involves collecting data in a non-numerical form (Easterby, Thorpe, and Lowe, 2005). Qualitative researchers use various methods to collect data, sometimes creating it themselves and other times using existing data (Morgan, 2022). Methods of data collection include observation, diary techniques, reviewing visual or textual data from books or videos, and interviews (Morgan, 2022). The most common methods are interviews (individual or group) and focus groups (Legard et al., 2003).

The primary source of data in the research are structured individual and group interviews. To ensure research credibility, obtained categories and themes are verified through the analysis of documentary sources. Table 2 outlines methods for data generation.

Table 2: Choice of methods for generating data

Method	*Research topic*	*Type of data*	*Sampling method*	*Sample*
Documentary source analysis	Orphan Drugs Rare diseases HTA	Qualitative data	Purposeful sampling	Written and electronic sources
Semi-structured individual interviews	Associations between rare disease awareness, orphan drug availability and HTA	Qualitative data	Purposive sampling Theoretical sampling	Experts People diagnosed with a rare disease (patients)

Semi-structured group interviews	Associations between rare disease awareness, orphan drug availability and HTA	Qualitative data	Purposive sampling Theoretical sampling	People diagnosed with a rare disease (patients)

For the research, a set of key questions has been formulated for interviews with research participants:

- How do you evaluate the recognition, diagnosis, and treatment of rare diseases in Slovenia?
- What strategies could enhance the recognition and diagnosis of rare diseases?
- What is your perspective on the accessibility of treatment and medications for rare diseases?
- How crucial do you deem the establishment of a registry/registries for rare diseases (including untreatable diseases) to be?
- Do you engage in international collaboration related to rare diseases, and if so, in what capacities (information exchange...)?
- What role do you think the EU should play in ensuring access to orphan drugs on the market post-marketing authorization?
- How familiar are you with the use of HTA and evidence-based medicine as tools in your field?
- From your standpoint, what aspects of our healthcare system are well-regulated concerning rare diseases, and where do you perceive opportunities for enhancement?
- Do you believe that Centres of excellence would enhance the treatment of rare diseases?
- How could a primary level healthcare provider be supported (e.g. GP) in identifying rare diseases?

2 Results

2.1 Sample homogeneity analysis and preliminary analysis

Before starting the analysis, sample homogeneity analysis and preliminary data analysis were carried out, to familiarise with the collected data.

Sample Homogeneity Analysis

The reliability and homogeneity of the sample were tested and confirmed for each group of participants separately by calculating the Pearson correlation coefficient for the sample (r). This calculation assumes of a linear relationship between two normally distributed variables (Riffenburgh and Gillen, 2020). In certain cases, the correlation coefficient for the sample (Pearson's r) is considered better than unbiased and nearly unbiased evaluators. Therefore, an effect size index is recommended for determining the strength of the linear relationship between two variables (Shieh, 2010).

The evaluation and analysis of the sample of experts demonstrated a high level of reliability and homogeneity, indicating a strong understanding of the topic. The reliability and homogeneity of the sample of experts were confirmed by the calculation of the Pearson coefficient, which indicated a similarity of sources with an amount of $r = 0.80$. Figure 2 illustrates the connection of texts among experts based on similarity.

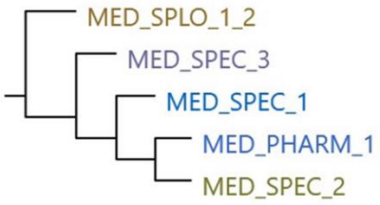

Figure 2: Texts grouped by word similarity - experts

Like experts, the examination and analysis of the patient samples demonstrated a high level of reliability and consistency, suggesting a good understanding of the topic. This was supported by the calculation of the Pearson coefficient, which indicated a similarity of sources with a value of r = 0.83. Figure 3 illustrates the connection between texts among patients based on similarity.

Figure 3: Texts grouped by word similarity - patients

Preliminary Analysis

Preliminary analysis of textual data can provide valuable insights into the perspectives and experiences of participants, revealing themes and patterns that are most important to them. Researchers should pay attention to word or phrase repetition, local terminology, metaphors, and linguistic connections, as these can be the basis for developing important themes (Ryan and Bernard, 2003).

The commonly spoken words among patients were related to the identification, diagnosis, and treatment of rare diseases, as well as the accessibility of orphan drugs. The emphasized words included "Slovenia", "or", "disease/diseases", and "diagnosis". The commonly spoken words among experts included "Slovenia", "or", "disease/diseases", "patient", and "treatment".

Unlike commonly spoken words, key words are those perceived as most important for research, as they reveal recurring concepts essential for understanding the research topic. Keywords are selected based on frequency and topic content (Kronberger and Wolfgang, 2020). Keywords identified included "support", "information", "therapy", "diagnosis", "awareness", "genetics", and "orphan drugs".

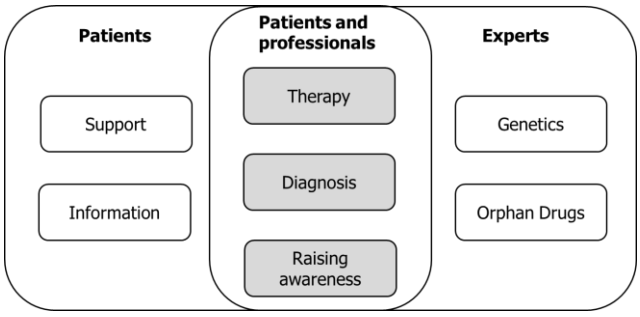

Figure 4: Comparison of keywords in both groups of participants

2.2 Conducting the interviews

The study involved individual semi-structured interviews with experts and group interviews with family doctors and patients to answer the research questions. All participants were asked the same questions in the same order. The interviews were recorded and transcribed. Recording interviews is the best way to capture data. It is only appropriate to record interviews if both the researcher and the research participant agree (Jamshed, 2014). We therefore recorded the interviews with the written consent of the participants. Once the interviews were recorded, we transcribed them, coded the texts and deleted the audio recordings, in accordance with the written consent for recording signed by the participants. The interviews took place between December 2022 and February 2024 at the interviewees' workplaces and lasted between 18 and 50 minutes. The first two interviews were more extensive, at 50 and 49 minutes, while the following interviews were shorter, at up to 33 minutes. The group interview was also longer, at 45 minutes.

2.3 Synthesis of the conceptual marketing model

Marketing orphan drugs presents unique challenges that necessitate a deep understanding of the underlying dynamics and decision-making processes. The key aspect theoretical models in pharma market are the integration of pharmacokinetic and pharmacodynamic principles (Sheiner and Steimer, 2000). By grasping drug-specific factors, marketers can better forecast clinical effectiveness and potential aspects of pricing and reimbursement for orphan drugs (Gobburu and Lesko, 2009). Incorporating pharmacokinetic and pharmacodynamic models, along with disease progression models, can provide a more comprehensive understanding of the overall value of orphan drugs (Gobburu and Lesko, 2009).

When it comes to rare diseases, ethical considerations become essential as treatment for rare diseases is economically unsustainable. One potential approach to address this complexity and explore alternative paths for introducing orphan drugs to the market is using GT, a qualitative research methodology that enables the systematic development of a conceptual model based on empirical data. Several authors (Bergen, Dutta, and Walker, 1992; Gobburu and Lesko, 2009; Lublóy, 2014) emphasize the crucial role of various stakeholders in the conceptual model derived from GT analysis

By developing a conceptually grounded model, this research offers a comprehensive framework for understanding the intricacies of marketing orphan drugs and provides insights that can inform strategies and policies to improve patient access. The evolution of concepts from codes and categories within both groups is outlined in Table 3.

Table 3: Evolution of Concepts

"Patients" Group	
Code	Category
Rare disease awareness at all levels levels of health care Access to new orphan drugs	Marketing and Regulatory Environment
Healthcare ethics	
Support and information for patients	Raising awareness of rare diseases
The role of the ZRBS and patient societies	
Access to health services and specialist care	Accessibility and coverage of treatment costs
Access to orphan drug treatment	
Cooperation between primary, secondary and tertiary levels Communication between patients and health professionals	The importance of stakeholder cooperation
Strategic marketing planning and marketing model design	Marketing strategies and market entry

"Experts" Group	
Code	Category
Registration of medicinal products	Marketing and Regulatory Environment
Health policy and legislation	
Impact of the pharmaceutical industry	
Raising awareness on rare diseases	Raising awareness of rare diseases and education
Educational initiatives	
Communication between clinicians	
Access to healthcare	Access to medicines and healthcare infrastructure
HTA	
Efficacy and safety of medicinal products	
System regulation	Systems approaches and international cooperation
International networking	
National registries of rare diseases	

2.4 Proposal of the conceptual model

The fundamental assumption of the model is that effective marketing of orphan drugs depends on a comprehensive approach, which combines a clear regulatory environment, intersectoral cooperation, widespread awareness of rare diseases, and strategic marketing planning. The categories are grouped into concepts and represent a proposal for a conceptual marketing model (Figure 5) designed on three levels. The first level represents the marketing and legislative environment, the second level, proposes the preparation of a strategic plan for market entry and future marketing and the third level focuses on specific tasks related to raising awareness, education, reimbursement and cooperation between the stakeholders.

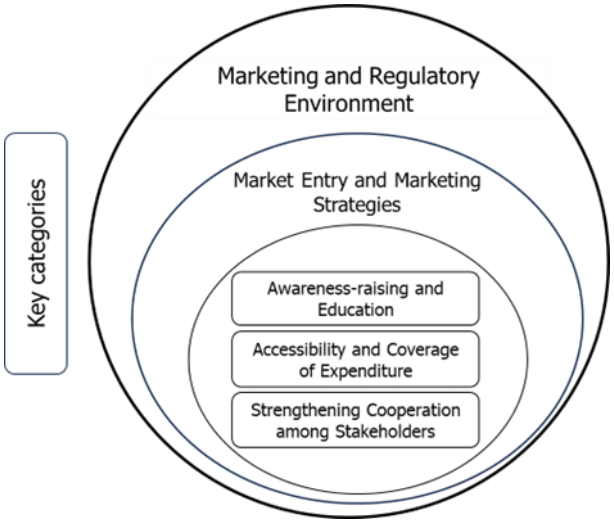

Figure 5: Synthesis of the conceptual model "Market entry of orphan medicines"

Marketing and Regulatory Environment

The legislative framework should be designed to facilitate a smooth marketing authorization process for new medicines, ensuring that orphan drugs are quickly accessible to those in need after authorization. The European Medicines Agency (EMA) harmonizes and centralizes the marketing authorization process across the EU. Once authorization is granted, the

product's inclusion in national treatment plans and reimbursement costs are determined by the individual regulatory and market environments of each EU Member State. Aligning national orphan drugs legislation and common reimbursement procedure would promote the availability of orphan medicines.

Market Entry and Marketing Strategy

Developing a strategic plan for market entry and operational marketing strategies is crucial to meet the strict regulatory requirements in the medicinal products industry, particularly in the orphan medicinal products market. The advertising of prescription-only medicinal products is limited to professional audiences such as prescribers and dispensing pharmacists. Strategic marketing planning involves analysing the marketing environment, utilizing target marketing principles to segment the market accurately, selecting target markets, positioning new medicines in the market, developing marketing messages, and choosing communication strategies.

Awareness-Raising and Education

Raising awareness and educating people are crucial in promoting understanding of rare diseases among both the public and healthcare professionals. Effective awareness-raising about rare diseases can help in speeding up the identification and diagnosis process, increasing awareness of available treatment options, It also helps in enhancing the health system's capability to quickly recognize symptoms and provide the necessary diagnosis and treatment. Consistent education ensures continuous knowledge transfer between various stakeholders, leading to more positive treatment outcomes. Awareness-raising and education play a significant role at all levels of the healthcare system and should be tailored to specific needs.

Accessibility and Coverage of Expenditure

The accessibility of orphan drugs is a major concern that is extensively researched and debated in policy discussions. Regulatory initiatives such as the EU's Orphan Medicines Regulation have facilitated the development and approval of an increasing number of orphan drugs. However, the high costs of these medicinal products create significant financial barriers hindering patient access. This highlights the need for a more sustainable and equitable pricing structure to ensure patients can afford the necessary treatments. Access to treatments for rare diseases and orphan drugs is directly linked to marketing, regulatory frameworks, access to healthcare, and evaluation of innovative health technologies. Without sufficient funding and supportive policies for integrating new therapies into national health systems, patients miss out on medical advancements. Sharing financial risks and expenditures amongst stakeholders is a crucial step towards improving access.

Strengthening Cooperation among Stakeholders

Collaboration amongst all stakeholders is vital for effectively implementing marketing strategies. This entails partnerships between patients, healthcare givers, regulatory bodies and health insurance providers. The innovative pharmaceutical industry also plays a significant role and needs to engage with public institutions while adhering to legal and ethical frameworks. Transparency and data sharing among stakeholders are crucial for better understanding access to medicines. All stakeholders should recognize the importance of approaching the issue of orphan drugs as collaborative partners, utilizing a holistic approach to ensure that patients with rare diseases receive improved care and treatment.

3 Discussion

The evolution of science has led to the development of technologies and techniques that support the creation of innovative new medicines. The emergence of new medicines and advancements in disease diagnostics are happening at the same time, resulting in the development of the niche field of rare diseases. Alongside scientific progress, legislation regarding rare diseases has also advanced. In 2000, the EU implemented Regulation (EC) No 141/2000 of the European Parliament and of the Council on orphan medicinal products (Official Journal of the EU L 018).

The EU provides various incentives and support systems (legislative, financial, and operational incentives) to orphan drug manufacturers to promote the production and availability of these medicines for patients with rare diseases. After obtaining marketing authorisation, marketing authorization holders are subject to market conditions. In some cases, this leads to barriers preventing patients from accessing necessary medicines. Overall, it is evident that there is a lack of awareness and preparation in the market for the specificities of orphan drugs and their unique contexts.

Based on the findings of the research, a conceptual model of market entry for orphan drugs is proposed and a tailored marketing model is developed, which differs significantly from the approaches used in the pharmaceutical industry so far. Unlike the marketing of medicinal products for common diseases, where diagnosis is quick, simple, and readily available, rare diseases involve a lengthy process of disease identification, resulting in a long time from disease onset to treatment initiation, up to 30 years (EURODIS, 2007). This means that all mechanisms for early identification of patients and enabling them to receive high-quality, reliable diagnosis and timely treatment must be included in orphan drug entry planning, even if a cure for their condition already exists.

Further improvements of medicines legislation are possible, especially after the market entry of orphan drugs, as some market entry requirements, such as national packaging, are costly and financially unacceptable due to the small number of patients. Raising awareness of rare diseases and educating all relevant stakeholders, including the public, are essential to understanding the field. Market accessibility of orphan drugs is linked to careful planning of their expenditure and financial incentives for countries and EU marketing authorization holders to increase post-market accessibility.

4 Conclusion

The research focuses on the relevant categories for entering the market of orphan drugs from the perspective of the pharmaceutical industry. The research questions specifically explore topics that are important for marketers when planning the entry of a new medicine. The pharmaceutical industry plays a crucial role in identifying and diagnosing rare diseases, as well as being an active partner in the entry and promotion of orphan drugs, collaborating with stakeholders such as payers, experts, and patient associations while adhering to regulatory requirements. This collaboration is key to making new medicinal products accessible and ensuring successful treatment outcomes.

The state and healthcare payers have valid concerns regarding the financial sustainability of funding new orphan drugs. The high costs of medicinal products due to research and development investments, coupled with the small patient populations, result in high treatment costs per patient. There are also doubts about the effectiveness of new treatments, as clinical trials involve a limited number of patients due to the rarity of diseases. By regulating market entry timing and pricing agreements, payers and the pharmaceutical industry aim to strike a balance to make treatments accessible to all in

need. However, delays in access to orphan drugs can lead to worsened conditions or even death for individual patients.

The market entry and marketing of orphan drugs present a dynamic and evolving area for development and future research. The qualitative approach utilized in this research uncovers insights that quantitative methods may not fully capture. Based on the research findings, it is believed that implementing knowledge effectively in marketing strategies tailored to the unique needs of the orphan drug market, along with incorporating new discoveries, can lead to the creation of innovative marketing models that consider all stakeholders' needs.

References

1. Aaker, D. A., and Weinberg, C. B. (1975). Interactive marketing models. *Journal of Marketing*, 39(43), pp. 16–23.
2. Abozaid, G. M., Kerr, K., McKnight, A., and Al-Omar, H. A. (2022). Criteria to define rare diseases in orphan drugs: a systematic review protocol. *BMJ Open*, 12(7), e062126. https://doi.org/10.1136/bmjopen-2022-062126
3. Althobaiti, H., Seoane-Vazquez, E., Brown, L. M., Fleming, M. L., and Rodríguez-Monguió, R. (2023). Disentangling the cost of orphan drugs marketed in the United States. *Multidisciplinary Digital Publishing Institute*, 11(4), pp. 558–558. https://doi.org/10.3390/healthcare11040558
4. Anamul, H., and Alam, Z. (2012). Business analysis of pharmaceutical firms in Bangladesh: Problems in prospects. *Journal of Business in Technology* (Dhaka), 6(1), pp. 61-77.
5. Bergen, M., Dutta, S., and Walker, O. C. (1992). Agency relationships in marketing: A review of the implications and applications of agency and related theories. *Journal of Marketing*, 56(3), pp. 1–24. https://doi.org/10.1177/002224299205600301
6. Borden, N. H. (1964). The concept of the marketing mix. *Journal of Advertising Research*, 4(1), pp. 2–7.
7. Boulden, J. B., and Buffa, E. S. (1970). Corporate models: online real-time systems. *Harvard Business Review*, 48(4), pp. 65–83.
8. Brody, H. (2007). Hooked: Ethics, the medical profession, and the pharmaceutical industry. Lanham, MD: Rowman & Littlefield.
9. Brody, H., and Light, D. W. (2011). The inverse benefit law: how drug marketing undermines patient safety and public health. *American Journal of Public Health*, 101(3), pp. 399–404.
10. Charmaz, K. (2014). Constructing grounded theory: A practical guide through qualitative analysis (2nd ed.). London: Sage.
11. den Exter, A. (2017). The right to healthcare under European law. *Diametros*, 51, pp. 173-195.
12. Denzin, N. K., and Lincoln, Y. S. (Ed.). (2005). *The handbook of qualitative research* (3rd ed.). Thousand Oaks, CA: Sage Publications.
13. Easterby-Smith, M., Thorpe, R., and Lowe, A. (2005). *Raziskovanje v managementu*. Koper: Fakulteta za management.
14. EMA. (2020). *Legal framework: orphan designation*. Available at: https://www.ema.europa.eu/en/human-regulatory/overview/orphan-designation/legal-framework-orphan-designation (Accessed: April 19, 2021).
15. EURORDIS. (2007). *Survey of the delay in diagnosis for 8 rare diseases in Europe (´EurordisCare2`)*. Available at: https://www.eurordis.org/sites/default/files/publications/Fact_Sheet_Eurordiscare2.pdf (Accessed: March 8, 2021).
16. Glaser, B. G., and Strauss, A. L. (1967). The discovery of grounded theory: Strategies for qualitative research. Chicago: Aldine.
17. Gobburu, J. V. S., and Lesko, L. J. (2009). Quantitative disease, drug, and trial models. *Annual Reviews*, 49(1), pp. 291–301. https://doi.org/10.1146/annurev.pharmtox.011008.145613
18. Groft, S. C., Posada, M., and Taruscio, D. (2021). Progress, challenges, and global approaches to rare diseases. *Wiley-Blackwell*, 110(10), pp. 2711–2716. https://doi.org/10.1111/apa.15974
19. Jamshed, S. (2014). Qualitative research method-interviewing and observation. *Journal of basic and clinical pharmacy* 5, pp. 87-88. DOI: 10.4103/0976-0105.141942.
20. JAZMP. (2021). Homepage. Available at: https://www.jazmp.si/humana-zdravila/farmakovigilanca/ (Accessed: April 19, 2021).
21. Kehayov, A. (2016). Modern approach in exercising the right to health care. *Journal of Medical*

in Dental Practice, 3, pp. 484–487. https://doi.org/10.18044/Medinform.201632.484
22. Kesič, D. (2004). Model tržnega prilagajanja farmacevtskih družb iz tranzicijskih držav v procesu globalizacije trga (Doktorska disertacija). Ekonomska fakulteta, Maribor.
23. Kotler, P., and Keller, K. L. (2016). *Marketing management*. New Jersey: Pearson Education Limited.
24. Kronberger, N., and Wagner, W. (2000). *Keywords in context: Statistical analysis of text features*. v M. W. Bauer in G. Gaskell (Ed.), Qualitative researching with text, image, and sound (pp. 300-317). London: Sage.
25. Legard, R., Keegan, J., and Ward, K. (2003). In-depth interviews. In J. Ritchie in J. Lewis (Ed.), *Qualitative research practice: A guide for social science students and researchers* (pp. 139–169). London: Sage Publications.
26. Lublóy, Á. (2014). Factors affecting the uptake of new medicines: a systematic literature review. *BioMed Central*, 14(1). https://doi.org/10.1186/1472-6963-14-469
27. McCarthy, E. J. (1960). *Basic marketing: A managerial approach*. Homewood, IL: Richard D. Irwin Inc.
28. McIntyre, S. H. (1982). An experimental study of the impact of judgement-based marketing models. *Management Science*, 28(1), pp. 17–32.
29. Montgomery, D. B., and Weinberg, C. B. (1973). Modelling marketing phenomena: A managerial perspective. *Journal of Contemporary Business*, 2(4), pp. 17–43.
30. Morgan, H. (2022). Conducting a qualitative document analysis. *The Qualitative Report*, 27(1), 64-77. https://doi.org/10.46743/2160-3715/2022.5044
31. Riffenburgh, R. H., and Gillen, D. L. (2020). Statistics in medicine (4th ed.). San Diego, CA: Academic Press.
32. Ryan, G. W., and Bernard, R. H. (2003). Techniques to identify themes. Field Methods, 15, 85–109. http://dx.doi.org/10.1177/1525822X02239569
33. Sheiner, L. B., and Steimer, J. L. (2000). Pharmacokinetic/pharmacodynamic modeling in drug development. Annual Reviews, 40(1), 67–95. https://doi.org/10.1146/annurev.pharmtox.40.1.67
34. Shieh, G. (2010). On the misconception of multicollinearity in detection of moderating effects: Multicollinearity is not always detrimental. Multivariate Behavioral Research, 45(3), pp. 483–507. https://doi.org/10.1080/00273171.2010.483393
35. Strauss, A. L., and Corbin, J. (1998). The basics of qualitative analysis: Grounded theory procedures and techniques (2nd ed.). Thousand Oaks, CA: Sage.
36. European Parliament and Council (2000). Regulation (EC) No 141/2000 on orphan medicinal products. Official Journal of the EU, No. L 018.Vukasović, T. (2012). Trženje – od temeljev trženja do strateškega tržnega načrtovanja. Koper: Založba Univerze na Primorskem.