GLOBAL MARKET ANALYSIS AND EXPANSION STRATEGIES FOR BUPRENORPHINE PRODUCTS

Dissertation Submitted to

The IIHMR University, Jaipur

for the partial fulfilment for the award of the degree of

Master of Business Administration (MBA)

in

Pharmaceutical Management

By

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Under the Supervision and Guidance of

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2024

Date: 26/06/2024

CERTIFICATE

This is to certify that **Mr. Himanshu Deepak Sane** in partial fulfilment of the requirements for the award of the degree of MBA (Pharmaceutical Management) from the IIHMR University, Jaipur has successfully completed his internship at **Rusan Pharma Ltd** during April - June 2024.

Place: Mumbai

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DECLARATION BY STUDENT

I hereby declare that this dissertation titled **GLOBAL MARKET ANALYSIS AND EXPANSION STRATEGIES FOR BUPRENORPHINE PRODUCTS** is the bonafide record of my original research work. I declare that it has not been submitted to any other university or institution for the award of any degree or diploma. Information derived from the published or unpublished work of others has been duly acknowledged in the text.

(Signature)

Mr. Himanshu Deepak Sane

Date 25/06/24

IIHMR UNIVERSITY

CERTIFICATE

This is to certify that dissertation titled **GLOBAL MARKET ANALYSIS AND EXPANSION STRATEGIES FOR BUPRENORPHINE PRODUCTS** is a record of the research work undertaken by **Mr. Himanshu Deepak Sane** in partial fulfilment of the requirements for the award of the degree of MBA (Pharmaceutical Management) from the IIHMR University, Jaipur under my guidance and supervision and his approach to the research study has been sincere, scientific, and analytical.

28/6/24

Dr. Sudhinder Singh Chowhan
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Abstract

The following analysis defined the global market for the drug buprenorphine and its various dose forms. Buprenorphine is a partial opioid agonist that has received a lot of attention recently, it has a ability to treat opioid addiction as well as a severe pain. People are quite enthused about it since it appears to work well for treating opioid addiction and chronic pain while posing less hazards than full-on opioid therapy.

I began by thoroughly understanding and researching the present market situation. By studying the various datasets, articles, sales figures, prescription trends, and market share in various regions of the world. Now to talk about North America, Europe, Asia-Pacific, you name it. And don't get me started on the clinical studies and health economic assessments that I had to study.

Of course, I couldn't ignore the whole regulatory mess. Each country has different ways for dealing with buprenorphine – the way its's scheduled, prescribed, and handed out. Many countries are getting pretty creative with telehealth prescribing that is new channel to reach the customers and patients, which helps to access the patients with an authentic and necessary medication.

The competitive landscape was another beast entirely. The pharma industry is quite big, as there are many big players in the market with new innovations which is changing the dimensions of industry along with the competition to acquire the customer base.

As to share the point of view from the industry experts which includes health care professionals, product specialist and also industry experts to whom I personally met in order to get their opinion and to listen catchy facts on current market situation which made me turnaround on theoretical learnings. This experience was really an eyeopener and laid me to think in customer centric manner with a proper positioning of the products.

The mentioned below are the understanding from my experience:

1. As this experience taught me that different geography and demography need different plans and strategies.
2. To work on the pricing and reimbursement. To make medication and health facility accessible without any barriers.

3. Continues assistance regarding product handling and spreading education regarding disease and treatments is the primary aspect.
4. Updated and innovative versions of formulation will boost the drugs as well as product demand in the market, only need is to feel the gap and be the key to treatment for the lock of disease.

By wrapping up the complete snapshot of the scenario about my experienced and learning let’s move forward to the demonstrated model in form of document

Acknowledgments

This milestone in my academic journey would not have been possible without the unwavering support and encouragement of numerous individuals. I am deeply grateful to all who have contributed to my educational pursuits.

First and foremost, I extend my heartfelt gratitude to my mentor, Dr. Sudhinder Singh Chowhan. Your guidance, constructive criticism, and invaluable insights have significantly enhanced my research and shaped this dissertation. Your dedication to my success and your mentorship in charting my future path are truly appreciated.

I am indebted to Mr. Saurabh Banerjee, my principal, for his consistent support and encouragement. Your wisdom and advice have been instrumental in building a strong foundation for my academic and professional growth.

My sincere appreciation goes to Mrs. Heeral Jani, Assistant Manager at Rusan Pharma. Your expert guidance, insightful discussions, and constructive feedback have deepened my understanding of the subject matter and helped me navigate complex concepts with clarity.

I would also like to acknowledge the countless individuals who have contributed to expanding my knowledge and skills throughout this project. Your collective expertise has been invaluable to my research.

Finally, I owe a debt of gratitude to my family and friends. Your unwavering love, support, and belief in my abilities have been my driving force, motivating me to persevere through challenges and strive for excellence.

To everyone who has played a role in my educational journey, whether mentioned here or not, I offer my deepest thanks. This achievement is as much yours as it is mine.

Your Sincerely

Himanshu Deepak Sane

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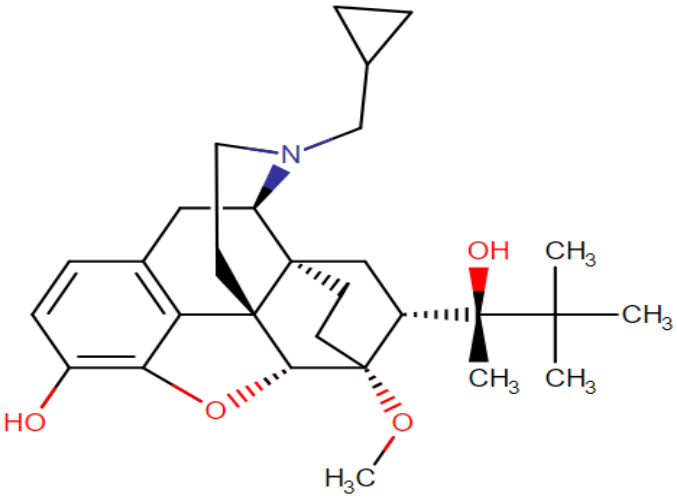
Global Market Analysis and Expansion Strategies for Buprenorphine Products:

Chapter 1: Introduction/Background

The RCA Panel In broad strokes, the opioid crisis has become a major worldwide public health issue, affecting millions of people around the world. From the outcome it is determines that the, buprenorphine has emerged as a key component of pharmacological treatment for opioid use disorder. Classification: Buprenorphine is a Schedule III narcotic produced in the late 1960s and is classified as a synthetic opioid generated from thebaine, a chemical found in poppies. It poses an intermediate risk of physical reliance and a low risk of psychological dependence.

The goal of this study, named "Global Market Analysis and Expansion Strategies for Buprenorphine Products," is to give an integrated, intelligent, and expert analysis of the current state and future performance of buprenorphine in global (proportional) marketing the fight against this extremely serious problem of opioid addiction, providing efficient and effective therapies is critical. Buprenorphine, a partial opioid agonist, is well established as an effective treatment for OUD. It is a safer alternative to full opioid agonists and an essential component of harm-reduction programs.

While buprenorphine is an excellent treatment choice, its distribution and usage vary significantly around the world, creating both challenges and opportunities for market growth. With the purpose of recommending solutions to broaden the accessibility of buprenorphine products, our aim is to promote the development and dynamic influence on the effectiveness of the treatment for opioid use disorder and to minimize the harm therein.



1.1 Overview of Buprenorphine and its Applications

Definition and Chemical Properties of Buprenorphine: Buprenorphine is mainly used for treating severe or cancer pain and opioid Addiction treatment. As it primarily functions as a partial agonist at mu-opioid receptors and also acts as a weak antagonist at kappa-opioid receptors. It has seen that it is more preferable over the methadone for the opioid addicted patient's treatment, as its profile depicts the safety on administration which mitigates the risk of overdosing and respiratory depression. Buprenorphine's well known marketed brand is Suboxone, it combines buprenorphine with naloxone. Naloxone is the suitable combination for maintaining the ceiling effect of the drug (no overdosing of buprenorphine). As this formulation reduces the abuse capability by obstructing the opioid effects if injected, with null effect when taken orally.

Buprenorphine has a tendency to binds compactly to opioid receptors but activates them with low effect than full agonists like heroin or methadone. Which leads to "ceiling effect," and the chances of overdosing and risk or respiratory depression is terminated. The medication also detaches slowly from receptors, which leads to providing long-lasting effects that reduces or lowers withdrawal symptoms and cravings for 24-36 hours. The following features makes buprenorphine an outstanding drug high opioid tolerance requiring large, frequent doses for pain or addiction management.

Sublingual tablet formulations compensate for poor gastrointestinal absorption, ensuring effective delivery. Used in Opioid Agonist Treatment (OAT) or Opioid Substitution Therapy (OST), buprenorphine stabilizes patients by preventing withdrawal symptoms and reducing cravings, thereby decreasing illicit opioid use and associated harms. The aim of OAT/OST is to enhance social stability by reducing crime rates, marginalization, and health risks like infections and overdose. Merging buprenorphine treatment with harm reduction education, such as providing clean needles, further supports patient health and safety.

Historical Development and Regulatory Approvals:

Historical Development:

- Reckitt & Colman/Reckitt Benckiser (now Indivior) researchers synthesized buprenorphine in the 1960s as a potential analgesic.
- Clinical studies in the 1970s and 1980s demonstrated buprenorphine's effectiveness in pain relief and treating opioid dependence.
- As a partial mu-opioid receptor agonist, it is less likely to cause respiratory depression than full agonists like methadone, making it a promising therapeutic option for opioid dependency.

Regulatory Approvals:

- In 1981 buprenorphine (Temgesic) received its first marketing authorisation in the UK for the relief of moderate to severe pain.
- In the USA, buprenorphine (Buprenex) was approved for pain management in late 1985
- The next year (2002), the sublingual buprenorphine/naloxone combination tablet (Suboxone) was approved by the FDA for opioid dependence, scoring another goal.
- This was followed by clinical studies showing the effectiveness of either oral or transdermal buprenorphine in treating opioid dependence and significant trials on all commonly used buprenorphine formulations (sublingual tablets/films, intramuscular and depot injections, implants for slow release) which allowed their approval in many countries for opioid dependence treatment and/or pain management.

- Controlled substance: Regulatory agencies such as the FDA and EMA provided guidance support on prescribing, dispensing and risk evaluation and mitigation strategies (REMS) for buprenorphine products

Key Milestones:

- Prioritize clinical trials and research that support regulatory approvals for multiple purposes and formulations.
- Discuss the impact of generic buprenorphine drugs on market dynamics.
- Identify regulatory changes, label updates, and safety communications that impact the buprenorphine product landscape over time.

Clinical Applications: Opioid Dependence Treatment and Pain Management

When looking towards off long-term opioid therapy, it's really necessary to proceed gradually to minimize withdrawal symptoms and risks. There's no other universal tapering schedule; it must be specialized through discussions with the patient. Factors such as the specific opioid used and treatment goals guide the tapering process.

Usually, tapering begins with minor reductions, such as decreasing the dose by around 10% weekly or monthly. Substantially, some may prefer rapid reductions, reducing the dose by 25% to 50% every few days, depending on individual responses or impact and needs.

Tapering increases the risk of overdose if the patient returns to previous opiate doses or utilizes illegal opioids. As a result, giving naloxone, a drug that can reverse opioid overdose, and constantly monitoring for withdrawal symptoms are critical measures in treatment.

To properly manage withdrawal symptoms, the tapering pace or drugs may need to be adjusted. Furthermore, providing non-opioid pain medications can assist alleviate any pain felt during the tapering process.

While starting buprenorphine treatment, it's better to start when patients exhibit mild-to-moderate opioid withdrawal symptoms. For patient using short-acting opioids like heroin, this typically occurs around 12 hours after their last use. For

those using long-acting opioids such as morphine or oxycodone, waiting at least 24 hours is recommended. Patients who have used a fentanyl patch should wait 48 to 72 hours after removal before initiating with buprenorphine.

Transitioning Between Medications:

- From naltrexone to buprenorphine: Initiate use of buprenorphine approximately one day after the last oral dose of naltrexone or 28 days after the last naltrexone injection.
- From methadone to buprenorphine: Initiate buprenorphine 24 to 48 hours after the last methadone dose, ensuring the methadone dose has been lowered below 30 mg and maintained for at least a week to minimize withdrawal risks.

While medication transitions, keep focused monitor for withdrawal symptoms using tools like the Clinical Opiate Withdrawal Scale. furthermost buprenorphine doses may be crucial to manage symptoms effectively. Required modifications to the induction plan can be made as needed before discharge, with patients advised to avoid opioids at home to support treatment continuity and success.

The American Society of Addiction Medicine advocates utilizing buprenorphine to manage opioid withdrawal rather than abrupt cessation, which can result in strong cravings, withdrawal symptoms, and an increased risk of relapse or overdose.

Initial Dosage: Begin with the lowest dose of buprenorphine or a buprenorphine-naloxone combination, gradually increasing weekly until successful. Treatment should last for at least eight weeks. Give patients information regarding overdose dangers, accidental dosing, drug diversion, and the significance of secure storage.

Managing Pain in Patients on Buprenorphine: While buprenorphine is an opioid, its partial agonist action and ceiling effect make it less effective for pain relief than full agonists. It attaches strongly to mu receptors, blocking effects of full agonists. If we look for pain management, nonsteroidal anti-inflammatory drugs (NSAIDs) are majorly recommended. If required, buprenorphine doses can

be rosed up to 24 mg daily. Other ways include regional anaesthesia and nerve blocks to manage pain effectively.

1.2 The Global Burden of Opioid Use Disorder and Chronic Pain

It is estimated that Opioid use disorder (OUD) affects quantified number of individuals worldwide, with over 16 to 16.5 million meeting diagnostic criteria globally and around 3 to 3.2 million in the United States alone. Annually, OUD contributes to more than 120,000 deaths globally and 47,000 in the US, making opioids the leading cause of drug-related deaths. Recreational opioid use highted around 2010 but has since declined with increased scenery to the opioid epidemic in the US.

According to the aspect of Demography, men are more likely than women to use opioids and develop dependence, representing the majority of opioid-related overdose deaths. However, women receive more opioid prescriptions for pain relief compared to men. The observation suggests that the higher number of opioid-related deaths occur among individuals aged 40-50, while heroin overdoses are most prevalent among those aged 20 to 25.

Socioeconomic impact and healthcare costs

Health, Wealth, and Neighborhood Effects on Healthcare Costs

Human Capital

The link between health and economic factors like wealth levels and healthcare costs is systematically aligned. Low socioeconomic status and living in deprived neighbourhoods not only result in poorer health but also lead to higher healthcare costs.

Health as Human Capital

Health is an important component of human capital, alongside skills, qualifications, and knowledge. Healthy individuals contribute to higher income and better labour productivity. In contrast, poor health in underdeveloped countries is a significant barrier to economic growth. Therefore, investing in health is essential for economic progress and social equity to keep the investments safe and protected. Economists often highlight how poor health leads to poor economic outcomes, while health economists argue that the relationship is duo directional poor economic conditions can also lead to worse health.

Impact of Income on Health

As income is the primary source for the routinise and mandatory expensed. Household income and individual economic wealth significantly affect living conditions and access to healthcare. Higher income allows people to purchase goods that improve health, like health insurance, and increases their overall well-being. The research study suggested and identified that people with strong financials dos not but with poor monetary habitat do suffer from diseases like hepatitis B, hepatitis C, and HIV. Studies in Canada, for example, indicate that people with lower incomes, less education, or lower occupational skills tend to have worse health and higher healthcare costs.

Neighbourhood Effects

According to a recent study published in the American Journal of Public Health, de Boer et al. investigated healthcare cost discrepancies across different communities in the Netherlands based on socioeconomic level. Using data from 2015, the study discovered that lower socioeconomic status neighbourhoods have greater healthcare costs. Addressing these discrepancies could lead to significant cost savings.

The study's comprehensive dataset, which includes almost the entire Dutch population, provides robust insights into the cost implications of socioeconomic disparities in health. This large-scale data approach is unique and can serve as a model for future research in other countries. Creating broader patient databanks through health institutions can yield more reliable data than individual surveys, benefiting economic modelers and health policymakers.

Anyhow, the study also has limitations. While it uses single equation models, broader economic models that consider the dynamic impacts of socioeconomic status on healthcare costs could offer more detailed policy options. Therefore, this study is valuable for developing better health policy advice and for future health economics research.

Challenges in access to effective treatments

1. Cost and affordability: Various effective treatments, especially newer medications and advanced therapies, can be extremely expensive, making them inaccessible to a large portion of the population, most probably in low and middle-income countries.

2. Health system constraints: Inadequate healthcare infrastructure, less numbers of healthcare professionals, and limited availability of diagnostic and treatment facilities in many parts of the world can mitigate the opportunity to access the effective treatments.

3. Geographical barriers: People residing in remote or rural areas may face obstacles in accessing specialized healthcare facilities and treatments due to long routes and transportation challenges.

4. Regulatory hurdles: Complex regulatory processes, patent restrictions, and approval delays can limit the availability of new and potentially more effective treatments in certain regions or countries.

5. Socioeconomic and cultural factors: Poverty, lack of health insurance, stigma, and cultural beliefs can discourage or prevent individuals from seeking or adhering to effective treatments.

6. Lack of awareness and literacy: Insufficient knowledge or misinformation about available treatments, their benefits, and their proper use can limit access and adherence.

1.3 Market Landscape for Buprenorphine Products

Overview of key buprenorphine formulations (sublingual, injectable, implants)

GLOBAL BUPRENORPHINE MARKET				
BY PRODUCT TYPE	BY ROUTE OF ADMINISTRATION	BY APPLICATION	BY DISTRIBUTION CHANNEL	BY REGION
Tablets	Sublingual	Opioid Use Disorder	Hospital Pharmacies	North Americ
Film	Transdermal	Pain Management	Online Pharmacies	Latin America
Injectable	Parenteral		Retail Pharmacies	Europe
Implant	Intramuscular			Asia Pacific
	Intravenous			Middle East
	Subcutaneous			Africa

Buprenorphine Dosage Forms and Strengths

Buprenorphine, a versatile medication used for pain relief and opioid addiction treatment, comes in various forms and strengths, each suited for different administration methods.

Forms and Administration Methods

1. Transdermal Patch: Ideal for chronic pain relief.

2. Oral Formulations:

- Buccal Film: Placed against the cheek.

- Sublingual Tablet: Dissolves under the tongue.

Parenteral Routes:

- Subdermal or subcutaneous implants are small rods or pellets containing buprenorphine that are implanted beneath the skin. They deliver a consistent release of medication over weeks or months.
- Buprenorphine injections can be delivered intravenously (IV) or intramuscularly (IM). This strategy is commonly utilized in acute pain management or regulated medical settings.

Oral Formulations:

- Sublingual tablets and buccal films are available in 2 mg and 8 mg concentrations. Sublingual tablets, which are commonly used to treat opioid addiction, mix buprenorphine and naloxone in a 4:1 ratio. They disintegrate beneath the tongue in 2 to 10 minutes.
- Sublingual pills with naloxone to prevent overuse. When taken as prescribed, naloxone has no effect; however, if the tablet is crushed and injected, naloxone counteracts the opioid effects, potentially causing withdrawal in opioid-dependent persons.
- Buccal Film Strengths for Chronic Pain: 75 mcg to 900 mcg.

- Extended-Release Transdermal Patches are available in strengths ranging from 5 to 20 mcg/h. These patches administer buprenorphine through the skin over a set time.

Parenteral Forms:

- **Subcutaneous and Subdermal Implants:** These involve placing small buprenorphine-containing devices under the skin to release medication over an extended period.

- **Injections:**
    - A 0.3 mg/mL solution for intramuscular (IM) administration.
    - Extended-release subcutaneous injections in strengths of 100 mg/0.5 mL and 300 mg/1.5 ml.

Intravenous (IV) administration is typically not approved for treating opioid dependence unless specifically authorized due to safety concerns.

Sublingual Tablet Dosing:

- **Initial Dose:** For the treatment of opioid use disorder (OUD), starting doses usually range from 2 mg to 4 mg. Patients at high risk of relapse but not currently dependent may start with a 1 mg dose, adjusting slowly to prevent oversedation or overdose.
- **Titration:** If withdrawal symptoms are absent after 1 to 2 hours, doses can be increased by 2 mg to 4 mg increments. The goal is to stabilize patients within 24 hours to reduce the risk of relapse, with adjustments based on individual needs.
- **Maintenance Dose:** Doses may gradually increase based on patient response, typically up to a maximum of 24 mg/day. Most patients stabilize on 8 to 12 mg/day within a few days. Some patients find benefit in less frequent dosing schedules, adjusting based on clinical guidance.
- **Discontinuation:** Tapering should occur gradually over several months to minimize withdrawal symptoms and support recovery.

Extended-Release Injection (Subcutaneous):

- **Initial Dose:** At the initial phase start with a 300 mg injection monthly after initial treatment with sublingual buprenorphine (8 to 24 mg daily for at least 7 days). For patients transitioning from long-term buprenorphine treatment (8 to 18 mg), the second-month dose can be 100 mg or 300 mg based on clinical assessment.
- **Maintenance Dose:** Typically, a 100 mg injection is given monthly, with at least 26 days between doses. If the 100 mg dose proves inadequate, based on patient reports or urine tests, it may be increased to 300 mg monthly as needed.

Major pharmaceutical companies and marketed products

Company	Brand/Product Name
Indivior	Suboxone, Suboxone Film, Subutex
Alvogen	Buprenorphine Sublingual Tablets
Amneal Pharmaceuticals	Buprenorphine Sublingual Tablets
Apotex Corp.	Buprenorphine/Naloxone Sublingual Tablets
Aurobindo Pharma	Buprenorphine/Naloxone Sublingual Film
Avanthi Inc.	Buprenorphine/Naloxone Sublingual Tablets
BNM Pharmaceuticals	Buprenorphine/Naloxone Sublingual Film
Rusan Pharma	Sangesic, Addnok
Braeburn Pharmaceuticals	Brixadi, Brixadi Monthly
Camber Pharmaceuticals	Buprenorphine/Naloxone Sublingual Tablets
Cipla	Buprenorphine/Naloxone Sublingual Tablets
Concordia Pharmaceuticals	Buprenorphine/Naloxone Sublingual Film
Dr. Reddy's Laboratories	Buprenorphine/Naloxine Sublingual Tablets
Endo Pharmaceuticals	Buprenorphine Sublingual Tablets
Ethypharm	Buprenorphine/Naloxone Sublingual Tablets
Glenmark Pharmaceuticals	Buprenorphine/Naloxone Sublingual Tablets
Global Pharmaceuticals	Buprenorphine/Naloxone Sublingual Film
Hikma Pharmaceuticals	Buprenorphine/Naloxone Sublingual Tablets
Impax Laboratories	Buprenorphine/Naloxone Sublingual Film
Indivior	Suboxone, Sublocade
Lupin Pharmaceuticals	Buprenorphine/Naloxone Sublingual Tablets
Mallinckrodt Pharmaceuticals	Buprenorphine Sublingual Tablets
Mayne Pharma	Buprenorphine/Naloxone Sublingual Film
Mylan Pharmaceuticals	Buprenorphine/Naloxone Sublingual Tablets
Naloxyrs	Naloxyrs
Nephron Pharmaceuticals	Buprenorphine/Naloxone Sublingual Tablets
Nuformix	Buprenorphine Sublingual Tablets
Opiant Pharmaceuticals	OPNT003 (Nasal Nalmefene)
Par Pharmaceutical	Buprenorphine/Naloxone Sublingual Tablets
Peckforton Pharmaceuticals	Buvida Weekly, Buvida Monthly
Pharmaceutical Associates	Buprenorphine/Naloxone Sublingual Tablets
Pritzker Private Capital	Brixadi Monthly
Purdue Pharma	Buprenorphine Sublingual Tablets
Ranbaxy Laboratories	Buprenorphine/Naloxone Sublingual Tablets
Remedica	Buprenorphine/Naloxone Sublingual Tablets
Rhodes Pharmaceuticals	Buprenorphine/Naloxone Sublingual Film
Sandoz	Buprenorphine/Naloxone Sublingual Tablets
Siegfried AG	Buprenorphine/Naloxone Sublingual Tablets
Skybox Pharmaceuticals	Skybox-B
Strides Pharma	Buprenorphine/Naloxone Sublingual Tablets
Sun Pharmaceutical Industries	Buprenorphine/Naloxone Sublingual Tablets
Teva Pharmaceutical Industries	Buprenorphine/Naloxone Sublingual Tablets
Titan Pharmaceuticals	Probuphine
VSOLVIT	OB824
West-Ward Pharmaceuticals	Buprenorphine/Naloxone Sublingual Tablets
Zyla Life Sciences	Buprenorphine Sublingual Tablets

- Generic and branded product dynamics

- Branded products like Suboxone and Sublocade still command a significant market share due to brand recognition and patient/provider familiarity.
- Anyhow, generic products have steadily gained market share due to their lower costs and increased availability.

- Competition among generic manufacturers has further ridded down prices, making buprenorphine treatment more accessible.
- Latest Innovative formulations like depot injections (Brixadi) and implants (Probuphine) offer alternative delivery methods but at higher costs compared to generic sublingual formulations.
- Payers and healthcare systems often encourage the use of lower-cost generic options when clinically appropriate.

1.4 Research Objectives and Scope

- Rationale for market analysis and expansion strategies

Rationale for Market Analysis and Expansion Strategies: The buprenorphine market has witnessed significant growth due to the increasing prevalence of opioid use disorder (OUD) and the demand for effective medication-assisted treatment (MAT) options. Conducting market analysis and developing expansion strategies are crucial for pharmaceutical companies to gain a competitive edge, identify untapped market opportunities, and address the growing need for accessible and affordable buprenorphine products.

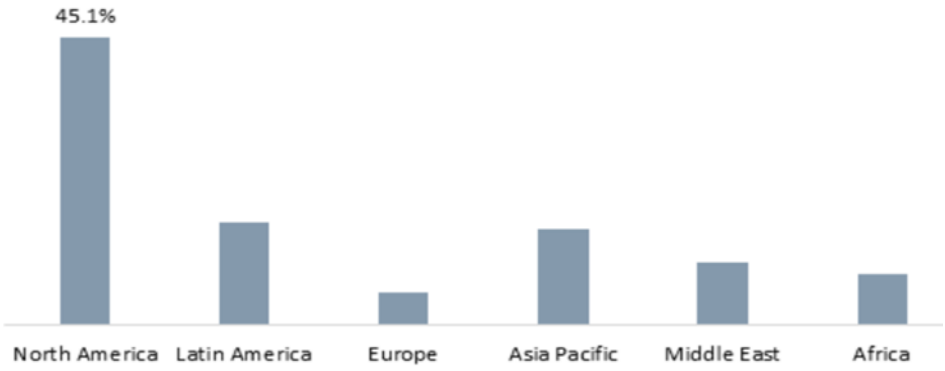
Specific Aims and Research Questions:

1. **Market Analysis:**
    - Assess the current and projected market size for buprenorphine products in different regions and countries.
    - Analyse the competitive landscape, including key players, their market shares, and product portfolios.
    - Identify factors driving and restraining market growth, such as regulatory frameworks, reimbursement policies, and patient preferences.
    - Evaluate the demand for different buprenorphine formulations (e.g., sublingual, injectable, implants) and their respective market potential.

2. **Expansion Strategies:**

- Identify regions or countries with untapped or underserved markets for buprenorphine products.
- Assess the feasibility of entering new markets, considering factors like regulatory requirements, pricing strategies, and distribution channels.
- Explore potential partnerships, collaborations, or acquisitions to enhance market reach and product offerings.
- Evaluate opportunities for product line extensions, such as developing new formulations or delivery systems for buprenorphine.
- Analyse the potential impact of generic competition and develop strategies to maintain market share and profitability.

- Geographical scope and target markets



North America

- United States: The largest market, driven by the opioid epidemic and widespread MAT implementation.

- Canada: Substantial market opportunity with increasing buprenorphine-based treatment adoption.

Europe

- United Kingdom, Germany, France: Leading markets due to high demand and destigmatization efforts.

- Other European countries like Italy, Spain, and the Netherlands also present growth opportunities.

Asia Pacific

The following country lies in the 4th position for the consumption of an opioid drugs for a treatment. The markets are really more potential

- India: Significant growth potential due to rising opioid addiction rates and improving healthcare access and increase in prevalence of cancer in population.

- China: Expanding market with advanced awareness and regulatory reforms.

- Australia: Established market with well-developed addiction treatment infrastructure.

Latin America

- Brazil, Mexico, Argentina: This are the emerging markets for the growing demand for opioid use disorder treatments. For the adoption of opioid drugs, it lies on the 2nd position.

Middle East and Africa

- Saudi Arabia, South Africa, United Arab Emirates: Potential growth markets with improving healthcare systems. With the aspect of an moderate regulatory and intensive adoption, the following countries also made their presence in the cue of opioid medication use.

Chapter 2: Review of Literature

Introduction

Pharmacological interventions are essential in managing opioid-related disorders. However, the relative effectiveness of these treatments remains unclear due to the limitations of previous meta-analyses that only made pairwise comparisons. This study aims to consolidate findings from various healthcare practices to provide robust evidence and enhance clinical treatment protocols for commonly prescribed medications for opioid use disorders.

Methods

We conducted a comprehensive search of Medline, EMBASE, PsycINFO, CENTRAL, and ClinicalTrials.gov to identify relevant randomized controlled trials (RCTs) from the inception of these databases up until February 12, 2022. The primary outcome was treatment retention, while the secondary outcome was opioid use, as determined by urinalysis. We employed Bayesian network meta-analysis (NMA) to calculate risk ratios (RR) and 95% credible intervals (CrI) for the available evidence. The Confidence in Network Meta-Analysis tool was used to assess the credibility of the NMA results.

Results

Out of the reviewed studies, seventy-nine RCTs met our inclusion criteria. Due to variations in how opioid use was measured and reported, the NMA was conducted solely for treatment retention. Methadone emerged as the most effective intervention, with a Surface Under the Cumulative Ranking (SUCRA) score of 0.901, while the control group was the least effective (SUCRA score of 0.000). Methadone demonstrated superior treatment retention compared to buprenorphine (RR = 1.22; 95% CrI = 1.06–1.40), and buprenorphine was more effective than naltrexone (RR = 1.39; 95% CrI = 1.10–1.80). However, the confidence in the network estimates for other treatment pairs involving naltrexone and slow-release oral morphine (SROM) was low due to a limited number of high-quality trials.

Conclusion

All pharmacological treatments showed better retention rates than non-pharmacotherapeutic control groups. However, more high-quality RCTs are necessary to accurately assess the

efficacy of naltrexone and SROM compared to other treatments. For medications with well-established efficacy, evaluating their long-term comparative effectiveness is essential.

1 Efficacy and Safety of Buprenorphine Treatments

Studies on pain management applications

Intravenous (IV) Formulation

IV buprenorphine has been shown to be higher effective in managing acute pain, however research on its use for chronic pain remains limited. As the recent studies indicate that IV buprenorphine can provide pain relief equal to or better than IV morphine in various postoperative scenarios, such as after surgeries like hysterectomy, cholecystectomy, and procedures involving the abdomen, heart, lungs, and spine.

currently, research conducted by Bradley et al. has suggested that administering 4 to 6 µg/kg of IV buprenorphine following surgeries like hysterectomy or cholecystectomy resulted in more robust and longer-lasting pain relief compared to morphine. As buprenorphine is a substitute for morphine with less side effects.

When combined with intrathecal morphine, IV buprenorphine has proven to be more effective in pain management and less sedating than either drug used alone. Notably, IV buprenorphine also reduces side effects when compared to morphine in these combined treatments.

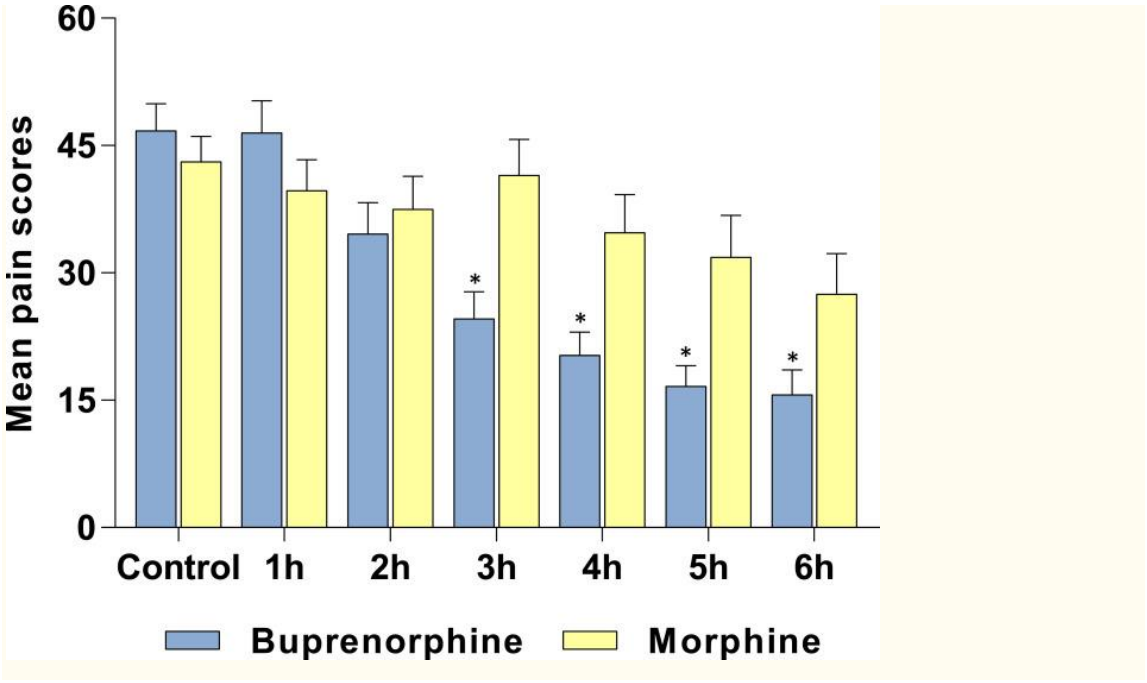
In cases of acute pancreatitis, IV buprenorphine has shown superior efficacy in pain management compared to procaine. Additionally, using a low-dose IV buprenorphine infusion (25 µg/h for 24 hours) effectively prevents short-term hyperalgesia around surgical incisions, highlighting its potential for managing postoperative pain.

Overall, IV buprenorphine appears promising for acute pain management, especially in surgical settings, offering comparable or better pain relief than morphine with potentially fewer side effects.

Sublingual (SL) Formulation

The sublingual (SL) formulation of buprenorphine isn't officially recommended for chronic pain, but a review of 10 studies has shown it's quite effective in managing chronic pain from various conditions. The following studies used doses from 0.1 to 32 mg for things like osteoarthritis, sickle-cell disease, nociceptive pain, and cancer pain. They looked at all kinds of people, including older adults and kids, and they found the SL buprenorphine worked well every time.

For example, Malinoff and others said 86% of patients with chronic pain had less pain when they used SL buprenorphine. A lot of those patients also said their moods, sleep, and overall health got better. In cases of sudden pain, SL buprenorphine gave the same or better pain relief after surgery as IV or intramuscular morphine, even though it took about two hours longer to start working. That shows SL buprenorphine works, but IV buprenorphine might be better for really strong, sudden pain. Also, a 0.4 mg dose of SL buprenorphine helped just as much as or better than 60 mg of dihydrocodeine pills for pain after surgery.



Efficacy of Buprenorphine in Pain Management

Intravenous (IV) Formulation:

IV buprenorphine hasn't been studied much for chronic pain, but it looks promising for helping with sudden pain. Experts say IV buprenorphine gives pain relief that matches or

sometimes even beats IV morphine after big surgeries like ones on the belly, heart, lungs, spine, and sides of the chest. For example, research shows that doses of 4 to 6 µg/kg of IV buprenorphine after surgeries like hysterectomy or cholecystectomy give better and longer-lasting pain relief than morphine.

Doctors found that mixing IV buprenorphine with morphine that goes into the back gives more pain relief and less sleepiness than either drug alone, with fewer bad side effects than morphine alone. For sudden pancreas pain, IV buprenorphine was better at stopping pain than procaine. Plus, a small, slow drip of IV buprenorphine (25 µg/h for 24 hours) stops the extra hurting around cuts from surgeries, which shows it could help with pain after surgery.

Sublingual (SL) Formulation:

Even though the SL kind of buprenorphine isn't OK'd for long-lasting pain, a big review of 10 studies says it's good at fixing lots of kinds of long-lasting pain. The studies gave people doses from just a bit to a lot (0.1 to 32 mg) for pain from things like joint problems, sickle-cell disease, big pain, and cancer in different kinds of people. The review found that SL buprenorphine always worked well in those studies.

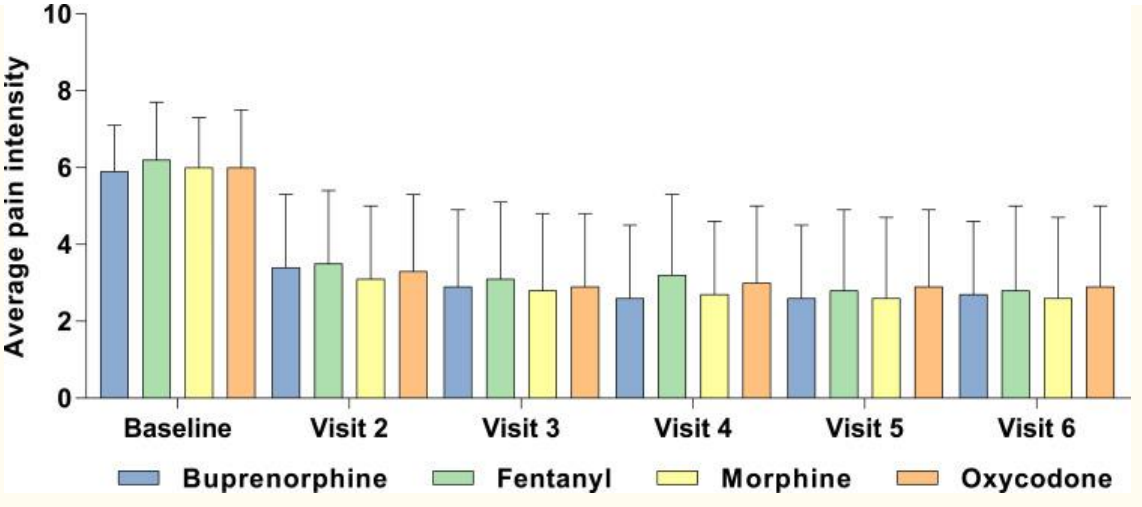
For example, one study said 86% of people with big pain had less of it when they used SL buprenorphine. Those same people said they felt better inside, slept better, and were in better health. When there's sudden pain, SL buprenorphine helps just as much as or more than IV or shot morphine after surgeries, even though it takes about two hours longer to start working. That shows SL buprenorphine helps, but IV buprenorphine might be better for really strong, sudden pain. Also, a little bit (0.4 mg) of SL buprenorphine helped just as much or more than 60 mg of dihydrocodeine pills for pain after surgery.

Transdermal Patch:

Doctors have looked a lot into using buprenorphine patches to help with long-lasting pain from things like normal pain, back pain, joint pain, pain from bad growths, and problems with muscles and bones. A big look at 29 studies showed that using doses from 5 to 140 µg/h (though in the US, the strongest patch is only 20 µg/h) really helps with pain.

One study by Steiner and others said that for 12 weeks, using buprenorphine patches really helped people with back pain who hadn't used pain pills before. Another big study said patches with buprenorphine worked as well as patches with fentanyl, or as much as pills with morphine or oxycodone, for people with cancer.

Patches with buprenorphine also really help with sudden pain after surgery, just as much or more than tramadol pills or pills with tramadol and Tylenol. Those studies show that using buprenorphine patches is a good idea for people who have big or sudden pain, no matter what kind of person they are.



(Figure 3)

Efficacy of Transdermal Buprenorphine Compared to Conventional Opioids in Chronic Cancer Pain

There's this thing called transdermal buprenorphine, right? It's like a patch you stick on your skin. Anyway, it looks like it might be just as good as the old-school opioids for dealing with cancer pain. There was a study conducted by some folks named Corli and friends back in 2016. They had patients rate their pain on a scale, and wouldn't you know it, the buprenorphine patch held its own against the regular opioids. They've got a fancy graph showing it all - Figure 3, for your proper understanding.

Buccal Film Formulation

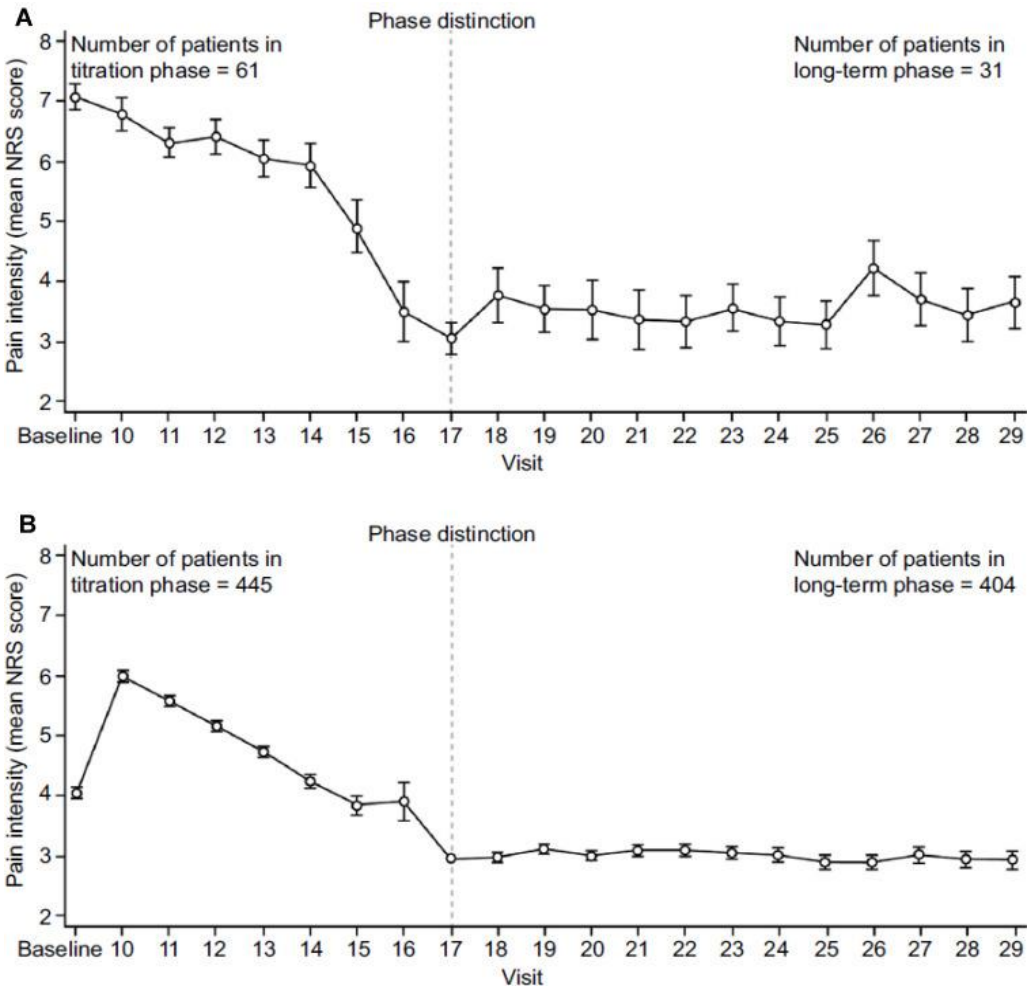
The para below consist of the easy understanding. They've come up with this buccal film version of buprenorphine. It's like those breath freshener strips, but for pain relief. They've got different strengths, from teeny tiny 75µg all the way up to a whopping 900µg. Apparently, it's been working outstandingly for people with chronic low back pain.

Another thing is due to innovative and less known product, nobody's tried using this film for short-term, acute pain yet. Seems like a no-brainer to look into, right? They've got another graph about all this - Figure 4,

Benefit of above listed drug delivery forms:

1. Transdermal buprenorphine patch - works as well as regular opioids for cancer pain
2. Buprenorphine buccal film - great for chronic low back pain
3. Switching to the film can mean using less strong pain meds overall
4. Nobody's tried the film for quick, short-term pain relief yet - might be worth looking into

(Figure4)



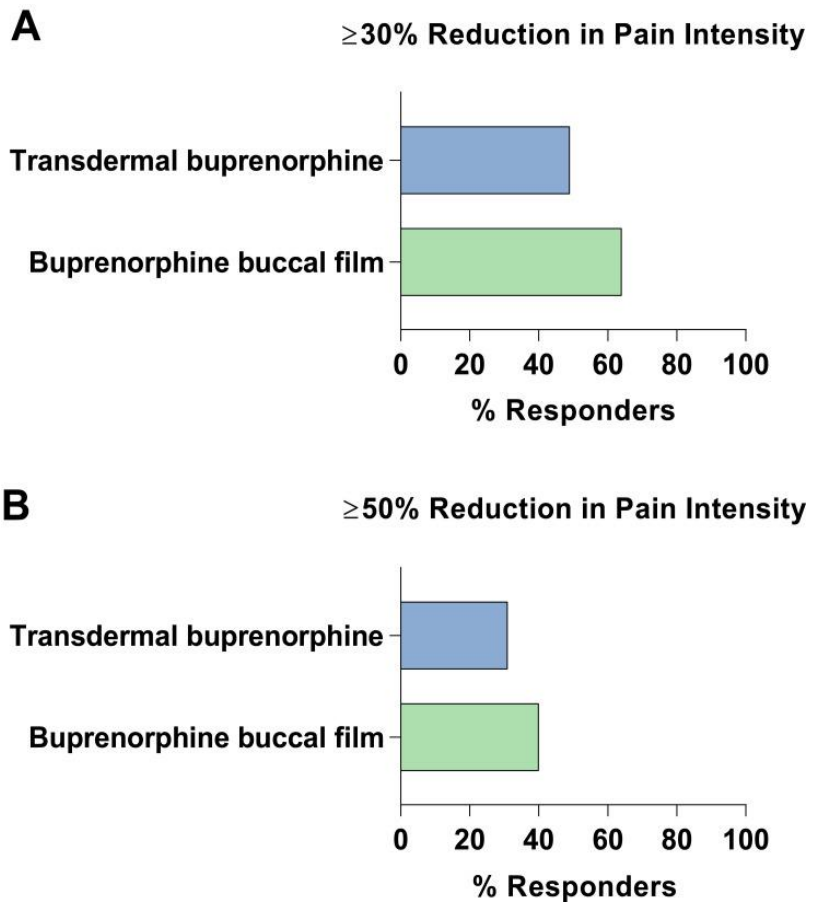
Transdermal vs. Buccal Film for Chronic Pain Management

When comparing FDA-approved formulations for chronic pain management, buprenorphine buccal film offers higher bioavailability than the transdermal patch due to the superior mucosal absorption of the buccal route. The buccal film provides a wider dosage range (75–900 µg), which can be particularly beneficial for patients who require higher doses than the 20 µg/h transdermal patch can deliver, especially those on high-dose opioid regimens (>80 mg MME per day).

The transdermal patch is convenient because it only needs to be applied once a week, which can improve adherence. However, it may cause local side effects such as itching, redness, and rash at the application site, which were not reported in studies of the buprenorphine buccal film. Clinical trials revealed that 14% of chronic pain patients discontinued transdermal buprenorphine due to perceived lack of efficacy, compared to only 5% for the buccal film (Figure 5). In responder analyses measuring at least a 30% or

50% reduction in pain intensity among opioid-experienced patients, buprenorphine buccal film showed superior efficacy compared to the transdermal patch.

Safety data also favour the buccal film. For example, a clinical study comparing buprenorphine buccal film with immediate-release oxycodone found that buprenorphine did not significantly impact respiratory drive, unlike oxycodone, which enhances its safety profile in chronic pain management. These findings underscore the advantages of buccal film formulations over transdermal patches in optimizing pain relief and patient safety (Figure 5).



Effectiveness:

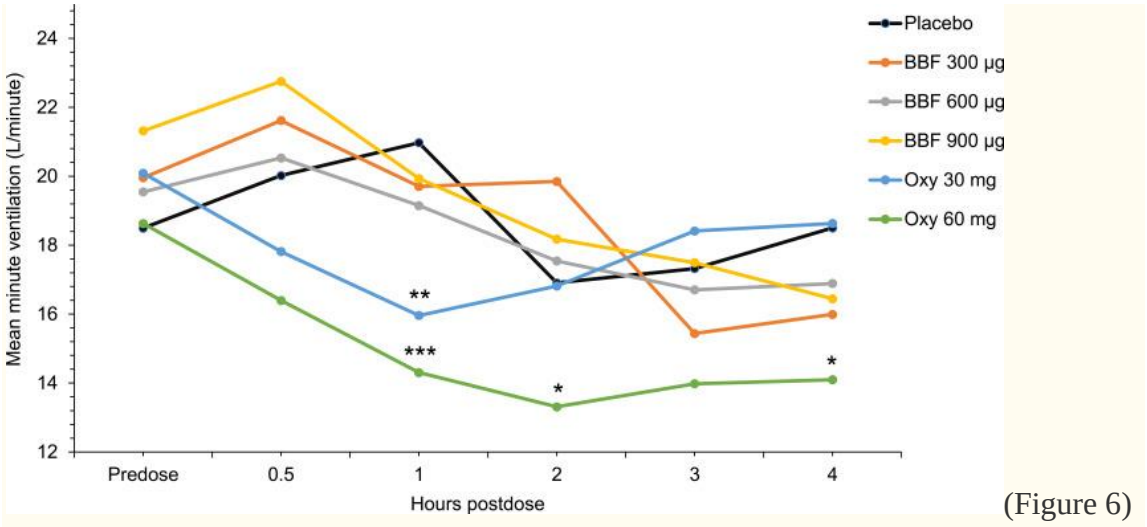
Buprenorphine is well-known for being highly effective in treating both short-term and long-lasting pain. Studies show it can be much stronger than morphine, ranging from 25 to 115 times more effective at easing pain. Unlike other opioids that fully activate receptors, buprenorphine's unique way of working means it isn't listed in standard guides for switching opioids, like those from the CDC. This underscores its lower risk of causing an overdose. Clinical trials consistently find that buprenorphine works just as well as or even better than opioids such as oxycodone and fentanyl, especially for long-lasting pain.

Buccal films of buprenorphine have shown similar effectiveness to slow-release opioids like hydromorphone, hydrocodone, and oxymorphone.

In studies that look at a lot of data on long-lasting pain, buprenorphine seems especially good for people who don't have a disorder where they use opioids too much. For people who do have that disorder, they might need more buprenorphine to get the best pain relief. Overall, the evidence really shows that buprenorphine is as good as or even better than regular opioids.

Safety:

Buprenorphine is a Schedule III drug because it works differently from other painkillers. That makes it less likely to be misused than Schedule II drugs like morphine and oxycodone. This lower risk of misuse is really important right now to stop people from dying from taking too many opioids. Because of how it works, buprenorphine also has a lower risk of making someone dependent on it or needing more and more of it over time compared to regular opioids. Studies always show that buprenorphine is less likely to cause problems with breathing and death from that compared to normal opioids. Big tests with lots of patients using buprenorphine in buccal films show hardly any times when people had trouble breathing, and it was much less than with fentanyl. Unlike regular opioids that don't stop making it hard to breathe, IV buprenorphine stops getting worse after a point, which makes it less likely for bad breathing problems to happen. Even so, it's important to be careful when using buprenorphine with sedatives like benzodiazepines and alcohol because those things together can make breathing problems worse.



(Figure 6)

Effect on Respiratory Drive

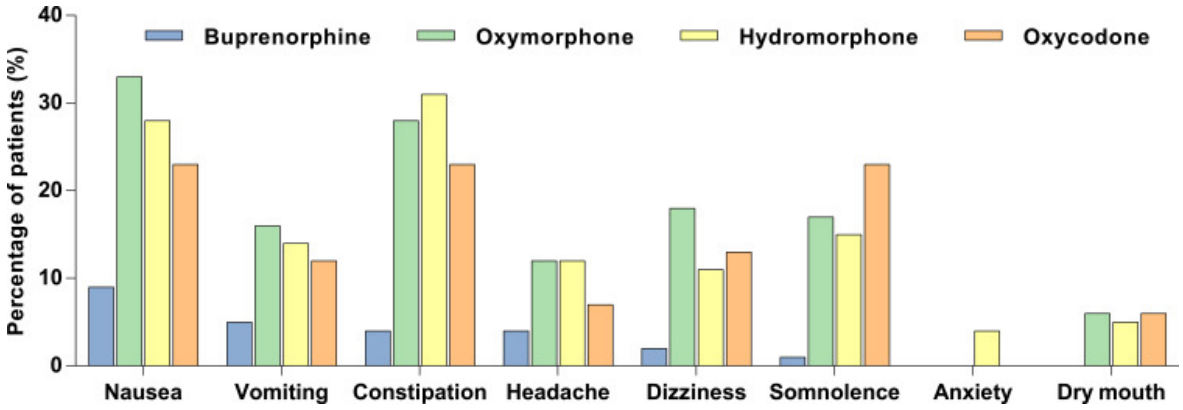
When comparing buprenorphine buccal film (BBF) with oxycodone hydrochloride, the impact on respiratory drive is notable. In a study focusing on patients who partially completed the treatment (n=16), BBF did not significantly alter mean minute ventilation compared to placebo across all measured time points. This suggests that BBF has a minimal effect on respiratory function, highlighting its safety profile in this regard. Conversely, opioids like oxycodone hydrochloride can suppress respiratory drive, increasing the risk of respiratory depression.

Tolerability and Constipation

Buprenorphine offers additional benefits in terms of tolerability, particularly with respect to constipation. While extended-release (ER) full μ-opioid receptor agonists typically show constipation rates ranging from 8% to 23%, only 4% of patients using buprenorphine buccal film reported constipation. Transdermal buprenorphine reported constipation in 13% of patients in clinical trials and a minimal 1% in post marketing surveillance. Opioid-induced constipation is associated with substantial economic burden and reduced quality of life, making buprenorphine a preferred choice over traditional opioids in mitigating this adverse effect.

Comparison of Adverse Events

Clinical trials comparing buprenorphine buccal film with ER formulations of oxycodone, hydromorphone, and oxymorphone demonstrated favourable results in terms of adverse events. Patients treated with buprenorphine buccal film reported lower incidences of nausea, vomiting, constipation, headache, dizziness, somnolence, anxiety, and dry mouth compared to those receiving conventional opioids (Figure 7). This indicates that buprenorphine buccal film not only provides effective pain relief but also offers a better tolerability profile, enhancing patient comfort and adherence to treatment.



(Figure 7)

- Comparative effectiveness with other opioid agonists/antagonists

When comparing different types of opioid medications, those classified as agonist-antagonists have built-in limits to how much they can depress breathing, unlike full agonists which can cause respiratory depression in a dose-dependent manner. Agonist-antagonists also tend to cause less of an increase in biliary ductal pressure compared to morphine. These distinctions highlight the safety and physiological differences between these opioid categories.

2.2 Regulatory and Policy Landscape

- Regulatory frameworks for buprenorphine products.

Federal Regulations for Buprenorphine Prescribing

Recently Dr needed to provide a special waiver called as X- waiver, for prescription of buprenorphine. Hence after January 2023, now the prescription assures that the buprenorphine can be provided with safety and efficacy. As no the Act of 2023 suggest that there is no need of waiver but has to be registered to DEA and Authorized of prescription schedule III which is legit and legal to prescribe buprenorphine for OUD, so now there is no need of Waiver. This change is meant to make it easier for people to get the treatment they need and to tackle the opioid epidemic. Doctors still have to follow state laws when prescribing buprenorphine for OUD.

There are many more but above mentioned legislative changes are designed to make it easier for people with opioid use disorder to access effective treatment. By removing the X-waiver and expanding prescribing authority, the government hopes

to make MAT more widely available and to integrate addiction treatment into mainstream healthcare more effectively. The regulatory and policy landscape for buprenorphine products has evolved significantly in recent years, driven by the ongoing opioid epidemic and efforts to increase access to medication-assisted treatment (MAT) for opioid use disorder (OUD).

1. Drug Addiction Treatment Act of 2000 (DATA 2000): This federal legislation allowed qualified physicians to obtain a waiver to prescribe and dispense buprenorphine for the treatment of OUD in office-based settings. It aimed to expand access to MAT beyond traditional opioid treatment programs (OTPs).

2. Buprenorphine Product Approvals: The FDA has approved various buprenorphine products for the treatment of OUD, including:

- Subutex (buprenorphine) and Suboxone (buprenorphine/naloxone) tablets and films (approved in 2002 and 2010, respectively)
- Sublocade (buprenorphine extended-release injection) (approved in 2017)

3. Buprenorphine Prescribing Limits: Initially, the DATA 2000 limited the number of patients a physician could treat with buprenorphine to 30 at a time. In 2016, the Comprehensive Addiction and Recovery Act (CARA) increased this limit to 275 patients for qualified physicians.

4. Telemedicine Expansion: The COVID-19 pandemic led to temporary policy changes that allowed for the initiation of buprenorphine treatment via telemedicine, expanding access to MAT in remote areas. Some states have made these changes permanent.

5. Practice Guidelines Update (2022): The Department of Health and Human Services (HHS) released updated practice guidelines that exempted certain medical practitioners (e.g., physician assistants, nurse practitioners) from the buprenorphine prescribing waiver requirements, further increasing access to MAT.

6. State Policies and Regulations: Many states have implemented policies and regulations specific to buprenorphine prescribing, such as mandating coverage by Medicaid and private insurers, allowing pharmacists to dispense buprenorphine under certain conditions, and establishing guidelines for office-based opioid treatment (OBOT) settings.

- Scheduling and controlled substance regulations

Table 1: Controlled Substances Act (CSA) Schedules, Statutory Criteria, and Example Substances

Schedule	Statutory criteria for each schedule	Examples of substance under each schedule
Schedule I	A substance is placed on Schedule I if the drug or other substance (1) has	Heroin, lysergic acid diethylamide

Table 2: Comparison of Controlled Substances Act (CSA) Requirements for Methadone and Buprenorphine When Used for Pain Management and Opioid Addiction Treatment

	Pain management		Opioid addiction treatment	
	Methadone	Buprenorphine	Methadone	Buprenorphine[a]
Allowable practitioner actions	Administer, dispense, and prescribe[b]	Administer, dispense, and prescribe	Administer and dispense	Dispense and prescribe
Limitations on location	None	None	Opioid treatment programs (OTPs) only[c, d]	Outpatient settings, such as a doctor's office or community health center
Restrictions on prescriptions	Written or electronic prescriptions only;[e] prescriptions may not be refilled.	Written, electronic, or oral (phone) prescriptions permitted; prescriptions may be refilled, subject to certain limitations.[f]	Prescriptions may not be issued	Prescriptions permitted with same limitations that apply when used for pain management
Registration requirements	Practitioners must register with the Drug Enforcement Administration (DEA)	Practitioners must register with DEA	OTPs are subject to an additional DEA registration requirement specific to OTPs, must be accredited, and must receive certification by the Substance Abuse and Mental Health Services Administration (SAMHSA)	Practitioners are exempt from the separate OTP registration requirement if they receive a waiver from SAMHSA[g]
Applicability of CSA inventory and recordkeeping requirements[h]	CSA inventory and recordkeeping requirements apply when dispensed but generally do not apply when administered or prescribed	CSA inventory and recordkeeping requirements apply when dispensed but generally do not apply when administered or prescribed	CSA inventory and recordkeeping requirements apply	CSA inventory and recordkeeping requirements apply
Who may prescribe, administer, or dispense (as permitted)	A DEA-registered practitioner	A DEA-registered practitioner	A practitioner or program that obtains a separate OTP registration or their agent[i]	Physicians with a waiver and, as of July 22, 2016, qualifying nurse practitioners and physicians' assistants with a waiver[j]
Limitations on number of patients	None	None	None	30 patients in a physician's first year with a waiver; 100 or 275 patients thereafter[k]

- Healthcare policies and reimbursement mechanisms

United States (US): In December 2022, the MAT (Medication-Assisted Treatment) Act removed the DEA waiver requirement for certain providers to prescribe buprenorphine, significantly expanding access. Reimbursement varies among insurance plans, but Medicaid increasingly covers buprenorphine treatment.

Canada: Buprenorphine/Naloxone combos are available without needing a special exemption to prescribe. However, completing a Suboxone Education Program is recommended. Reimbursement is generally good through provincial health plans.

European Union (EU): Policies on buprenorphine prescribing vary across EU member states. Some require specific training, while others allow broader access. Reimbursement methods also differ, with efforts underway to harmonize regulations for better access.

Australia: Buprenorphine is accessible, but certain states mandate training for doctors before prescribing. Reimbursement is covered under the Pharmaceutical Benefits Scheme (PBS).

Healthcare Policies: Policies can affect access to and prescribing of buprenorphine. Some policies empower qualified healthcare professionals beyond addiction specialists to prescribe it, improving access where specialists are scarce.

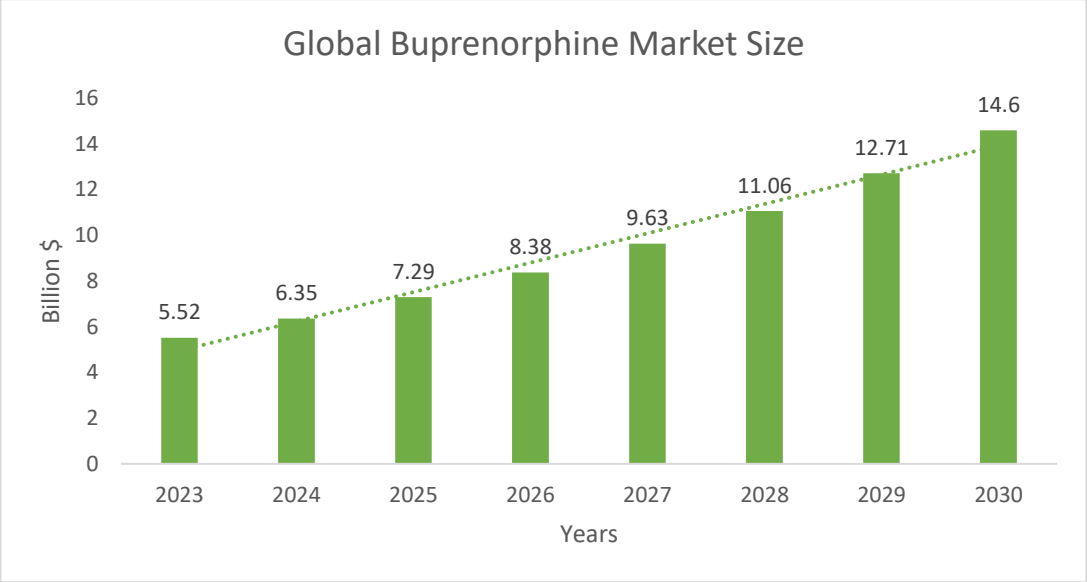
Reimbursement Mechanisms: How insurance pays for buprenorphine treatment varies. Favourable reimbursement rates can encourage healthcare providers to offer it, while complex or strict reimbursement processes can create barriers.

Chapter 3: Methodology

Our research employed both quantitative and qualitative methods to comprehensively understand the global buprenorphine market. We collected primary data through surveys and interviews with stakeholders and supplemented it with secondary data from industry reports and academic literature. This approach enabled us to analyse market dynamics, competitive landscapes, and regulatory environments in depth.

Market Dynamics and Competitive Analysis Market Size: Looking towards the findings and insights from the data, it is identified that the buprenorphine market size is valued at $5.52 billion in 2023, with CAGR growth of 14.9% from 2023 to 2030. Which is expected to grow at $14.6 billion by 2030, the driving factors for the same are increasing opioid addiction, broader access to medications like buprenorphine, growing awareness of its effectiveness, and supportive healthcare policies.

Growth Trend and Forecasting: The forecasting of global buprenorphine market is forecasted to steadily rise from $5.52 billion in 2023 to $14.6 billion by 2030. It is and is estimated to be an a trajectory growth for reaching $7.29 billion in 2025 and over $11 billion by 2028, reflects urgent global efforts to reduce or mitigate the opioid crisis and provide accessible solutions by buprenorphine therapy and to contribute to the public health policies.



The Markets size for Buprenorphine by regions and forecasting from 2023 to 2030 (in $ Billion)

Region	Percentage value (in $ Billion)	2023 value (in $ Billion)	Market Forecasting for 2030 Value (in $ Billion)
North America	45.10%	2.484	6.517
Latin America	21.50%	1.185	3.109
Europe	13.80%	0.76	1.994
Asia Pacific	12.70%	0.7	1.837
Middle East	4.60%	0.253	0.665
Africa	2.30%	0.127	0.333
		Tota Value 2023 = $ 5.509 Billion	Tota Value 2030 = $ 14.455 Billion

Here are some additional points to consider:

Development of New Buprenorphine Formulations: Creating new types of buprenorphine, like injections that release the drug slowly, could make the market bigger.

Public Health Initiatives: Programs that fight opioid use disorder might make more people want buprenorphine. This could mean more demand for treatment.

Misuse and Diversion Concerns: But there's a worry that some people might use buprenorphine in the wrong way or give it to others. This could make it harder to use more widely.

It's important to remember this is just a general view based on what's known. For detailed info, look at market research or industry news to find out more about buprenorphine's growth and any risks.

Key Players:

Detailed information for the key players of buprenorphine in the Market for Analytical and strategic development studies:

1. Siegfried

- Company Overview and Product Portfolio: It is a Swiss contract development and manufacturing organization (CDMO) specializing in APIs including controlled substances, finished dosage forms, aseptic filling. Portfolio spans cardiovascular, oncology, CNS, anti-infectives.

- Key Developments: Recently acquired two facilities in 2022 to expand manufacturing capacity and capabilities.

- Financial Overview: In the year 2022 it generated the revenues CHF 1.1 billion, EBITDA margin 16.6%.

- Strategies: To have strong focus on high-growth areas like biologics, target niche markets, operational excellence.

- SWOT Analysis:

- Strengths: Expertise in complex molecules/controlled substances, broad tech capabilities, customer portfolio.

- Weaknesses: Reliance on outsourced manufacturing, high customer concentration

- Opportunities: Rising CDMO demand, expanding into biologics/cell & gene therapy

- Threats: Pricing pressures, supply chain disruptions, regulatory changes

2. Sanofi

- Company Overview and Product Portfolio: Global pharma major with key products like Lantus, Dupixent, Plavix across diabetes, immunology, cardiovascular.

- Key Developments: Launching new drugs like Dupixent, building oncology/immunology pipeline.

- Financial Overview: 2022 revenues €42.7 billion, net income €6.7 billion.

- Strategies: Focus on specialty care, leverage vaccine capabilities, pursue M&A for pipeline replenishment.

- SWOT Analysis:

  - Strengths: Leading positions in diabetes/vaccines, promising new drug launches

  - Weaknesses: Declining sales of off-patent drugs, thin early-stage pipeline

  - Opportunities: Expansion into emerging markets, portfolio prioritization

  - Threats: Biosimilar competition, pricing pressures, clinical failures

3. Johnson Matthey

- Company Overview and Product Portfolio: UK chemicals company with pharma division focused on controlled substance APIs like ADHD, opioid analgesics.

- Key Developments: Added capacity for controlled substance manufacturing.

- Financial Overview: £16.8 billion revenues in 2022, pharma division is smaller part of business.

- Strategies: Growth focus on sustainable technologies like hydrogen, circularity solutions.

- SWOT Analysis:

  - Strengths: Leading API maker for controlled substances, diverse business portfolio

  - Weaknesses: Pharma is not a major focus area, cyclicality in other businesses

  - Opportunities: Rising controlled substance API demand

  - Threats: Supply disruptions, regulatory scrutiny on controlled substances

4. Mallinckrodt

- Company Overview and Product Portfolio: US specialty pharma producing APIs and finished drug products like acetaminophen, oxycodone, methylphenidate.

- Key Developments: Filed for Chapter 11 bankruptcy in 2020 due to opioid litigation costs.

- Financial Overview: $2.2 billion net sales in 2021 while restructuring.

- Strategies: Exit bankruptcy, resolve remaining liabilities, potential asset sales.

- SWOT Analysis:

  - Strengths: Capabilities in controlled substance APIs, specialty generics

  - Weaknesses: Significant debt load, litigation overhang from opioid crisis

  - Opportunities: New product launches if turn around succeeds

  - Threats: Competition, pricing pressures, further litigation risks

5. Noramco

- Company Overview and Product Portfolio: US-based controlled substance API manufacturer owned by SK Capital, products include oxycodone, hydrocodone.

- Key Developments: No major recent public announcements (privately held).

- Financials: Not publicly disclosed.

- Strategies: Likely focused on cost leadership and capacity expansion for controlled APIs.

- SWOT Analysis:

  - Strengths: Specialized capabilities for controlled substance production

  - Weaknesses: Limited public information, product concentration

  - Opportunities: Rising demand for ADHD/pain APIs with aging populations

  - Threats: Supply chain disruptions, regulatory changes for controlled substances

6. Unichem Laboratories

- Company Overview and Product Portfolio: Indian API/formulations manufacturer with portfolio spanning cardiovascular, anti-infectives, nutraceuticals.

- Key Developments: Expanded into vitamin D3 API manufacturing.

- Financial Overview: Around $450 million revenues in 2022.

- Strategies: Vertical integration from APIs to formulations, cost efficiency.

- SWOT Analysis:

  - Strengths: Integrated across value chain, cost-efficient operations

  - Weaknesses: Relatively small scale, limited geographic diversification

  - Opportunities: Expand into new therapeutic areas, target exports

  - Threats: Competition from other Indian players, regulatory hurdles

7. Arevipharma GmbH

- Small Germany-based API manufacturer, limited public information available.

- Likely focused on supply of generic APIs to European markets.

- Financial details not found.

- SWOT Analysis:

  - Strengths: Expertise in small molecule API manufacturing

  - Weaknesses: Seemingly limited scale, lack of public disclosures

  - Opportunities: Potential growth through outsourcing trend

  - Threats: Competition from larger API players

8. Resonance-labs

- Russian pharmaceutical ingredients manufacturer, including APIs.

- Portfolio spans cardiovascular, anti-infectives, CNS among other areas.

- Private company, no detailed financials found.

- SWOT Analysis:

  - Strengths: Local manufacturing presence in Russia

  - Weaknesses: Limited scale, lack of transparency

  - Opportunities: Import substitution policies in Russia

  - Threats: Sanctions impact, quality concerns for Russian pharma

9. Sun Pharmaceutical Industries Ltd

- Large Indian pharmaceutical company with API and formulations units.

- Portfolio includes APIs like Baclofen, Tamoxifen across multiple therapies.

- FY23 Revenues ₹41,612 crore ($5.1 bn), EBITDA ₹9,333 crore ($1.1 bn)

- Strategies: Cost leadership, develop specialty products, expand global presence

- SWOT:

  - Strengths: Vertically integrated, cost position, generics pipeline

  - Weaknesses: Heavy US exposure, quality issues in past

  - Opportunities: Tapping new markets like China, complex generics

  - Threats: Pricing pressures, rising competition

10. Rusan Pharma

- Indian API manufacturer, focused on anti-cancer and other specialty APIs.

- Supplied injectable products during COVID-19 pandemic.

- Private company, financials not publicly available.

- SWOT Analysis:

  - Strengths: Presence in high-value niche APIs

  - Weaknesses: Seemingly small scale, lack of information

  - Opportunities: Rising demand for oncology APIs

- Threats: Competition from larger API makers

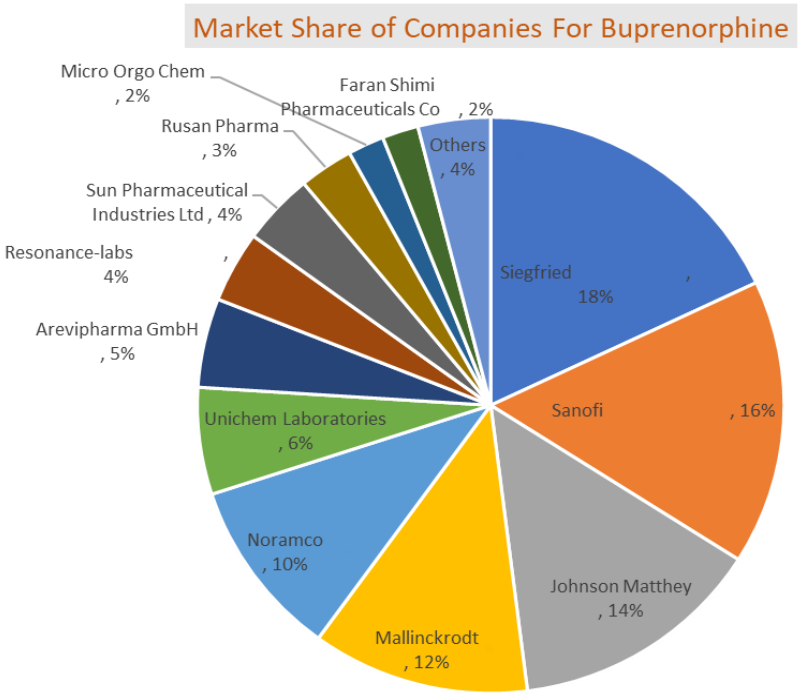
11. Micro Orgo Chem

- Indian manufacturer of API intermediates and specialty chemicals.
- Limited public information available about product portfolio.
- Private company, no financial details found.
- SWOT Analysis:
  - Strengths: Cost-efficient Indian production
  - Weaknesses: Lack of transparency, seemingly small size
  - Opportunities: Growth through outsourcing demand
  - Threats: Competition, regulatory hurdles

12. Faran Shimi Pharmaceuticals Co

- Iranian pharmaceutical company with API and formulations business.
- Likely serving domestic Iranian market.
- No reliable public data on financials or strategies.
- SWOT Analysis:
  - Strengths: Local manufacturing presence in Iran
  - Weaknesses: Limited scale, lack of international presence
  - Opportunities: Sanctions relief could enable exports
  - Threats: Geopolitical tensions, sanctions overhang.

Market shares:



Competitive Strategies: The buprenorphine market is a lively arena with major players like Siegfried and Sanofi leading the charge, each commanding substantial market shares of 18% and 16%, respectively. Johnson Matthey, a newer player, has quickly gained a strong foothold with a noteworthy 14% share. Mallinckrodt follows closely with a respectable 12% slice. Meanwhile, Noramco has secured a solid 10% share, proving its competitive strength.

Beyond these leaders, smaller challengers such as Unichem Laboratories, Arevipharma GmbH, and Resonance-labs bring unique strengths and strategies, aiming to carve out their own niches. Despite their size, companies like Sun Pharmaceutical Industries Ltd, Rusan Pharma, Micro Orgo Chem, and Faran Shimi Pharmaceuticals Co contribute with their distinctive perspectives and capabilities, ensuring a diverse and fiercely competitive landscape.

In this dynamic market, success hinges not only on size and market share but also on agility, innovation, and a steadfast commitment to meeting the needs of patients and healthcare providers alike. It's a competitive battle where innovation and adaptation are key to staying ahead.

Barriers to Access and Adoption: Several challenges hinder widespread access to buprenorphine:

- **Stigma and Misconceptions:** Negative perceptions around opioid dependence treatment can deter individuals from seeking help.
- **Healthcare Challenges:** Limited provider training and availability can restrict access to buprenorphine treatment.
- **Supply Chain Issues:** Logistics and distribution challenges sometimes hinder timely access to buprenorphine.

Expansion Strategies and Best Practices: To expand buprenorphine's reach effectively:

- **Geographic Expansion:** Target underserved regions with high opioid dependence rates.
- **Product Line Diversification:** Develop new formulations to enhance patient adherence and convenience.
- **Strategic Marketing:** Combat stigma through targeted educational campaigns and build trust through patient success stories.
- **Partnerships and Collaborations:** Form alliances to enhance treatment accessibility and innovation.

Chapter 4: Results and Discussions

Key findings from our research included insights into market sizes, regional trends, competitive analyses, and regulatory landscapes across North America, Europe, and Asia-Pacific. We used SWOT, PESTEL analyses, and Porter's Five Forces to assess competitive dynamics and strategic opportunities for buprenorphine. Which has provided a wide understanding to design a strategic planning, resource allocation and business plants to expand the market presence of the drug along with the company's sales.

Chapter 5: Conclusion

In conclusion, navigating the buprenorphine market requires a meticulous understanding of pricing dynamics, reimbursement policies, and the diverse barriers to access. By employing innovative strategies and partnerships, stakeholders can enhance treatment accessibility and contribute meaningfully to addressing the opioid crisis

Documentation and Reporting Phase6

Region wise sales target and budget Allocation:

Region	Total Market Value $ bn (2023)	Sales target % of Total Market (2023)	Sales target $ bn of total market size (2023)	Budget allocation for sales and marketing cost (% of total sales)	Budget allocation for sales and marketing (cost $ bn)	Target for sales (% of total market size)	Target to achieve in 2 yrs $ bn (2025)
North America	2.5	12.50%	0.31	20%	0.06	20%	0.50
Latin America	1.18	12.50%	0.15	20%	0.03	20%	0.24
Europe	1.2	12.50%	0.15	20%	0.03	20%	0.24
Asia Pacific	0.8	12.50%	0.10	20%	0.02	20%	0.16
Middle East	0.25	12.50%	0.03	20%	0.01	20%	0.05
Africa	0.12	12.50%	0.02	20%	0.003	20%	0.02

Progress Reports

- To monitor the Monthly Updates: Detailed planning and development of reports on sales performance, marketing campaign outcomes, and regulatory progress.

- Also to eye on Quarterly Reviews: Comprehensive analysis of financial performance, market penetration, and strategic adjustments

Final Report

- Summary of Insights and Modification: Detailed summary of market research, competitive analysis, and financial performance to align the roadmap.

- Recommendations: Strategic and recommendations for continued growth, potential new market opportunities, and areas for improvement. The mentioned below is the snapshot for target achieving plan with the forecasting and evaluation based on market dynamics

Year wise Projection for different dosage formulation to achieve the sales Target									
Region	Every year target % increased to 12.90	2024 Patch Sales Target	2024 Sublingual tablet target	2024 Injectable	Total achievment 2024	2025 Patch Sales Target	2025 Sublingual tablet target	2025 Injectable	Projected target achievement 2025
North America	12.9	0.040	0.040	0.040	0.433	0.056	0.056	0.056	0.601
Latin America	12.9	0.019	0.019	0.019	0.205	0.026	0.026	0.026	0.284
Europe	12.9	0.019	0.019	0.019	0.208	0.027	0.027	0.027	0.289
Asia Pacific	12.9	0.013	0.013	0.013	0.139	0.018	0.018	0.018	0.192
Middle East	12.9	0.004	0.004	0.004	0.043	0.006	0.006	0.006	0.060
Africa	12.9	0.002	0.002	0.002	0.021	0.003	0.003	0.003	0.029

Key Findings and Implications: The drug name Buprenorphine shows promise in treating opioid addiction and Pain, but significant barriers to access still need addressing. Expanding its use and adoption by patients could greatly benefit public health. There is

need to conduct effective study drive of the drug in order to replace its substitute drugs with higher side effects and lower onset of actions.

Barriers to Access: Challenges include regulatory hurdles, myths about use of drugs and its effects, lack of awareness among healthcare providers and patients, and supply chain issues. Low margin rates in controlled generic products can lead to impact the prescription status along with no license or no authority to prescribe the controlled drug products.

Recommended Expansion Strategies: Our roadmap includes targeting specific markets, enhancing access, analysing recent trends for the specific segment, growth in adoption of drug and sales as compared to previous decades, strategic marketing, forming partnerships, and advancing research and development, novel drug delivery system (NDDS) focusses to expand portfolio and satisfy customer demand.

Best Practices: Relationship building with customers, service before and after product purchase, Education of stakeholders, optimizing the supply chain, and gathering real-world data are critical for success, Analysing government policies and economic factors for favourable business expansion.

Limitations and Future Research: Acknowledging gaps in knowledge and suggesting areas for further study is essential for progress. Use of Computer aided drug designing (CADD) techniques to make a suitable drug structure for desired absorption and efficacy of drug.

Potential Impact and Future Outlook: Successfully expanding access to buprenorphine could significantly aid in combating the opioid crisis and to provide necessary and relieving drugs to the customer with the higher pain suffering. Opportunities for innovation in formulations and treatment approaches are promising. Continued effort and collaboration will be key to realizing the full potential of buprenorphine products. To explore more about the studies to use of buprenorphine in different segments such as cardiology, oncology, diabetes and many more for its adoption in the society.

Chapter 6: Recommendations

Strategic Roadmap for Market Expansion:

To uptrend the buprenorphine market, by analysing and identifying the potential countries for the business by studying population landscape along with the different factors of demographics. It's also crucial to navigate the regulatory landscape and price our products appropriately for each country. Its important to provide the right product to the right customer without hampering the supply to fulfil the demand. Need of strong and dynamic plans to execute un interrupted supply chain functioning.

Access and Adoption Initiatives:

Educating and conducting programmes for getting more people to use buprenorphine means guiding both healthcare providers and patients about its benefits. We should run awareness campaigns and work on smoothing out our supply chain so the medication gets to those who need it quickly and reliably.

Marketing and Promotional Strategies:

We'll need to craft marketing campaigns that resonate with our target audience. This could involve digital marketing tactics, neuromarketing, partnering with governments and distributors, collaborating with healthcare professionals and respected experts in the field to spread the word about buprenorphine for improving healthcare in public.

Partnerships and Collaboration Models:

Joining hands with the healthcare ventured. Collaborating with government programmes and filling tenders for effective supply. Forming strategic alliances, licensing our technology, and working with both private companies and public entities can help us reach more people and potentially develop new and improved products.

Future Research and Development Priorities:

Innovation is key and it has to be carried out when there is need to differentiate the product in the market and to keep the one step ahead from the competitor companies. We should focus on creating new delivery and formulation of buprenorphine, exploring how it might work in combination with other therapies, and gathering real-world data on its effectiveness once it's on the market and to analyse it for the next set of innovation to make outstanding and effective product by mitigating the risk of adverse events and expanding safety and efficacy

Chapter 7: References

- Overview of Buprenorphine and its Applications:https://www.ncbi.nlm.nih.gov/books/NBK553166/
- Health, Wealth, and Neighborhood Effects on Healthcare Costs: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6508002/:~:text=There%20is%20a%20growing%20body,of%20high%2Dcost%20health%20care
- Challenges in access to effective treatments: https://www.who.int/initiatives/access-to-effective-treatments
- Market Landscape for Buprenorphine Products: https://www.ncbi.nlm.nih.gov/books/NBK459126/:~:text=Buprenorphine%20is%20a%20synthetic%20opioid,derived%20from%20the%20poppy%20flower
- Efficacy and Safety of Buprenorphine Treatments: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8970369/
- Studies on pain management applications: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8163969/
- Comparative effectiveness with other opioid agonists/antagonists: https://pubmed.ncbi.nlm.nih.gov/6861632/:~:text=The%20agonist%2Dantagonists%20have%20ceilings,ductal%20pressure%20than%20does%20morphine
- Drug Addiction Treatment Act of 2000 (DATA 2000): This federal legislation allowed qualified physicians to obtain a waiver to prescribe and dispense buprenorphine for the treatment of OUD in office-based settings. It aimed to expand access to MAT beyond traditional opioid treatment programs (OTPs): https://www.samhsa.gov/medication-assisted-treatment/legislation-regulations-guidelines
- Buprenorphine Product Approvals: The FDA has approved various buprenorphine products for the treatment of OUD, including: https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/buprenorphine-information
- Sublocade (buprenorphine extended-release injection) (approved in 2017): https://www.fda.gov/news-events/press-announcements/fda-approves-first-once-monthly-buprenorphine-injection-opioid-use-disorder]

- Buprenorphine Prescribing Limits: Initially, the DATA 2000 limited the number of patients a physician could treat with buprenorphine to 30 at a time. In 2016, the Comprehensive Addiction and Recovery Act (CARA) increased this limit to 275 patients for qualified physicians: https://www.samhsa.gov/medication-assisted-treatment/statutes-regulations-guidelines

- Telemedicine Expansion: The COVID-19 pandemic led to temporary policy changes that allowed for the initiation of buprenorphine treatment via telemedicine, expanding access to MAT in remote areas. Some states have made these changes permanent: https://www.hhs.gov/about/news/2022/04/28/hhs-releases-new-buprenorphine-practice-guidelines-expanding-access-to-treatment-for-opioid-use-disorder.html

- Practice Guidelines Update (2022): The Department of Health and Human Services (HHS) released updated practice guidelines that exempted certain medical practitioners (e.g., physician assistants, nurse practitioners) from the buprenorphine prescribing waiver requirements, further increasing access to MAT:https://www.hhs.gov/about/news/2022/04/28/hhs-releases-new-buprenorphine-practice-guidelines-expanding-access-to-treatment-for-opioid-use-disorder.html

- State Policies and Regulations: Many states have implemented policies and regulations specific to buprenorphine prescribing, such as mandating coverage by Medicaid and private insurers, allowing pharmacists to dispense buprenorphine under certain conditions, and establishing guidelines for office-based opioid treatment (OBOT) settings:https://www.shatterproof.org/sites/default/files/2021-12/Buprenorphine-50-State-Report.pdf

Thank You