Bozok Journal of Science
Volume 2, No 2, Page 88-97 (2024)
Review Article DOI: 10.70500/bjs.1580533

Some of FDA-Approved Cancer Drugs Containing Aminopyrimidine Structure

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Abstract
Cancer is a complex condition characterized by the abnormal growth and multiplication of tumors, which can damage healthy tissues in the body and lead to various health issues. Factors such as genetics, environmental influences, and lifestyle choices play a role in cancer development, creating a unique risk profile for each individual. Early diagnosis and treatment strategies are crucial in the fight against cancer and can significantly alter the disease's progression. This study will provide information on research regarding the effects of FDA-approved drugs containing the Amino Pyrimidine ring.

Keywords: Cancer, Breast Cancer, Leukemia Cancer, Lung Cancer.

1. INTRODUCTION

Cancer is a disease that can develop in any part of the human body, which consists of trillions of cells. It arises when certain cells start to divide uncontrollably, with the potential to spread to other regions of the body. Globally, there are more than 100 distinct types of cancer, with carcinomas being the most widespread. The names of carcinomas vary according to the type of epithelial cell they affect. Breast, colon, and prostate cancers are among the most frequently occurring carcinomas worldwide [1]. As reported by the World Health Organization in 2020, breast cancer was the most frequently diagnosed type of cancer, with 2.26 million cases, among cancers that contributed to 10 million deaths. However, in terms of mortality rates, lung cancer ranked first, with 1.8 million deaths [2].

Each type of cancer demands a unique approach to treatment, making accurate diagnosis crucial for effective and appropriate care. A key initial step involves defining the treatment objectives. The primary aim is often to cure the cancer or to extend the patient's life significantly. Another essential goal is to support the patient in reaching optimal physical, psychosocial, and spiritual health, enhancing quality of life through palliative care during the terminal stage. This necessity contributes to a rising demand for cancer medications [3]. Pyrimidines are one of the two nitrogenous bases found in DNA and RNA (the other being purines). Pyrimidine analogs are synthetic compounds that resemble the natural pyrimidine bases, and they can interfere with DNA and RNA synthesis, making them effective as anticancer agents. Pyrimidine analogs have played a crucial role in cancer chemotherapy for decades, with several important drugs (such as 5-FU, gemcitabine, and cytarabine) being mainstays in the treatment of various cancers. Their ability to interfere with DNA and RNA synthesis in rapidly dividing cancer cells makes them effective, though resistance mechanisms are a significant challenge. Ongoing research aims to overcome these challenges and improve the specificity and efficacy of these drugs, making them even more potent tools in the fight against cancer.

Each year, the US Food and Drug Administration (FDA) receives hundreds of applications for drugs that may carry cancer risks, and a significant number of these applications result in market approval. Following these approvals, the FDA allows these active compounds to be sold commercially. In this research, FDA-approved cancer drugs were analyzed, focusing specifically on those containing an amino pyridine structure in their composition [4]. General information about the effective syntheses and biochemical studies of these compounds was presented.

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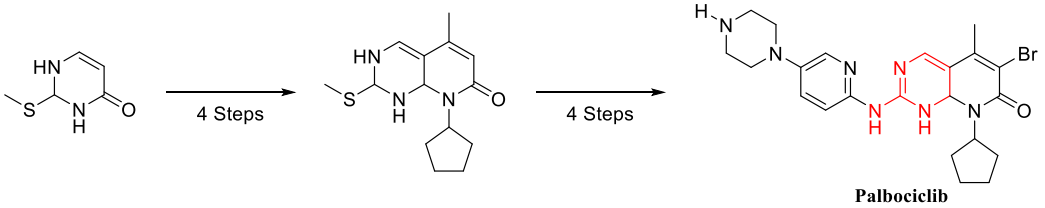
2. RESULTS AND DISCUSSION

According to cancer data from the World Health Organization, there are over one hundred different types of cancer. Each cancer type operates through a distinct mechanism in the body and has the potential to eliminate cancerous cells. The Aminopyrimidine framework discussed in this study was chosen due to its resemblance to the base units in DNA structure, and screenings of FDA-approved drugs containing this framework were conducted.

2.1. Breast Cancer drugs

2.1.1. Palbociclib

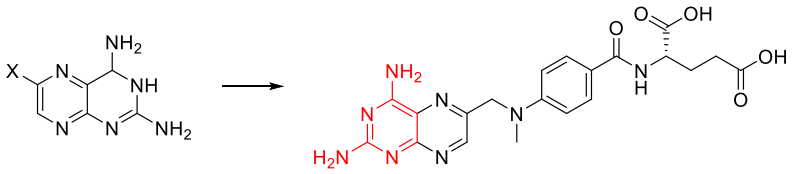
Palbociclib is primarily used to treat certain types of breast cancer. It belongs to the class of cyclin-dependent kinase (CDK) 4/6 inhibitors, working by blocking proteins that control the cell cycle and contribute to cancer cell proliferation. Approved on February 3, 2015, and developed by Pfizer for HR-positive and HER2-negative breast cancer, this drug is sold under the brand name Ibrance.[5].



Scheme 1. Synthesis of Palbociclib

2.1.2. Methotrexate

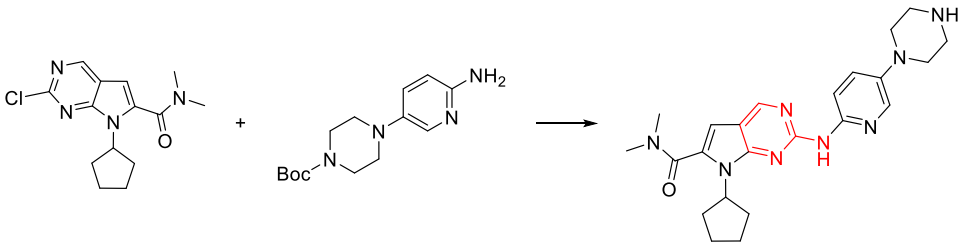
Introduced in 1947, this drug is less toxic compared to similar treatments and is used for breast cancer, leukemia, lung cancer, and lymphoma. Known by the brand names Trexall, Rheumatrex, and Otrexup, it was among the most widely prescribed medications globally in 2022 [6].



Scheme 2. Synthesis of Methotrexate

2.1.3. Ribociclib

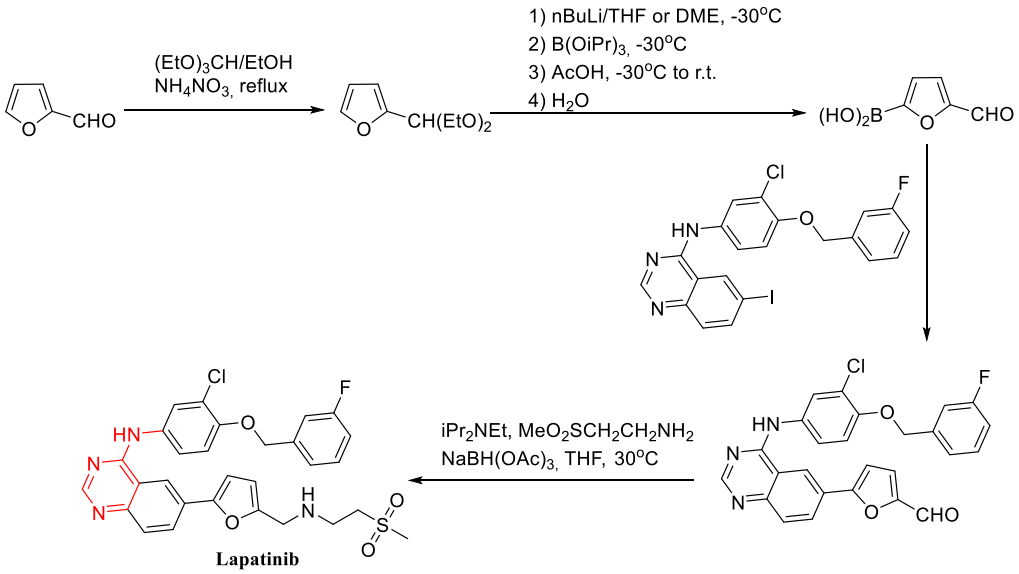
Ribociclib is a targeted cancer treatment classified as a cyclin-dependent kinase (CDK) 4/6 inhibitor. It is primarily prescribed for certain types of breast cancer. Sold under the brand name Kisqali, this drug was approved in March and August 2017 for breast cancer therapy [7].



Scheme 3. Synthesis of Ribociclib

2.1.4. Lapatinib

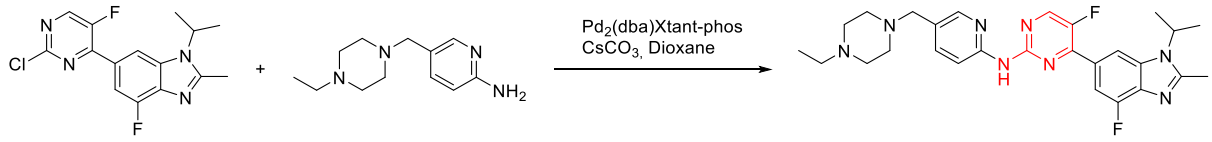
Lapatinib is a targeted therapy primarily used for breast cancer treatment. It acts as a small molecule tyrosine kinase inhibitor, specifically targeting the human epidermal growth factor receptor 2 (HER2) and epidermal growth factor receptor (EGFR) proteins. Approved by the FDA in March 2007, this drug is sold under the brand names Tykerb and Tyverb by Novartis and is effective not only against breast cancer but also other solid tumors [8].



Scheme 4. Synthesis of Lapatinib

2.1.5. Abemaciclib

Abemaciclib is a targeted cancer therapy classified as a cyclin-dependent kinase (CDK) 4/6 inhibitor. It is primarily used for the treatment of certain types of breast cancer. Sold under the brand name Verzenio, this drug was acknowledged by the FDA for its effectiveness against breast cancer in October 2015 and received formal approval in September 2017.

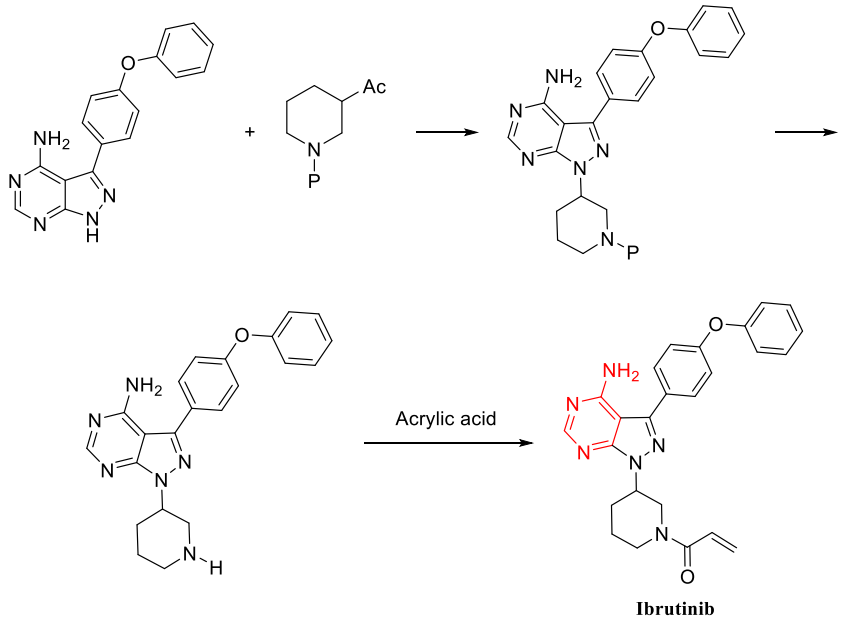


Scheme 5. Synthesis of Abemaciclib

2.2. Lymphoma Cancer Drugs

2.2.1. Ibrutinib

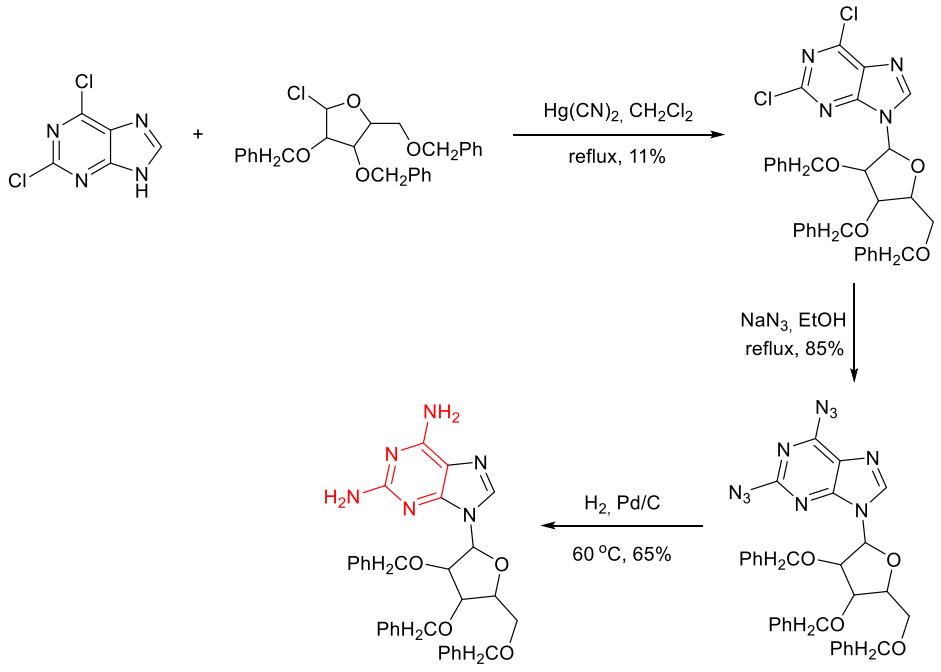
Ibrutinib is a targeted therapy primarily used for certain types of blood cancers. Functioning as a Bruton's tyrosine kinase (BTK) inhibitor, it is effective in managing conditions such as chronic lymphocytic leukemia (CLL) and mantle cell lymphoma (MCL). Listed on the World Health Organization's Essential Medicines list, this drug is sold under the brand name Imbruvica. It is a murine-based treatment that inhibits cancer cell growth by binding to the BTK protein [9].



Scheme 6. Synthesis of Ibrutinib

2.2.2. Fludarabine

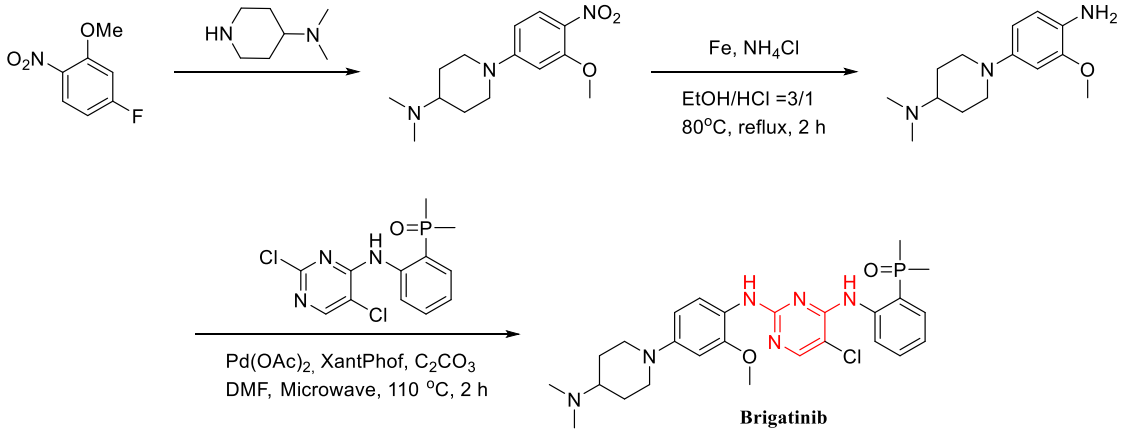
Fludarabine is a chemotherapy agent primarily used for the treatment of certain blood cancers, particularly chronic lymphocytic leukemia (CLL) and non-Hodgkin lymphoma. Approved in 1991, this medication is sold under the brand name Fludara and is applied in the management of both leukemia and lymphoma [10].



Scheme 7. Synthesis of Fludarabine

2.2.3. Brigatinib

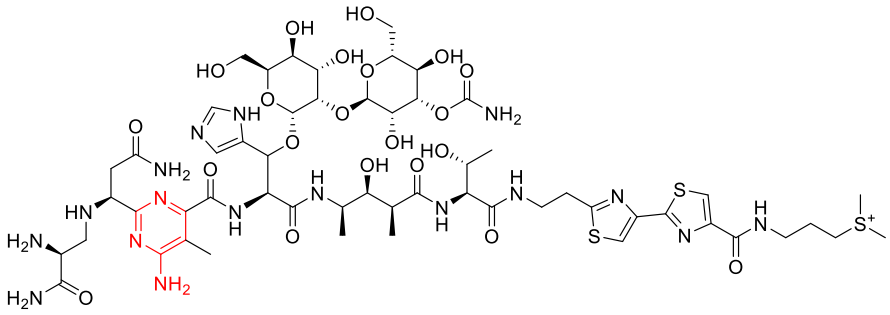
Brigatinib is a targeted therapy mainly used for certain types of lung cancer, especially non-small cell lung cancer (NSCLC) that is positive for anaplastic lymphoma kinase (ALK). This drug was approved by the FDA on April 28, 2017, and is sold under the brand name Alunbrig [11].



Scheme 8. Synthesis of Brigatinib

2.2.4. Bleomycin

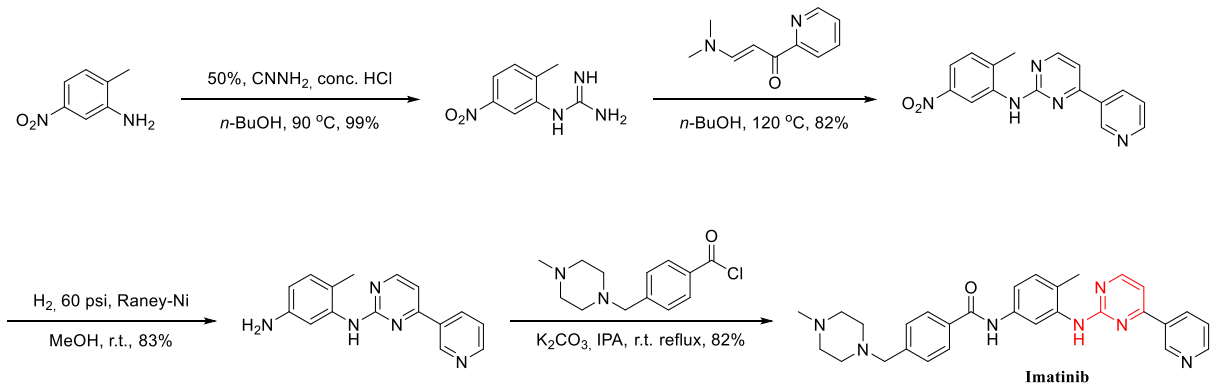
Bleomycin is a chemotherapy agent used to treat various types of cancer, particularly testicular cancer, Hodgkin's lymphoma, and certain types of squamous cell carcinoma. This medication, which was discovered in 1962, is sold under the brand name Blenoxane. It is also effective in treating breast cancer and other malignancies, and it appears on the World Health Organization's List of Essential Medicines [12].



Scheme 9. Structure of Bleomycin

2.2.5. Imatinib

Imatinib is a targeted therapy primarily used for certain types of cancer, especially chronic myeloid leukemia (CML) and gastrointestinal stromal tumors (GISTs). This medication received approval for medical use in 2001 and is listed among the World Health Organization's Essential Medicines. It is marketed under the brand names Gleevec and Glivec [13].

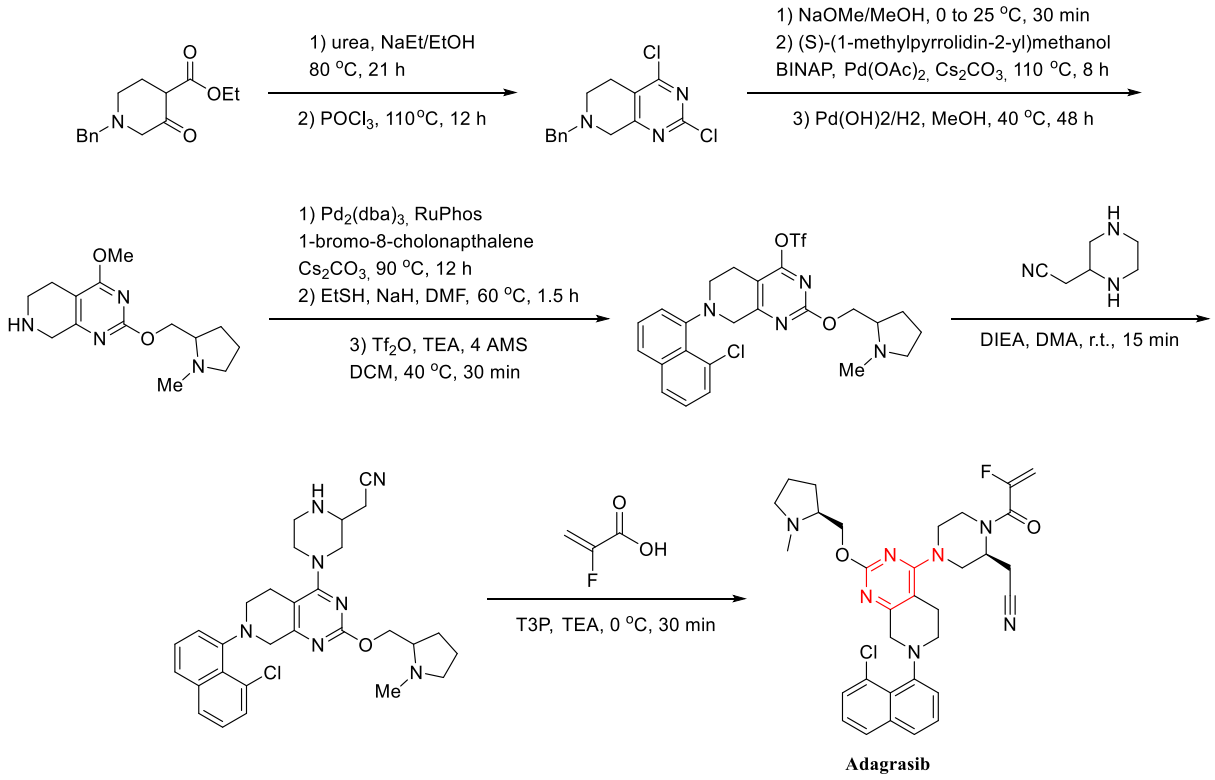


Scheme 10. Synthesis of Imatinib

2.3. Lung Cancer Drugs

2.3.1 Adagrasib

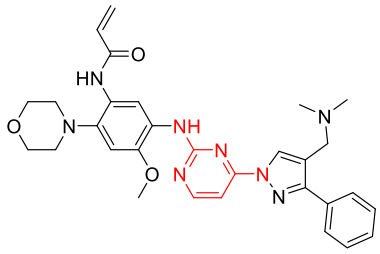
Adagrasib is a targeted therapy used for certain types of cancer, especially those with mutations in the KRAS gene, notably KRAS G12C. This drug was approved for medical use in December 2022 and is included in the World Health Organization's List of Essential Medicines, marketed under the brand name Krazati [14].



Scheme 11. Synthesis of Adagrasib

2.3.2. Lazertinib

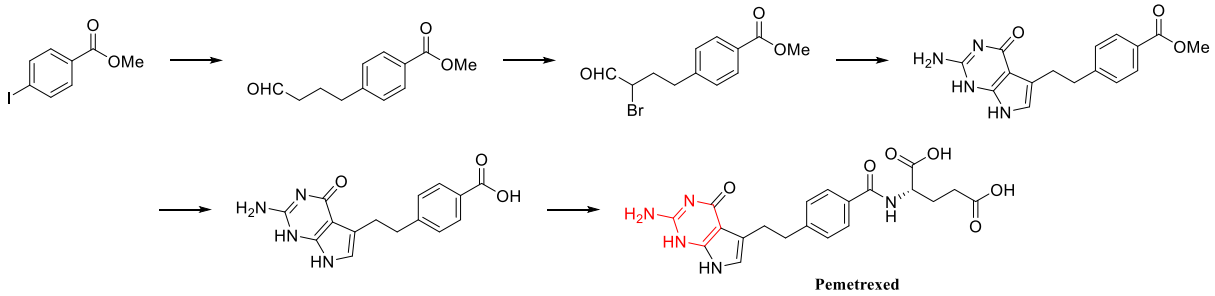
Lazertinib is an investigational drug primarily being studied for the treatment of certain types of cancer, particularly non-small cell lung cancer (NSCLC). Its synthesis generally includes several essential steps, such as building its core structure and adding specific functional groups. This medication received approval for medical use in August 2024 and is marketed under the trade name Lazcluze [15].



Scheme 12. Structure of Lazertinib

2.3.3. Pemetrexed

Pemetrexed is a chemotherapy agent primarily used to treat certain types of lung cancer and mesothelioma. This medication was approved for medical use by the U.S. Food and Drug Administration (FDA) in February 2004 and is available under the brand names Alimta, Pemfexy, and Ciambra [16].

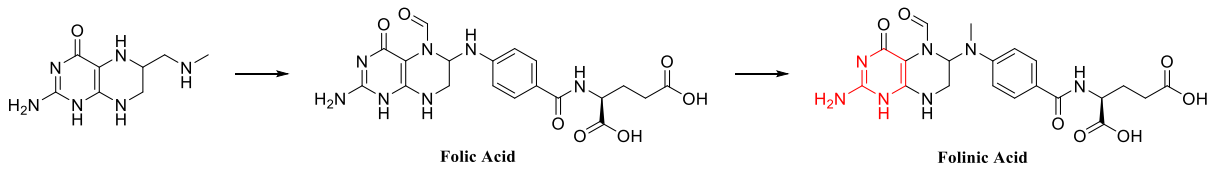


Scheme 13. Synthesis of Pemetrexed

2.4. Other Cancer Drugs

2.4.1. Folinic acid

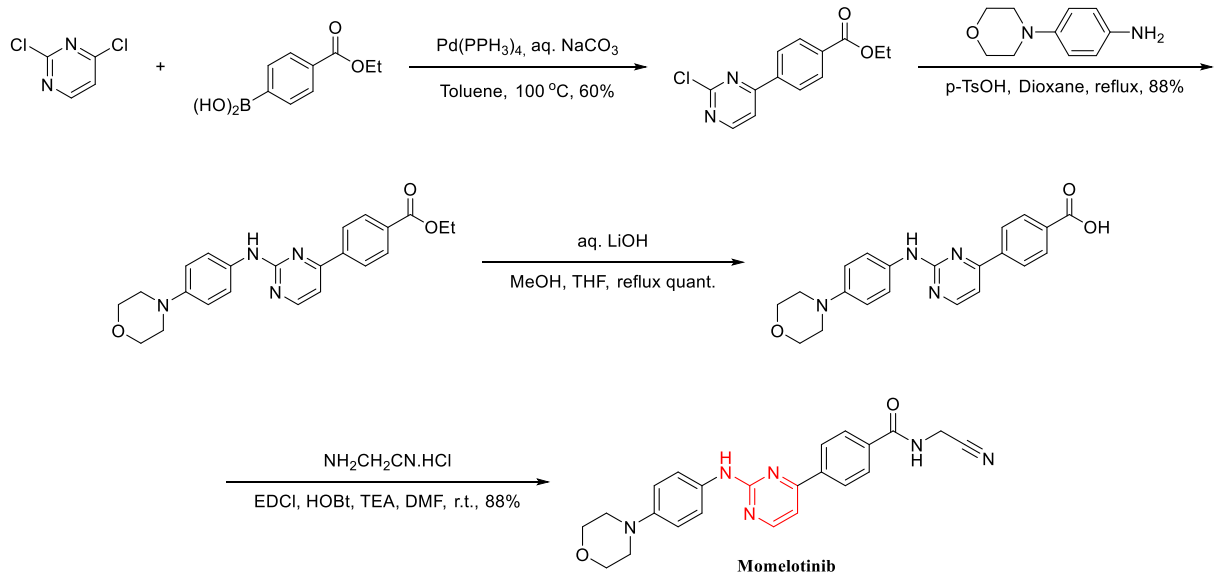
Folinic acid, also known as leucovorin, is a derivative of vitamin B9 (folate) that is used in medical treatments to minimize the side effects of specific chemotherapy drugs and to treat folate deficiency. This medication, which was first synthesized in 1945 and is included on the World Health Organization's List of Essential Medicines, can be found under the brand name Leucovorin. It is employed in the treatment of colon cancer [17].



Scheme 14. Synthesis of Folinic acid

2.4.2. Momelotinib

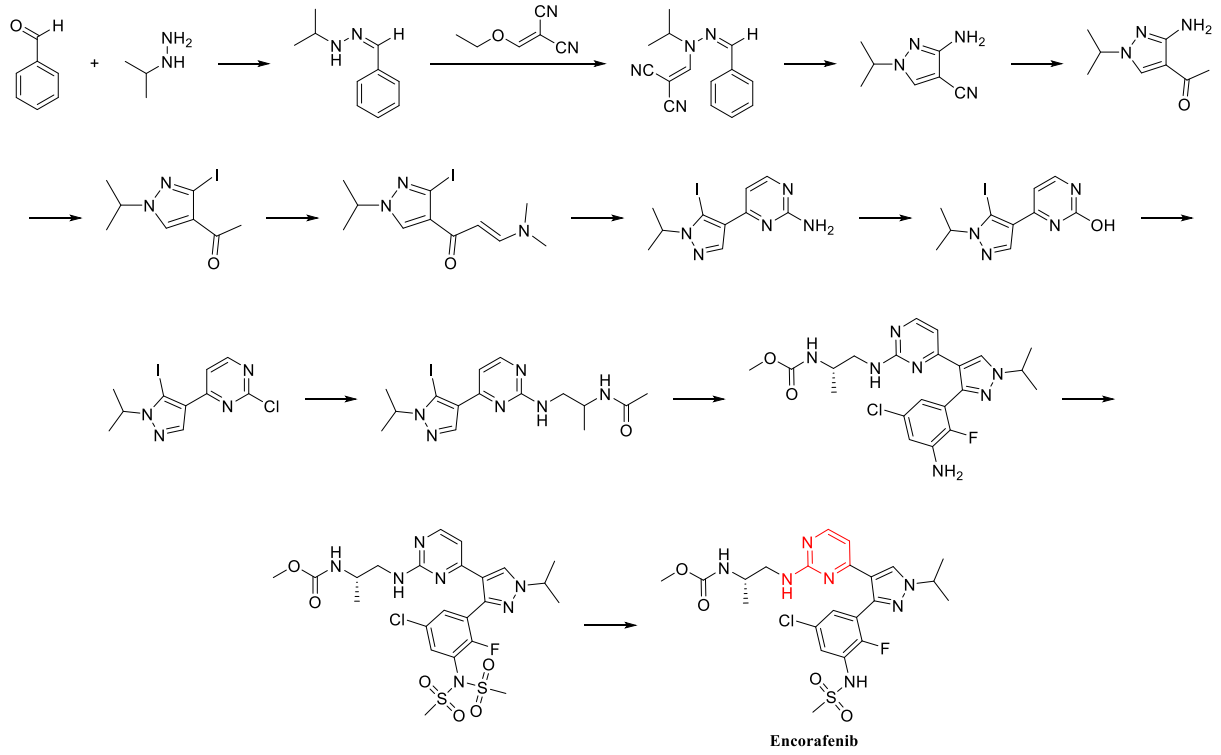
Momelotinib is an investigational medication that is being studied for the treatment of myelofibrosis, a type of bone marrow cancer that disrupts the body's normal blood cell production. This drug received approval in September 2023 and is marketed under the brand name Ojjaara. It is specifically used in the management of myelofibrosis [18].



Scheme 15. Synthesis of Momelotinib

2.4.3. Encorafenib

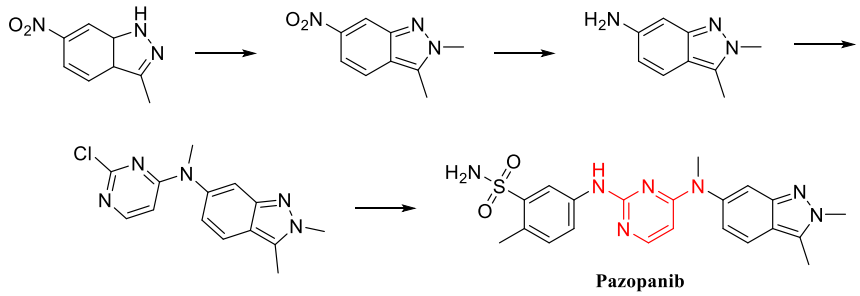
Encorafenib is a targeted therapy mainly used for certain types of cancers, particularly melanoma. This medication was approved for medical use by the U.S. Food and Drug Administration (FDA) in June 2018 and is available under the brand name Braftovi. It is specifically indicated for the treatment of select cases of melanoma [19].



Scheme 16. Synthesis of Encorafenib

2.4.4. Pazopanib

Pazopanib is a targeted therapy predominantly used for certain types of cancer, particularly renal cell carcinoma (kidney cancer) and soft tissue sarcoma. This drug was approved for medical use by the U.S. Food and Drug Administration (FDA) in October 2009 and is sold under the brand name Votrient. It is specifically indicated for the treatment of clear cell renal cell carcinoma, the most common histological subtype [20].



Scheme 17. Synthesis of Pazopanib

3. RESULTS AND DISCUSSION

4. CONCLUSION

Cancer remains one of the most formidable health challenges globally, impacting millions of individuals annually. Progress in research, early diagnosis, and treatment alternatives has notably enhanced survival rates and the quality of life for numerous patients. Nevertheless, the intricate nature of cancer, characterized by its diverse types and the underlying genetic and environmental influences, necessitates an ongoing dedication to research and innovation. This study explores FDA-approved cancer medications that feature an Aminopyrimidine structure and offers insights into several of these drugs.

AUTHOR'S CONTRIBUTIONS

All authors have made essential contributions to this study. The final version of the article has been read and approved by all authors.

CONFLICTS OF INTEREST

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

RESEARCH AND PUBLICATION ETHICS

The author declares that this study complies with Research and Publication Ethics.

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