WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
Coden USA: WJPRAP Impact Factor 8.453
Volume 15, Issue 1, 478-492. Review Article ISSN 2277–7105

A COMPREHENSIVE REVIEW ON ANTICANCER PHARMACOTHERAPY FOR BREAST CANCER

Sakshi Landge*, Dr. Amita Dongare, Prof. Vaishali Jagtap

Department of Pharmacy, Eknath Sitaram Divekar College of Pharmacy, Varvand, India.

Article Received on 05 Dec. 2025,
Article Revised on 26 Dec. 2025,
Article Published on 01 Jan. 2026

https://doi.org/10.5281/zenodo.18093905

***Corresponding Author**

Sakshi Landge

Department of Pharmacy, Eknath Sitaram Divekar College of Pharmacy, Varvand, India.

How to cite this Article: Sakshi Landge*, Dr. Amita Dongare, Prof. Vaishali Jagtap. (2026) A COMPREHENSIVE REVIEW ON ANTICANCER PHARMACOTHERAPY FOR BREAST CANCER. World Journal of Pharmaceutical Research, 15(1), 478–492.

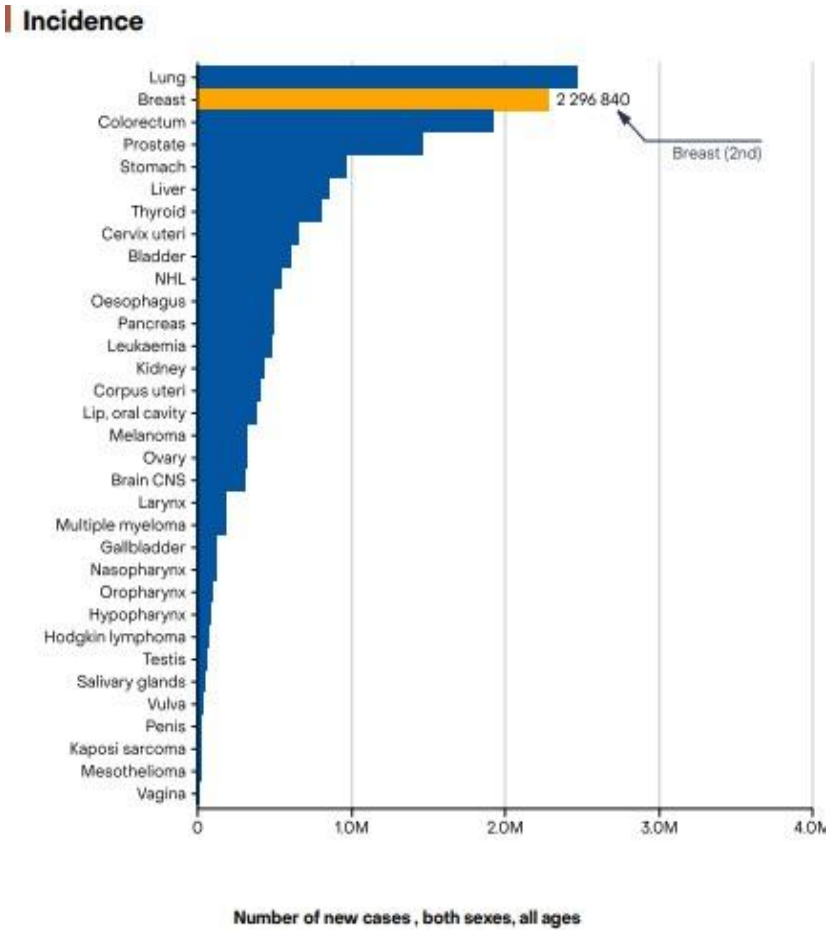
ABSTRACT

Background: Breast cancer remains the most prevalent malignancy worldwide and represents a major pharmacological and public health challenge due to its molecular heterogeneity and development of drug resistance. Conventional cytotoxic chemotherapy, although effective, is associated with significant systemic toxicity and limited specificity. **Objective:** This review critically evaluates the transition from conventional chemotherapy to precision-based anticancer pharmacotherapy in breast cancer, with emphasis on endocrine therapy, targeted agents, antibody–drug conjugates, and emerging molecular therapies. **Key Findings:** Advances in molecular classification and pharmacogenomics have enabled the development of highly specific therapies, including CDK4/6 inhibitors, HER2-targeted monoclonal antibodies, antibody–drug conjugates, PARP inhibitors, PI3K inhibitors, and oral selective estrogen receptor degraders. These therapies have significantly improved survival outcomes while reducing treatment-related toxicity in selected patient subgroups. **Conclusion:** The overarching conclusion of this review is that the future of oncology lies in the "de-escalation" of therapy—reducing the intensity of treatment without compromising the cure rate. By utilizing predictive biomarkers and high-efficiency targeted agents, we can spare patients from the debilitating side effects of traditional chemotherapy (such as alopecia, myelosuppression, and cardiotoxicity). This shift represents a fundamental change in the pharmacist's role, moving toward the management of highly specific drug-drug interactions and the monitoring of sophisticated biological therapies.

INTRODUCTION

Epidemiology: Global Burden of Breast Cancer

Breast cancer has surpassed lung cancer to become the most frequently diagnosed malignancy worldwide. According to the latest data from the World Health Organization (WHO) and the Global Cancer Observatory (GLOBOCAN), breast cancer accounts for approximately 11.7% of all new cancer cases globally. In 2024–2025, the estimated incidence has risen to over 2.3 million new cases annually, with mortality rates remaining disproportionately high in low-to-middle-income countries due to delayed diagnosis and limited access to targeted biological therapies. From a pharmaceutical and public health perspective, the "epidemic" of breast cancer is not uniform. While survival rates in developed nations exceed 90% for early-stage disease, the challenge persists in managing metastatic cases and aggressive subtypes. The increasing prevalence is attributed to a combination of genetic predispositions (such as BRCA1/2 mutations) and lifestyle-related risk factors, necessitating a more robust pipeline of affordable, high-efficiency pharmaceutical interventions.

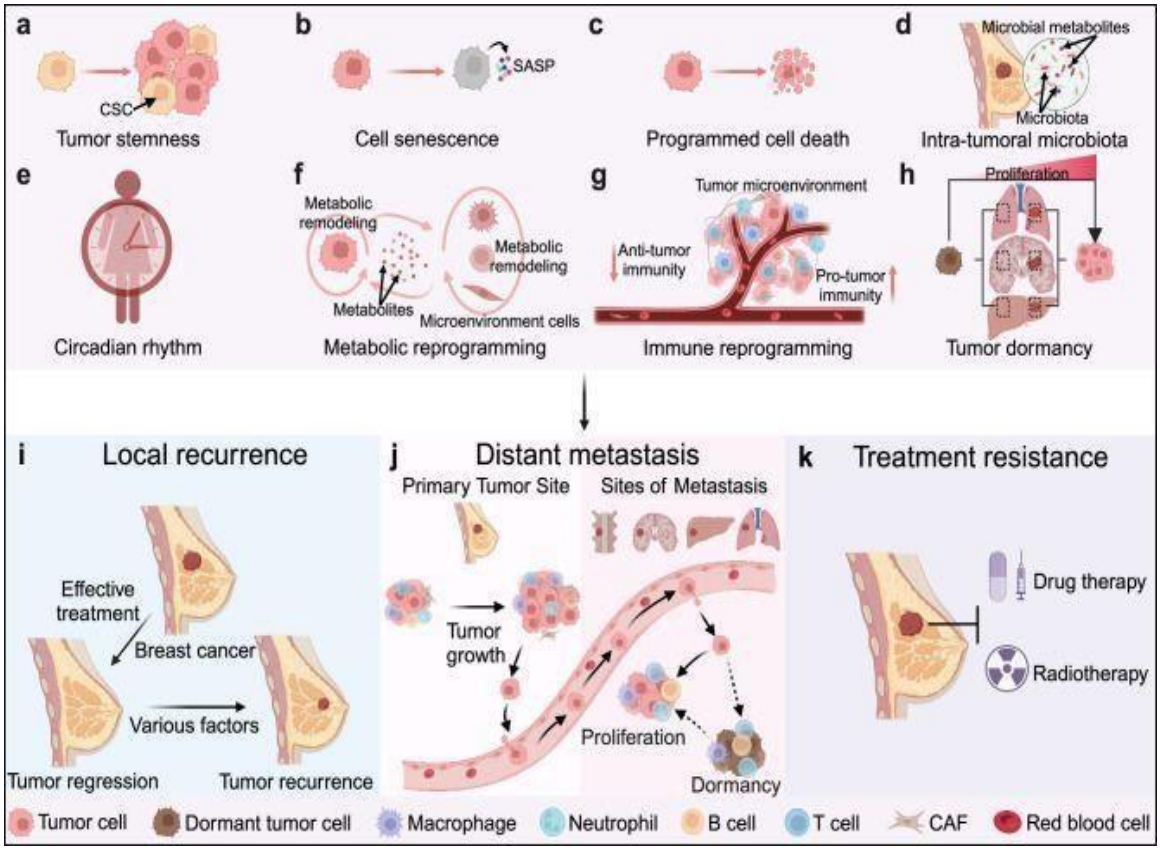


Pathophysiology: Malignant Transformation

Breast cancer develops through a multistep process involving genetic mutations and epigenetic alterations. Key mechanisms include oncogene activation (HER2, MYC), tumour suppressor gene inactivation (TP53, PTEN), and angiogenesis mediated by vascular endothelial growth factor (VEGF). These pathways form the pharmacological basis for modern targeted drug development.

Malignancy typically begins with Hyperplasia, where epithelial cells lose their sensitivity to inhibitory growth signals. This progresses to Carcinoma in situ, where the basement membrane remains intact, and finally to Invasive Carcinoma. At the molecular level.

For the pharmacist, understanding this "angiogenic switch" and the loss of apoptosis is critical, as these pathways serve as the primary targets for modern anti-cancer drug design.



Molecular Subtypes of Breast Cancer and Pharmacological Implications

Luminal A (ER^+ / PR^+ / $HER2^-$)

This is the most hormone-dependent and biologically calm subtype. Tumors grow slowly because they rely mainly on estrogen and progesterone signaling rather than aggressive

growth pathways. The proliferation marker Ki-67 is low, which explains the excellent prognosis and lower recurrence rate.

Pharmacologically, these cancers respond very well to endocrine therapy. Tamoxifen blocks estrogen receptors, while aromatase inhibitors (anastrozole, Letrozole) reduce estrogen synthesis, especially effective in postmenopausal women. Chemotherapy is usually not required unless high-risk features are present.

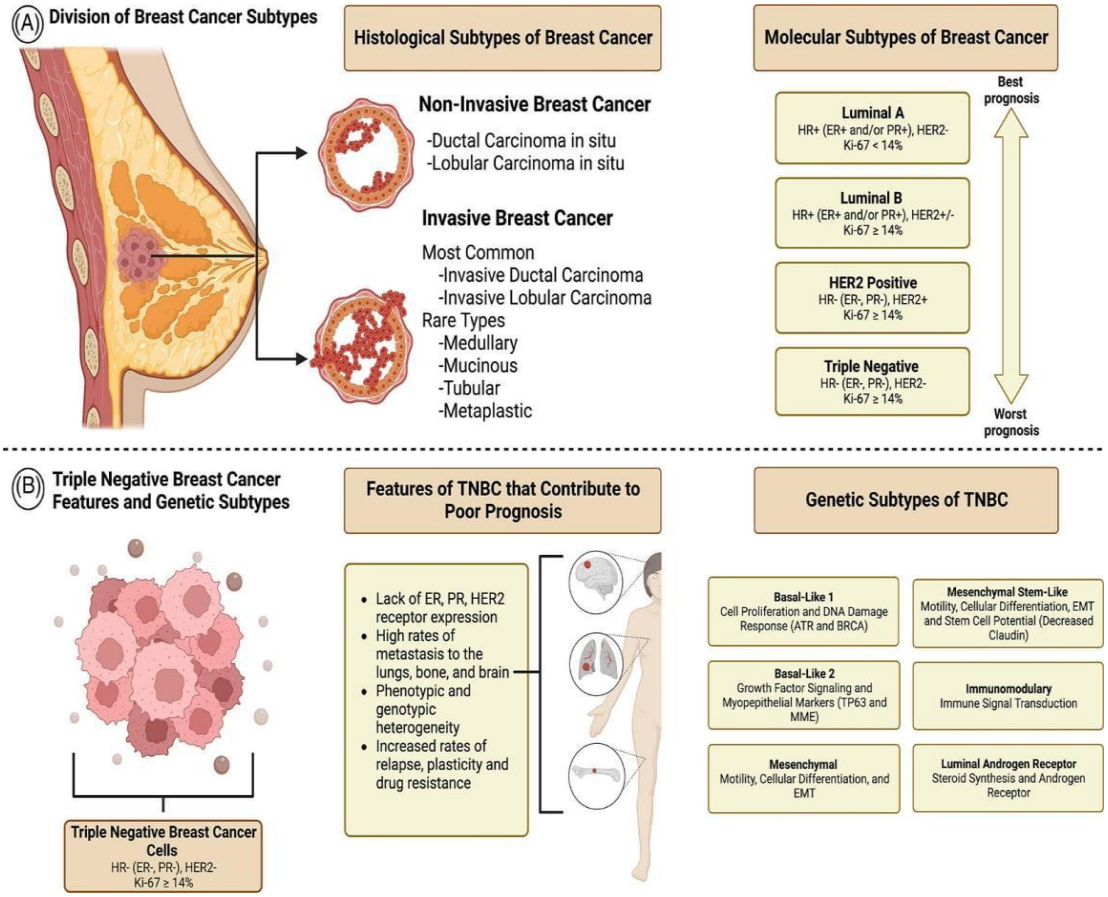
Luminal B (ER^+ / PR^+, ± HER2)

Luminal B tumors are still hormone-receptor positive but are more aggressive than Luminal A. They show a higher Ki-67 index, indicating faster cell division and a greater chance of recurrence. Some cases also express HER2, further increasing growth signaling. Endocrine therapy remains the backbone of treatment, but it is often combined with targeted agents. CDK4/6 inhibitors (palbociclib, ribociclib, abemaciclib) are commonly added because they block cell-cycle progression, improving progression-free survival. Chemotherapy is more frequently considered than in Luminal A cases.

HER2-Enriched Breast Cancer

This subtype is defined by overexpression or amplification of the HER2 receptor, which drives rapid and uncontrolled tumor growth. Historically, it was associated with poor prognosis and high relapse rates.

Pharmacological advances have dramatically changed outcomes. HER2-targeted therapies directly inhibit this pathway. Trastuzumab blocks HER2 signaling and promotes immune-mediated tumor destruction. Pertuzumab prevents HER2 dimerization, enhancing efficacy when combined with trastuzumab. Antibody–drug conjugates (e.g., T-DM1, trastuzumab deruxtecan) deliver cytotoxic drugs directly into HER2-positive cancer cells.
With these agents, survival rates have significantly improved.



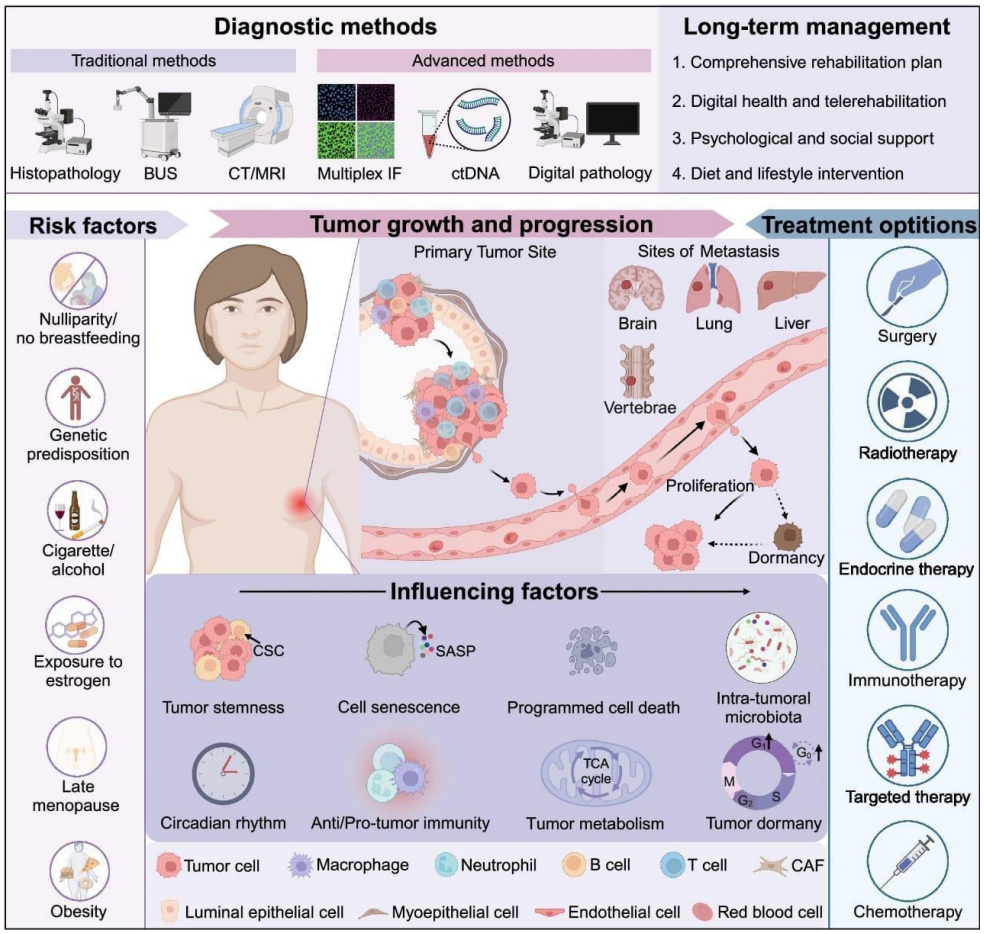
Conventional Treatment Modalities

Surgery and Radiation Therapy

Surgery remains the primary and most definitive treatment for localized breast cancer. The main objective is complete removal of the tumor with clear margins to minimize the risk of local recurrence.

Two major surgical approaches are used. Breast-conserving surgery (lumpectomy) involves excision of the tumor along with a rim of normal tissue and is preferred when the tumor is small and localized, as it preserves breast anatomy and cosmetic appearance. Mastectomy, which involves complete removal of the breast tissue, is indicated in cases of large tumors, multifocal disease, genetic predisposition (such as BRCA mutations), or patient preference.

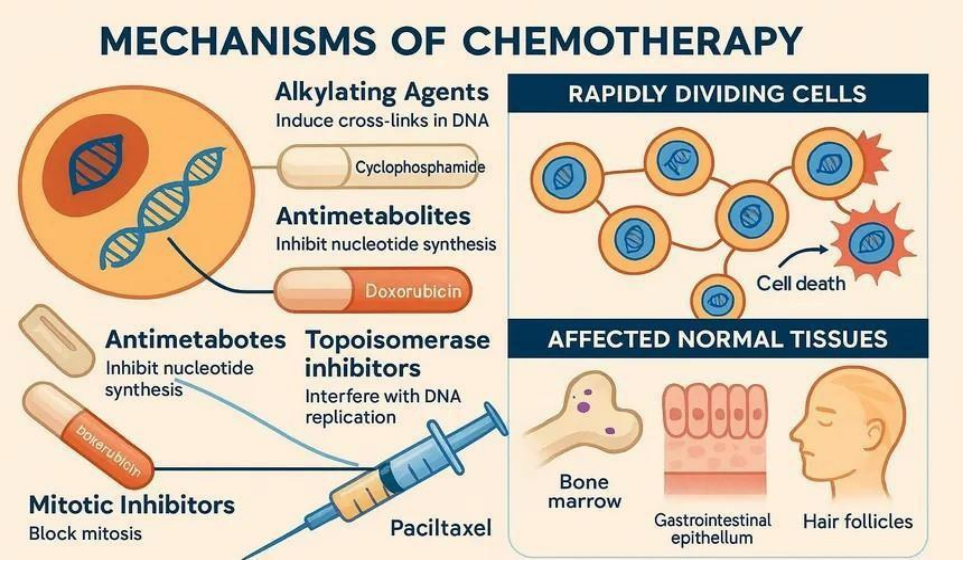
Assessment of regional lymph node involvement is a critical part of surgical management. Sentinel lymph node biopsy is commonly performed to determine metastatic spread while minimizing surgical morbidity. In cases of extensive nodal involvement, axillary lymph node dissection may be required, though it carries risks such as lymphedema and shoulder dysfunction.



Cytotoxic Chemotherapy

Cytotoxic chemotherapy plays a crucial role in the systemic management of breast cancer, particularly in patients with high-risk disease, aggressive tumor biology, or limited response to targeted therapies. **Anthracyclines**, such as doxorubicin, and **taxanes**, such as paclitaxel, form the backbone of most standard chemotherapy regimens due to their proven efficacy in reducing tumor burden and improving survival outcomes. Anthracyclines exert their anticancer effects by intercalating into DNA, inhibiting topoisomerase II, and generating free radicals, thereby disrupting DNA replication and transcription and leading to cancer cell death. Taxanes act by stabilizing microtubules and preventing their depolymerisation, which interferes with mitotic spindle formation and arrests tumor cells in the M phase of the cell cycle, ultimately inducing apoptosis. Despite their therapeutic benefits, the use of these agents is associated with significant toxicity. Anthracyclines are well known for their dose-dependent **cardiotoxicity**, which can result in irreversible cardiac dysfunction, while both drug classes commonly cause **myelosuppression**, increasing the risk of infections and anaemia. Additionally, taxanes frequently produce **peripheral neuropathy**, which may affect quality of life and limit treatment intensity. Consequently, careful patient selection, dose

optimization, and close monitoring are essential to maximize clinical benefit while minimizing adverse effects.



Endocrine Therapy

Approximately 70% of breast cancers are estrogen receptor–positive (ER^+), making hormonal signaling a central driver of tumor growth in the majority of cases. In these tumors, estrogen functions as a key mitogenic factor, binding to intracellular estrogen receptors and activating transcriptional programs that promote cell survival, proliferation, and resistance to apoptosis. Endocrine therapy is designed to disrupt this estrogen-dependent signaling axis, either by blocking the estrogen receptor itself or by reducing systemic estrogen levels, thereby suppressing tumor progression. Due to its targeted nature, endocrine therapy is generally associated with lower toxicity compared to cytotoxic chemotherapy and forms the backbone of long-term treatment in hormone receptor–positive breast cancer.

Selective Estrogen Receptor Modulators (SERMs)

Tamoxifen is a selective estrogen receptor modulator (SERM) that plays a pivotal role in the treatment and prevention of estrogen receptor–positive breast cancer. It acts by competitively inhibiting estrogen binding to estrogen receptors in breast tissue, thereby blocking estrogen-mediated transcriptional activity responsible for tumor cell proliferation. Through this mechanism, tamoxifen induces cell-cycle arrest in the G0/G1 phase, leading to reduced tumor growth and, in many cases, tumor regression. It is widely used as adjuvant therapy in both premenopausal and postmenopausal women and has demonstrated significant reductions in recurrence rates as well as improvements in overall survival.

However, tamoxifen exhibits tissue-selective agonist and antagonist properties, which explain both its therapeutic benefits and adverse effects. While it functions as an estrogen antagonist in breast tissue, it acts as a partial agonist in the endometrium, bone, and coagulation system. Consequently, long-term therapy is associated with an increased risk of thromboembolic events, including deep vein thrombosis and pulmonary embolism, as well as endometrial hyperplasia and endometrial cancer. Other commonly reported adverse effects include hot flashes, menstrual disturbances, and mood changes. Therefore, extended tamoxifen use requires regular clinical follow-up, gynaecological surveillance, and careful risk– benefit evaluation to ensure optimal therapeutic outcomes.

Aromatase Inhibitors

Aromatase inhibitors such as Letrozole, anastrozole, and exemestane are essential components of endocrine therapy in postmenopausal women, where estrogen production occurs primarily through peripheral conversion of androgens to estrogen by the aromatase enzyme. These agents exert their effect by inhibiting aromatase, resulting in profound suppression of estrogen synthesis and effective deprivation of estrogen-dependent tumor cells. Aromatase inhibitors are widely used as first-line adjuvant therapy, as sequential therapy following tamoxifen, and in the treatment of advanced or metastatic hormone receptor–positive breast cancer.

While aromatase inhibitors offer superior disease control in many postmenopausal patients, prolonged estrogen suppression is associated with adverse effects such as bone mineral density loss, increased fracture risk, and musculoskeletal symptoms including arthralgia and myalgia. As a result, patients receiving aromatase inhibitors require bone health monitoring and may benefit from calcium, vitamin D supplementation, or bone-protective agents to mitigate skeletal toxicity.

Selective Estrogen Receptor Degraders (SERDs)

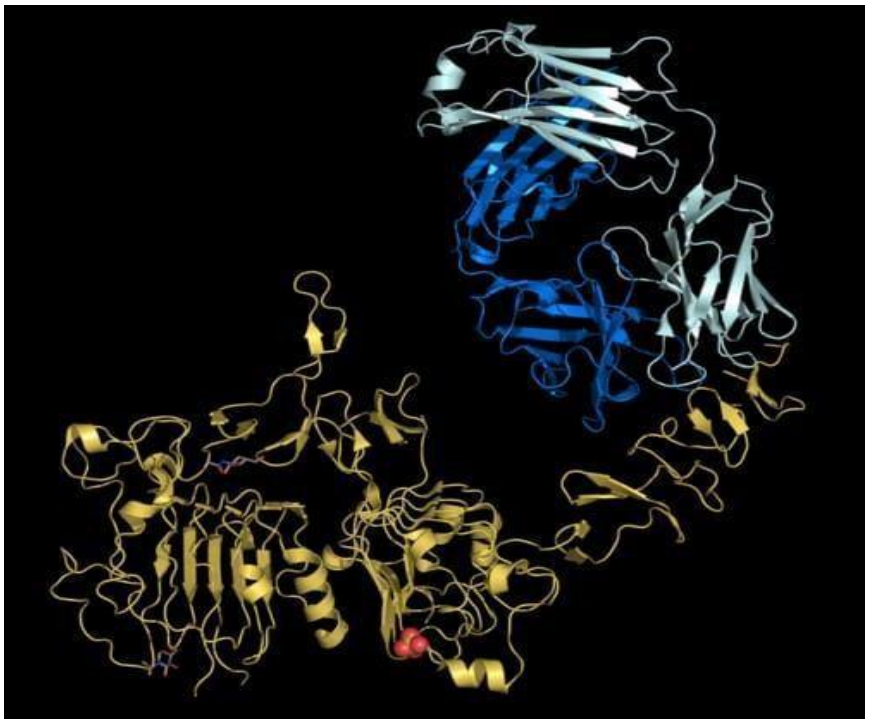
Selective Estrogen Receptor Degraders (SERDs) represent a more advanced endocrine strategy by directly targeting and eliminating the estrogen receptor, rather than modulating estrogen levels. Elacestrant is the first oral SERD approved for the treatment of ESR1-mutated metastatic breast cancer, a genetic alteration frequently associated with resistance to aromatase inhibitors and other endocrine therapies. Elacestrant binds to the estrogen receptor and induces conformational destabilization followed by proteasomal degradation, leading to sustained inhibition of estrogen-driven transcription and tumor proliferation.

The oral availability of elacestrant offers a clear advantage over earlier injectable SERDs such as fulvestrant, improving patient convenience, adherence, and long-term tolerability. Clinical studies have demonstrated its efficacy in patients with endocrine-resistant disease, particularly when ESR1 mutations are present. Common adverse effects include nausea, fatigue, and musculoskeletal discomfort, which are generally manageable. Overall, elacestrant represents a significant advancement in addressing endocrine resistance and expanding personalized treatment options for patients with advanced hormone receptor–positive breast cancer.

Targeted Therapies

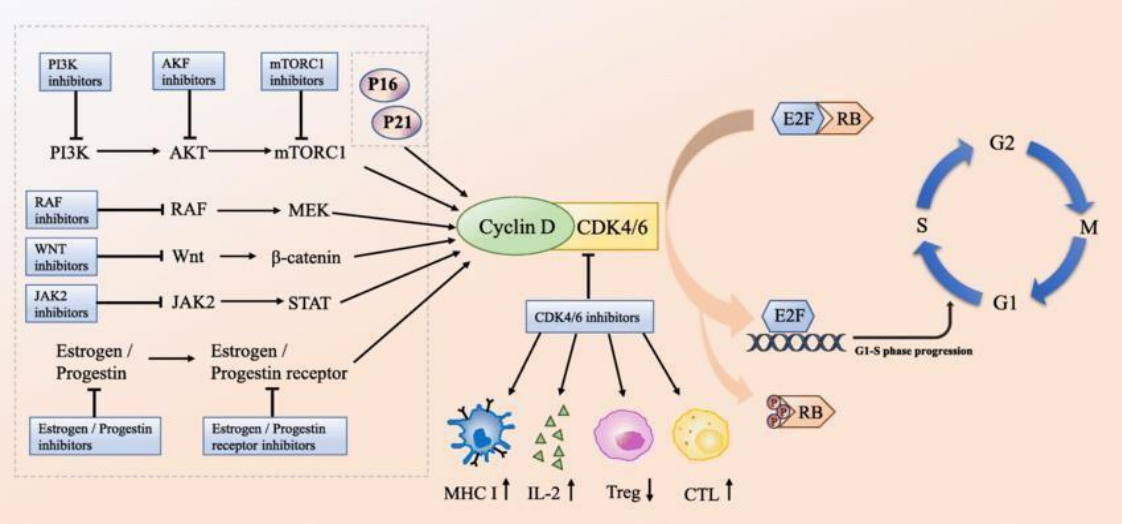
HER2-Targeted Agents

HER2-targeted agents have transformed the treatment landscape of HER2-positive breast cancer by specifically inhibiting the oncogenic HER2 signaling pathway. Trastuzumab and pertuzumab work synergistically to provide dual HER2 blockade, targeting different domains of the HER2 receptor. Trastuzumab binds to the extracellular domain IV of the HER2 receptor, inhibiting downstream signaling and mediating antibody-dependent cellular cytotoxicity, while pertuzumab binds to domain II, preventing HER2 dimerization with other HER family receptors. This complementary mechanism results in more effective suppression of tumor growth and has significantly improved survival outcomes in both early-stage and metastatic disease.



CDK4/6 Inhibitors

Agents that have become central to the treatment of hormone receptor–positive, HER2-negative breast cancer, particularly in advanced and metastatic settings. These drugs act by selectively inhibiting cyclin-dependent kinases 4 and 6, which are essential for phosphorylation and inactivation of the **retinoblastoma (Rb) protein**, a key regulator of the cell cycle. By maintaining Rb in its **active, hypo phosphorylated state**, CDK4/6 inhibitors prevent the transition from the G1 phase to the S phase of the cell cycle, thereby inducing sustained **G1 phase arrest** and suppressing tumor cell proliferation.



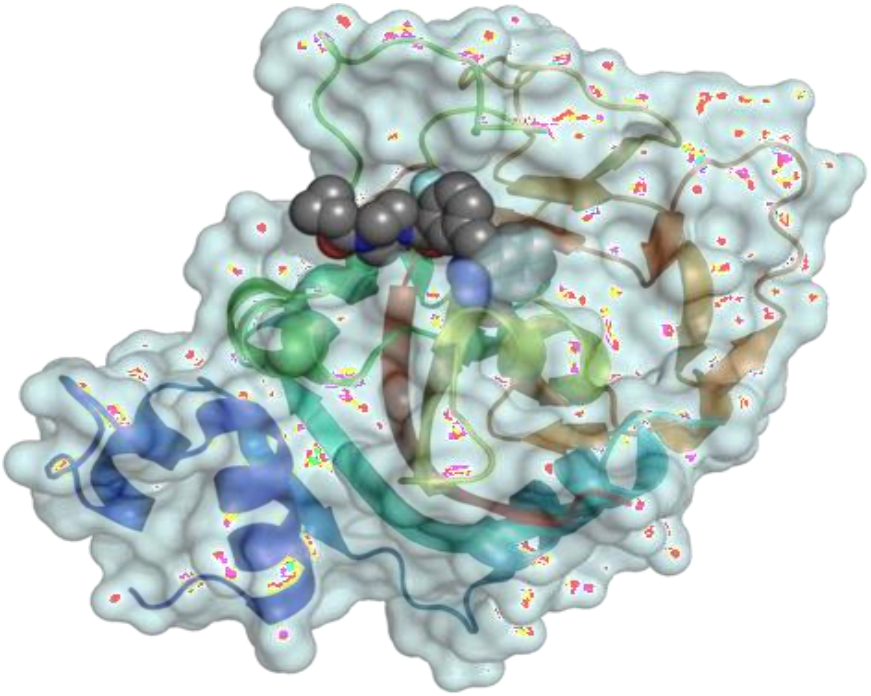
PARP Inhibitors

PARP inhibitors, such as olaparib, play a targeted role in the treatment of BRCA- mutated breast cancer by exploiting the principle of synthetic lethality. PARP enzymes are essential for repairing single-strand DNA breaks through the base excision repair pathway; when PARP is inhibited, these breaks accumulate and are converted into double-strand breaks during DNA replication. In normal cells, double- strand breaks are efficiently repaired by homologous recombination, but BRCA- mutated cancer cells lack this repair mechanism, leading to genomic instability and selective tumor cell death. This targeted action allows olaparib to effectively eliminate cancer cells while sparing normal tissue, resulting in improved clinical outcomes with a more favourable toxicity profile compared to conventional chemotherapy, though adverse effects such as anaemia, fatigue, and nausea may still occur.

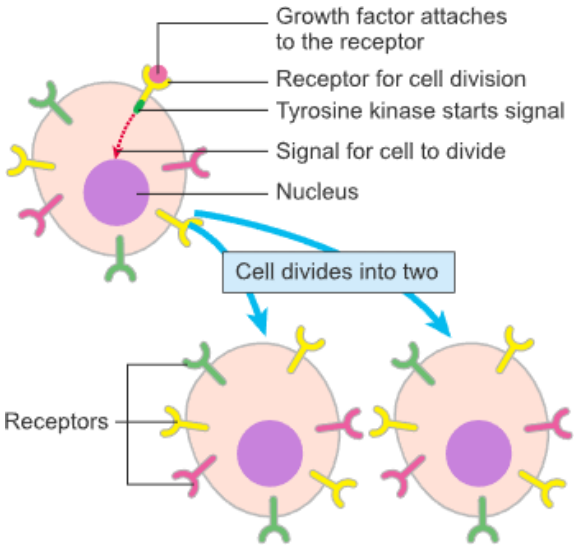
PI3K Inhibitors

PI3K inhibitors are designed to disrupt aberrant intracellular signaling that drives tumor growth and survival in hormone receptor–positive breast cancer. Involisib selectively targets

the PI3K alpha (PI3Kα) isoform, which is frequently activated by PIK3CA mutations in HR-positive disease. By inhibiting PI3Kα, involisib suppresses downstream AKT/m TOR signaling, leading to reduced cellular proliferation, enhanced apoptosis, and improved sensitivity to endocrine therapy. Its isoform selectivity helps preserve antitumor efficacy while limiting off-target effects seen with earlier, less selective PI3K inhibitors, resulting in manageable toxicity profiles such as hyperglycaemia, rash, and gastrointestinal symptoms. When combined with endocrine agents, involisib represents a precision-medicine approach that addresses endocrine resistance in PIK3CA-mutated breast cancer.



PARP inhibitors



An example of how growth inhibitors can block more than one action in a cell

Recent Approved and Emerging Therapies

Datopotamab Deruxtecan (TROP2-targeting ADC)

Datopotamab deruxtecan is an antibody–drug conjugate that targets TROP2, a transmembrane glycoprotein highly expressed in several breast cancer subtypes, including hormone receptor–positive and triple-negative breast cancer. The monoclonal antibody component selectively binds to TROP2-expressing tumor cells, after which the complex is internalized and releases a potent topoisomerase I inhibitor payload. This targeted delivery enables effective tumor cell killing while limiting systemic toxicity. Early clinical trials have demonstrated encouraging antitumor activity in heavily pre-treated patients, positioning datopotamab deruxtecan as a promising option for treatment-resistant disease.

Trastuzumab Deruxtecan plus Pertuzumab

The combination of trastuzumab deruxtecan with pertuzumab represents an important advancement in first-line therapy for metastatic HER2-positive breast cancer. Pertuzumab prevents HER2 receptor dimerization, while trastuzumab deruxtecan delivers a highly potent cytotoxic agent directly into HER2-expressing cancer cells. This dual approach provides both robust HER2 pathway inhibition and targeted chemotherapy, resulting in deep and durable responses. Clinical evidence suggests improved progression-free survival compared with earlier HER2-targeted regimens, though careful monitoring is required due to potential adverse effects such as interstitial lung disease associated with antibody–drug conjugates.

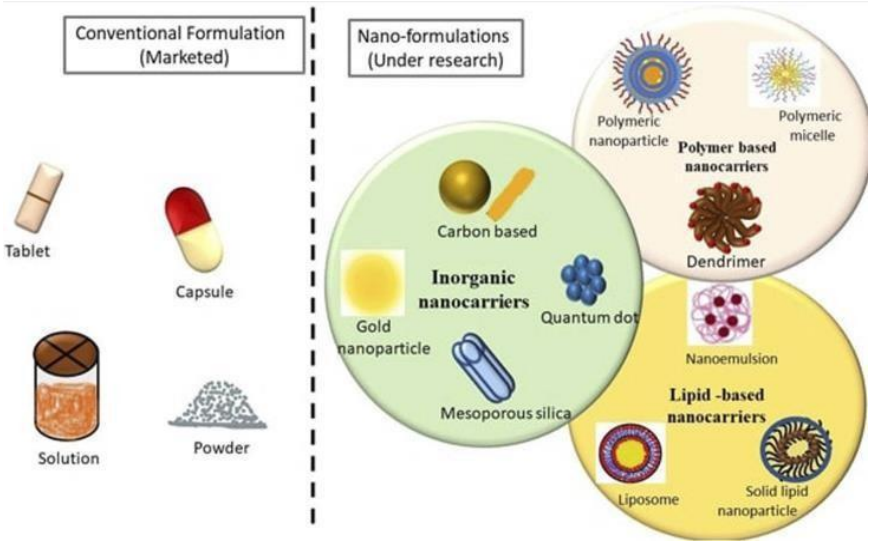
Imlunestrant (Oral SERD)

Imlunestrant is a next-generation oral selective estrogen receptor degrader developed for the treatment of estrogen receptor–positive breast cancer, particularly in cases with acquired endocrine resistance. It binds to the estrogen receptor and induces its degradation, leading to sustained suppression of estrogen- driven signaling. The oral route of administration improves patient convenience and long-term adherence compared to injectable SERDs. Ongoing studies indicate that Imlunestrant is effective both as monotherapy and in combination with CDK4/6 or PI3K inhibitors, making it a versatile option in advanced hormone-dependent disease.

Saruparib (Next-generation PARP1 Inhibitor)

Saruparib is an emerging next-generation PARP1-selective inhibitor designed to enhance antitumor efficacy while reducing off-target toxicity seen with earlier PARP inhibitors. By

selectively inhibiting PARP1, Saruparib induces DNA damage accumulation in tumors with defects in homologous recombination repair, such as BRCA-mutated breast cancer, leading to synthetic lethality. Its improved selectivity aims to minimize hematologic toxicity while maintaining strong anticancer activity. Early clinical data suggest that Saruparib may offer improved tolerability and effectiveness, particularly in patients who have progressed on first-generation PARP inhibitors.



Conventional and Novel formulations of various FDA approved anticancer Drugs used for Breast Cancer Indications.

Challenges and Future Perspectives

Despite remarkable progress in the understanding and treatment of breast cancer, several critical challenges continue to hinder optimal patient outcomes. One of the most significant issues is acquired drug resistance, which develops as cancer cells evolve under therapeutic pressure through genetic mutations, activation of alternative signaling pathways, and changes in tumor microenvironment. This resistance often leads to disease progression despite initial response to endocrine therapy, targeted agents, or chemotherapy. Another major challenge is the high cost of advanced treatments, including targeted therapies, antibody–drug conjugates, and immunotherapies, which limits their widespread use and places a heavy economic burden on both patients and healthcare systems. In developing countries, these problems are further aggravated by limited diagnostic and molecular testing infrastructure, lack of access to advanced imaging and biomarker assays, and delays in early detection, all of which restrict the implementation of personalized treatment strategies.

Looking ahead, future breast cancer management is expected to increasingly rely on innovative, technology-driven approaches aimed at improving precision and accessibility of care. Liquid biopsies are gaining prominence as a non-invasive tool for early cancer detection, monitoring minimal residual disease, and identifying emerging resistance mutations in real time, allowing timely modification of therapy. The integration of artificial intelligence in treatment planning holds promise for analysing large datasets encompassing genomics, radiology, pathology, and clinical parameters to support accurate risk stratification and individualized therapeutic decisions. Furthermore, the development of personalized cancer vaccines, designed to target patient-specific tumor antigens, represents an evolving immunotherapeutic strategy with the potential to provide durable immune control and reduce relapse rates. Collectively, these future directions aim to overcome existing challenges and shift breast cancer care toward a more adaptive, equitable, and patient-centred precision medicine paradigm.

CONCLUSION

Breast cancer therapy has evolved dramatically over the past few decades, shifting from largely non-specific cytotoxic chemotherapy to highly precise, mechanism- driven pharmacological strategies. A deeper understanding of tumor biology, molecular subtypes, and genetic alterations has enabled the development of targeted therapies, endocrine agents, antibody–drug conjugates, and immunotherapeutic approaches that selectively attack cancer cells while sparing normal tissues. This transition toward biomarker-guided treatment selection has led to significant improvements in survival outcomes, disease control, and overall quality of life, while also reducing the burden of treatment-related toxicity.

As therapeutic regimens become increasingly complex and individualized, the pharmacist's role has expanded beyond traditional dispensing functions. Pharmacists are now integral members of the oncology care team, contributing to treatment planning, therapeutic drug monitoring, management of adverse drug reactions, and patient education to improve adherence and safety. Their involvement is particularly critical in navigating drug–drug interactions, dose adjustments, and long-term toxicity monitoring associated with modern anticancer agents. Moving forward, the continued integration of precision medicine with multidisciplinary clinical care underscores the vital role of pharmacists in ensuring the safe, effective, and rational use of evolving breast cancer therapies, ultimately enhancing patient-centred outcomes.

In this rapidly advancing therapeutic landscape, the role of the pharmacist has become increasingly crucial. Pharmacists contribute not only to appropriate drug selection and dose optimization but also to the management of adverse effects, monitoring of drug interactions, and enhancement of patient adherence to complex treatment regimens. As breast cancer therapy continues to advance toward greater personalization and complexity, the pharmacist's expertise will remain essential in ensuring the safe, rational, and effective use of modern anticancer agents, ultimately supporting improved patient-centred care.

REFERENCES

1. Dent R A, et al. DESTINY-Breast09: Trastuzumab deruxtecan plus pertuzumab versus standard therapy in HER2-positive metastatic breast cancer. Journal of Clinical Oncology, 2025; 43: LBA1000.
2. Jhaveri K L, et al. Overall survival with Inavolisib in PIK3CA-mutated advanced breast cancer. New England Journal of Medicine, 2025; 393: 151–161.
3. Waks A G, Winer E P. Breast cancer treatment: Recent advances and future directions. JAMA, 2024; 321(3): 288–300.
4. Tolaney S M, et al. Sacituzumab govitecan plus pembrolizumab in advanced triple-negative breast cancer. Journal of Clinical Oncology, 2025; 43: LBA109.
5. Siegel R L, et al. Cancer statistics, 2024. CA: A Cancer Journal for Clinicians. 2024; 74(1): 12–49.
6. Cardoso F, et al. ESMO clinical practice guidelines for diagnosis, treatment, and follow-up of metastatic breast cancer. Annals of Oncology, 2025.
7. Slamon D J, et al. Ribociclib in early-stage HR-positive/HER2-negative breast cancer (NATALEE trial). Journal of Clinical Oncology, 2025; 43: 511.
8. Hanahan D. Hallmarks of cancer: New dimensions. Cancer Discovery, 2024; 12(1): 31–46.
9. World Health Organization. Breast cancer fact sheet. Global Cancer Observatory (GLOBOCAN), 2024.
10. National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology: Breast cancer. Version 1. 2025.