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(REVIEW ARTICLE)

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Regulatory requirements for the approval of anti-cancer drugs as per CDSCO in India comparison with Singapore

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Abstract

This study examines the regulatory requirements for anticancer medications in Singapore and India are compared in this abstract. It draws attention to the frameworks set up by Singapore's Health Sciences Authority (HSA) and India's Central Drugs Standard Control Organization (CDSCO). The procedures for clinical studies, approval schedules, and post-marketing surveillance are among the main distinctions. Singapore places a strong emphasis on strict safety and efficacy criteria, whereas India stresses a quicker clearance process to address pressing healthcare needs. The investigation highlights how various regulatory methods affect patient access, innovation, and medicine supply in both nations.

Recent decades have seen extraordinary improvements in the discovery of anticancer medications, transforming both cancer treatment and patient outcomes. With an emphasis on the main areas of anticancer therapeutics—chemotherapy, targeted therapy, immunotherapy, and hormone therapy—this study offers a thorough summary of the state of the field. We examine each drug class's methods of action, effectiveness, and difficulties while showcasing more recent developments like immune checkpoint inhibitors and CAR-T cell therapy. We also go over side effects, drug resistance, and how tailored medicine might improve the effectiveness of treatment. A look is also given to new developments in drug research, such as the application of nanotechnology and AI-driven drug discovery. The review attempts to shed light on the changing tactics used to fight cancer and the potential paths for anticancer medication development.

Keywords: Anticancer; Regulatory requirements; Singapore; CDSCO; Chemotherapy; Immunotherapy

1. Introduction

Cancer is characterized by rapid and uncontrolled formation of abnormal cells which may mass together to form a growth of tumor, or proliferate throughout the body, initiating abnormal growth at other sides.

Anticancer drugs are also known as antineoplastic operators, are utilized to treat cancer by coordinating and murdering cancer cells or restraining their development. Anticancer drugs are utilized to treat malignancies. Medicated treatment may be utilized alone or in combination with other medicines such as surgery or radiation therapy. Anticancer drugs murder the cancer cells by to begin with arrange energy implies concentration subordinate. Slaughtering is done by anti-cancer drugs for total remedy of cancer, all cancerous cells must be murdered as single cell able of creating cancer. There are several types of cancers, they are Bladder cancer, Breast cancer, Colorectal cancer, Kidney cancer, Lung cancer-non small cell, Lymphoma-Non-hodgkin, Melanoma, Oral and Oropharyngeal cancer, Pancreatic cancer, Prostate cancer, Thyroid cancer, Uterine cancer.

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Cancer treatment depends on the type and stages of Cancer, a type of treatment that uses drugs or other substances to treat cancer and most of the people receive combination of treatment some are "local" treatment like surgery, radiation therapy which are used to treat a specific tumar. Systemic treatment such as chemotherapy, immunotherapy, or targeted therapy etc because they affect the entire body.

Type of treatment for cancer are Surgery, Radiation therapy, Chemotherapy,Immunotherapy, Targeted therapy, Hormone therapy, Steam cell or Bone marrow transplant, Photodynamic therapy, Hyperthermia.

Cancer surgery is a procedure that removes cancer cell from the body and also helps to determine the stage of the cancer the type of surgery depend on the location of the cancer there are several types of surgery, they are Open surgery, Minimally invasive surgery, Keyhole surgery, Cryosurgery, Electro surgery, Laser surgery.

Radiation therapy uses high energy particles or radiation such as x - ray gamma rays electron beams or protons to destroy or kill cancer cell it is one of the most widely used cancer treatment.

Chemotherapy is a type of cancer treatment that uses drug to kill cancer cells or slow their growth, it is a systemic treatment, meaning it affects the entire body and is often used in combination with other treatment like surgery, radiation therapy or immunotherapy and chemotherapy is also called as “chemo”

2. Molecular basis of cancer

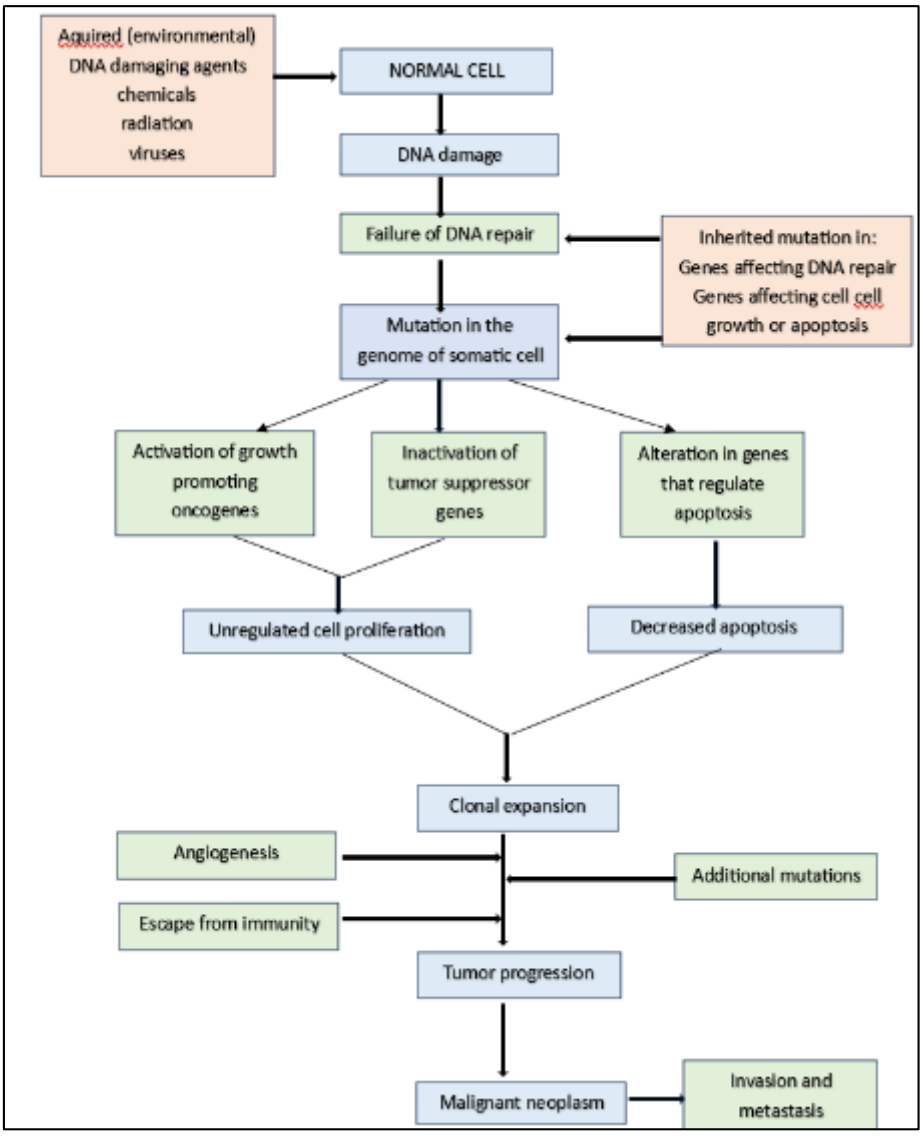

Figure 1 Molecular basis of cancer

3. Classification of anticancer drugs

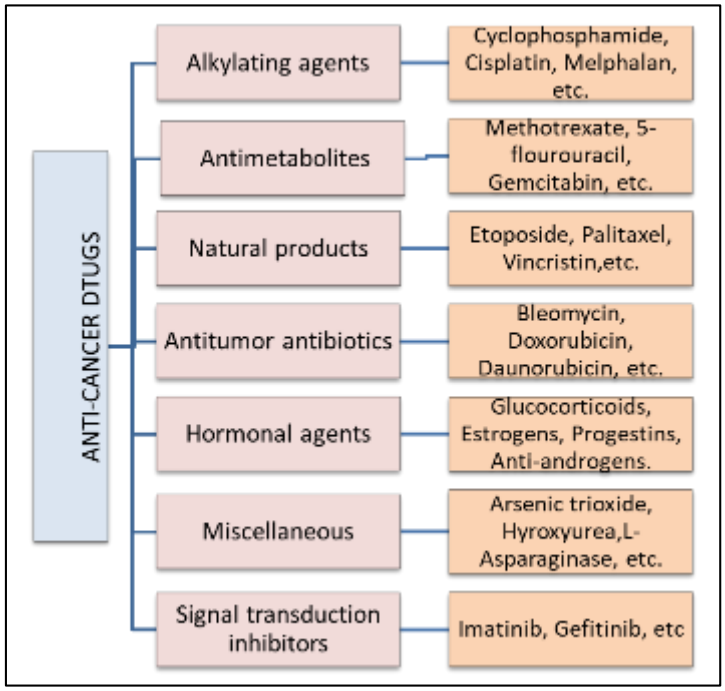

Figure 2 Classification of anti-cancer drugs

3.1. Alkylating agents

These agents that works by directly impairing or damaging the DNA of cancer cell by getting converting into azindinium ion bond with nitrogen atom at 7th position in the guanine of DNA. These agents are active against lymphomas, Hodgkin's disease breast cancer and multiple myeloma. Examples are Mechlorethamine, Cyclophosphamide, Chlorambucil, Thiotepa, Cisplatin.

3.2. Antimetabolites

These are a class of anticancer drug that interfere with DNA and RNA synthesis. They resemble the normal substrates of cellular metabolism and are incorporated into DNA or RNA, leading to disruption of cell division and growth.

3.3. Natural Products

Natural products have played a significant role in the development of Anti-cancer drugs , many of the currently used chemotherapeutic agents are derived from natural sources like plants, micro-organisms and marine organisms.

3.4. Antitumor antibiotics

Antitumor antibiotics are a class of anticancer drugs that interfere with DNA function and structure. Unlike traditional antibiotics that fight bacterial infections, these drugs are used specifically to treat cancer. They are derived from natural products produced by soil microorganisms, primarily from the genus Streptomyces. Their main mechanism of action involves damaging DNA and inhibiting essential cellular processes like replication and transcription, leading to cell de. Examples are: Anthracyclines, Bleomycine, Doxorubicin, Daunorubicin.

3.5. Hormonal Agents

Hormonal agents are class of anticancer drugs that target cancers that are sensitive to hormones. These agents are most commonly used in hormone-dependent cancers like breast cancer and prostate cancer. The main principle behind hormonal therapies is either to reduce the levels of certain hormones or block their effects on cancer cells.

3.6. Miscellaneous

Examples are Hydroxyurea, L-Asparginase, Arsenic trioxide.

Mechanism of action: Hydroxyurea interferes with conversion of RBC to DNA by Inhibiting ribonucleoside diphosphate reductase, this results in inhibition of DNA synthesis.

Asparaginase breaks down asparagine, an amino acid that certain cancer cells cannot synthesize themselves and depend on external sources for. By depleting asparagine, it starves these cells, leading to their death.

3.7. Signal transduction inhibitors

Signal transduction inhibitors are a class of anticancer drugs that interfere with the pathways that control the growth, survival, and proliferation of cancer cells. Cancer cells often have dysregulated signaling pathways that lead to uncontrolled cell growth. Signal transduction inhibitors target specific molecules within these pathways to disrupt cancer cell function. These are also called Tyrosine Kinase Inhibitors (TKIs).

Mechanism of Action: Tyrosine kinases are enzymes that play a crucial role in activating various signaling pathways involved in cell division and survival. TKIs block the activity of these enzymes, specifically targeting cancer cells. For example, imatinib inhibits the BCR-ABL tyrosine kinase, which is responsible for the abnormal proliferation of leukemic cells in chronic myeloid leukemia (CML). Other TKIs target growth factor receptors like EGFR (epidermal growth factor receptor), leading to reduced signaling and tumor growth Examples are: Imatinib, Gefitinib.

4. Background

Regulatory approval of oncology drugs is the cornerstone of the development process and approval characteristics shape eventual utilization. Approval trends and characteristics provide valuable information for drug developers and regulators and ultimately affect clinicians and patients.

Objectives

- Explain the role of chemotherapy in the management of patients with cancer
- Expalin the concept of “cell kill” in cancer patients
- Expalin the term “cell cycle specificity” and classify anti-cancer drugs based on their cell specificity
- Descibe the principles and advantages of combination therapy
- Expalin the mechanism of resistance to anti-cancer drugs.

4.1. Central drug standard control organization:

The Central Drugs Standard Control Organization (CDSCO) is India's national regulatory authority for drugs and medical devices. It operates under the Ministry of Health and Family Welfare government of India. CDSCO’s primary responsibility is to ensure the safety, efficacy, and quality of drugs, medical devices, diagnostics available in the Indian market.

The Drugs Controller General of India (DCGI), who is an official of the CDSCO, is the final authority for approving clinical trials in India. The DCGI is advised by the Drug Technical Advisory Board (DTAB) and the Drug Consultative Committee (DCC).

The Central Drugs Standard Control Organization (CDSCO) is the Central Drug Authority for discharging functions assigned to the Central Government under the Drugs and Cosmetics Act. CDSCO has six zonal offices, four sub-zonal offices, 13 port offices and seven laboratories under its control.

4.2. Goals of CDSCO:

- Ensuring Public Health Safety
- Regulatory Compliance
- Facilitating Access to Medicines
- Promoting Ethical Clinical Research
- Capacity Building and Training
- International Collaboration.

5. Organization of CDSCO

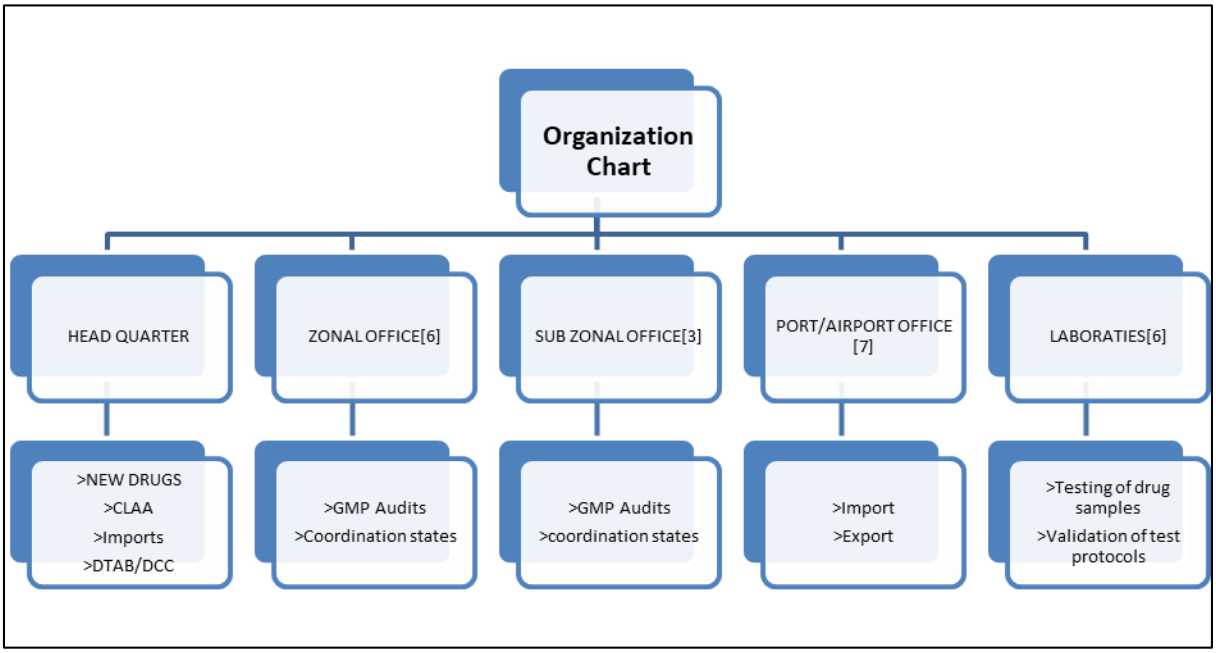

Figure 3 Organization of CDSCO

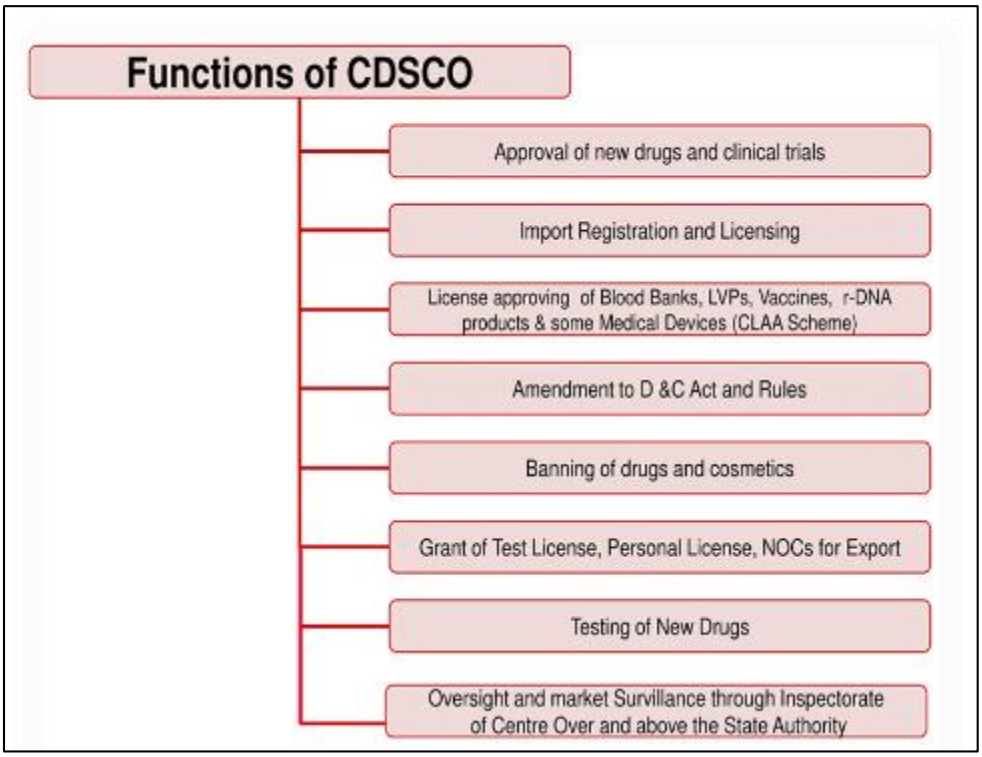

Figure 4 Functions of CDSCO

6. Approval Process for Anti-cancer Drugs in India

The approval process for anticancer drugs in India is overseen by the Central Drugs Standard Control Organization (CDSCO) under the Directorate General of Health Services, Ministry of Health & Family Welfare. The Drug Controller General of India (DCGI) is the authority responsible for approving drugs for manufacture, import, and sale. Below is the step-by-step process for the approval of anticancer drugs:

6.1. Preclinical Studies

Objective: To evaluate the safety, pharmacokinetics, and pharmacodynamics of the drug in animal models before human testing.

These studies are essential to provide basic data on the drug's toxicity and potential efficacy.

6.2. Clinical Trial Application

Before conducting clinical trials, the manufacturer or sponsor must submit a Clinical Trial Application (CTA) to the CDSCO.

The application includes data from preclinical studies, the proposed protocol for the clinical trials, information on investigators, and the study sites.

6.3. Clinical Trials

In India, clinical trials are carried out in four stages:

- Phase I: Tests the drug's safety, dosage range, and side effects in a small group of healthy volunteers or patients.
- Phase II: Focuses on the drug's effectiveness and further evaluates its safety in patients with the specific type of cancer.
- Phase III: Larger studies involving patients across multiple centers to confirm efficacy, monitor side effects, and compare the new drug to the current standard treatments.
- Phase IV: Post-marketing studies after the drug is approved and available to monitor long-term effects and any rare side effects.

CDSCO grants approval to move from one phase to the next based on the data submitted at each stage.

6.4. New Drug Application (NDA):

After successful clinical trials, the sponsor must submit a New Drug Application (NDA) to the CDSCO. The NDA contains:

- Results from preclinical and clinical studies.
- Proposed labeling information.
- Details of manufacturing processes and controls.
- Data on the drug's safety and efficacy in the context of the proposed cancer treatment.

6.5. Review and Approval by CDSCO

The DCGI reviews the NDA and may seek recommendations from expert committees like the New Drug Advisory Committee (NDAC) or the Oncology/Hematology Expert Committee.

The review process involves a thorough examination of the data on the drug's safety, efficacy, and quality.

If the DCGI finds the data satisfactory, it grants approval for the drug to be marketed in India.

6.6. Post-Approval Monitoring

Even after approval, the drug is subject to post-marketing surveillance (PMS) to track any long-term or rare side effects.

Manufacturers must submit periodic safety update reports (PSUR) to the CDSCO to monitor the drug's ongoing safety profile.

6.7. Regulatory requirements for Manufacture of Anti-cancer drugs in India

6.7.1. Step 1: Licensing:

- Obtain manufacturing license from State Licensing Authority (SLA)
- Obey with Good Manufacturing Practice (GMP) guidelines

6.7.2. Step 2: Drug Development:

- Conduct preclinical trials
- Submit Investigational New Drug (IND) application to CDSCO
- Conduct clinical trials (Phase I-III)

6.7.3. Step 3: New Drug Approval:

- Submit New Drug Application (NDA) to CDSCO
- Provide clinical trial data and regulatory documents
- Obtain New Drug Approval (NDA) certificate

6.7.4. Step 4: Manufacturing:

- Establish GMP-compliant manufacturing facility
- Obtain WHO-GMP or ISO 9001 certification
- Manufacture anticancer drugs

6.7.5. Step 5: Quality Control:

- Conduct quality control testing
- Ensure stability and bioequivalence
- Maintain batch records and documentation

6.7.6. Step 6: Labeling and Packaging:

- Comply with labeling and packaging regulations
- Ensure proper storage and distribution

6.7.7. Step 7: Post-Marketing Surveillance:

- Conduct pharmacovigilance and adverse event reporting
- Monitor drug safety and efficacy.

6.8. Comparison of the regulatory requirements for anti-cancer drugs in India [CDSCO] and singapore [HSA]

Figure 5 Comparison of the regulatory requirements for Anti-cancer drugs in India and Singapore

Table 1 Comparison of the regulatory requirements for Anti-cancer drugs in India and Singapore

SL NO	Aspect	India	Singapore
01	Regulatory Authority	Central Drugs Standard Control Organization (CDSCO) under the Ministry of Health and Family Welfare. Drug Controller General of India (DCGI) oversees approval. State Drug Regulatory Authorities manage local regulations.	Health Sciences Authority (HSA) under the Ministry of Health The Therapeutic Products Branch (TPB) is responsible for drug registration.
02	Legislative Framework	Drugs and Cosmetics Act, 1945 and Drugs and Cosmetics Rules, 1945 govern drug approvals. New Drugs and Clinical Trials Rules, 2019 specifically addresses clinical trials and new drug approvals	Health Products Act, 2007 governs all health products including anticancer drugs Medicines Act, 1975 also applies to certain pharmaceuticals product
03	Drug Approval Process	Manufacturer must obtain New Drug Approval from DCGI for anticancer drugs not marketed in India. Clinical trials need approval through CDSCO and Ethics Committees. Drugs undergo Bioavailability/Bioequivalence studies and are subjected to rigorous reviews.	Requires submission of a New Drug Application (NDA) to the HSA Singapore uses a risk-based evaluation framework where new drugs are categorized based on risk levels. Evaluation routes: Full, Abridged, Verification, and Immediate, depending on the drug's approval status in major jurisdiction.
04	Clinical Trials	Governed by the New Drugs and Clinical Trials Rules, 2019 Ethical clearance required, and trials results need submission to CDSCO for approval	Clinical trials must follow the Clinical Trials Regulations under HSA Requires approval from an Institutional Review Board (IRB) Follows ICH-GCP (Good Clinical Practices) guidelines
05	Import Regulations	Requires an Import License from CDSCO Drugs must be registered with CDSCO before import, under the Form 10 or Form 11 based on clinical trial or commercial use.	Requires an Import Licences from HSA Product Registration is necessary before import, and HSA also mandates the submission of import documents.
06	Manufacturing Regulations	Requires Manufacturing Licences under Drugs and Cosmetics Act -Good Manufacturing Practices (GMP) as per Schedule M are mandatory for pharmaceutical companies	Requires Manufacturing Licences under the Health Products Act. Follows Good Manufacturing Practices (GMP) guidelines under

			pharmaceutical inspection co-operation Scheme (PIC/S) standards.
07	Post-Marketing Surveillance	CDSCO manages pharmacovigilance Programme of India (PvPI) to monitor drug safety. Adverse drug reaction (ADR) must be reported.	HSA monitors post-market drug safety through the Pharmacovigilance System. ADR Reporting is mandatory and actively monitored by the authority.
08	Pricing Regulations	National Pharmaceutical Pricing Authority (NPPA) regulates the pricing of essential drugs, including some anticancer drugs	No direct price control for anticancer drugs, but HSA ensures affordable access and may regulate based on public health interests
09	Marketing Authorization	Marketing Authorization (MA) requires approval from DCGI Local manufacturers and importers must file a dossier for registration and approval.	Marketing Authorization (MA) Is given by HSA. HSA may grant Provisional Approval for novel therapies, especially for unmet medical needs.
10	Generics Drug	India has a robust generic drug industry Anticancer drugs can be generics, and a bioequivalence study may be required.	Generics must undergo registration with HSA Bioequivalence or biowaiver studies are required for generics.
11	Timeline for Drug Approval	Regular approval process may take 12-18 months Accelerated approval available for critical drugs.	Approval timelines vary, but expedited processes exists for certain conditions. Fast-track approval for unmet medical needs.
12	Intellectual Property (IP) Laws	India follows TRIPS Agreement but has provisions for Compulsory Licencing for Lifesaving drugs, including anticancer drugs.	Singapore follows TRIPS Agreement and has strong IP protection. Compulsory licencing is rare but available under specific conditions.
13	Distribution and Sale	Wholesale and retail licences are required under the Drugs and Cosmetics Act. Anticancer drugs may have restrictions on where they can be sold (eg. Specialized pharmacies)	Distribution and sale are regulated under the Health Products Act and Medicines Act. Certain anticancer drugs may only be sold in specific healthcare settings or with special restrictions.

7. Conclusion

The regulatory requirements for anticancer drugs in India and Singapore reveal significant differences that impact drug approval timelines, safety protocols, and market accessibility. India's regulatory framework, while evolving, often faces challenges related to resource constraints and infrastructure, which can lead to longer approval processes. In contrast, Singapore benefits from a more streamlined and efficient regulatory environment, characterized by rigorous scientific assessments and expedited pathways for innovative therapies.

These differences highlight the need for India to enhance its regulatory processes to improve efficiency and ensure patient safety, while also fostering an environment conducive to pharmaceutical innovation. Collaborative efforts and knowledge sharing between the two countries could help bridge these gaps, ultimately improving access to effective anticancer treatments for patients in India.

Compliance with ethical standards

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Disclosure of conflict of interest

No conflict of interest to be disclosed.

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