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A Comparative Regulatory Study on the Approval Requirements of Ripasudil Ophthalmic Solution for the Treatment of Glaucoma in Japan and India

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Abstract: *Glaucoma is a major cause of blindness worldwide with uncontrolled intraocular pressure (IOP) primary risk factor. Ripasudil is a novel Rho-kinase inhibitors offers an alternative therapeutic option by lowering IOP through different mechanism compared to conventional other anti-glaucoma medicines (AGMs). Every country has its own rules and regulations for approval requirements of drugs. Regulatory framework plays an important role for approval requirement and safety, efficacy and quality of such innovation before they reach market. This study compares the approval requirements process for ripasudil ophthalmic solution in Japan and India. Information was collected from official source of regulatory authority, including pharmaceutical and medical device agency (PMDA) in Japan and central drug and standard control organization in India, as well as published article, literature and guidelines. This comparative study focusses on application procedures, pre-clinical and clinical trial requirements, dossier submission formats, review timelines, and post-marketing surveillance.*

Keywords: Glaucoma, Ripasudil, ophthalmic solution, Japan, India, Regulatory affairs, Drug approval

I. INTRODUCTION

Glaucoma is a chronic, progressive eye disease that damage optical nerve which is carrying the visual information from the eye and sending to the brain. Optic nerve damage is mostly responsible by increased intraocular pressure (IOP). Sometimes glaucoma also occurs with the normal eye tension. Worldwide, glaucoma is affecting millions of people and most common leading cause of blindness. Glaucoma is more common in the age above 40 years but also affects in younger adults.

There is main two type of glaucoma:

1) Open angle glaucoma

The most common form, painless and slowly progression.

2) Close angle glaucoma:

Less common and more severe, suddenly raise in IOP with redness, blurred vision and pain.[1]

The main goal of glaucoma therapy is to reduce and control intraocular pressure (IOP), And slowing optical nerve damage and preserving vision of patients. Aqueous humours outflow playing major role in the glaucoma. There are two types of pathways for outflow of aqueous humours one is trabecular meshwork and second is uveoscleral pathways. Main pathway is trabecular meshwork which is responsible for 80% of total outflow. Uveoscleral pathway responsible for only 20% of outflow of aqueous humours. Ripasudil is called Rho-kinase inhibitors and novel drug in the treatment of glaucoma. Mechanism of ripasudil is work by inhibiting Rho-kinase enzyme that involved in regulating smooth muscle contraction and cellular adhesion in the trabecular meshwork. Ripasudil is work directly on the trabecular meshwork which is responsible for the 80% of total aqueous humours outflow while other anti-glaucoma medicines (AGMs) like Beta-blockers, Alpha-adrenergic agonists, Prostaglandin analogues (PGA), Carbonic anhydrase inhibitors (CAI) are work on the uveoscleral pathway were only 20% of aqueous humours outflow occurs.[2][3][9]

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Regulatory framework for the approval requirement is a crucial for the safety, efficacy, and quality before its market launch. Approval requirements process is varied significantly to country by country. In Japan, pharmaceutical and medical devices agency (PMDA) has been approving the new ophthalmic drug and in India, it's regulated by the central drugs standard control organizers (CDSCO).

This title is help to provide a comparative regulatory study of the approval requirements for ripasudil ophthalmic solution in Japan and India. By analyses the similarities and differences in the regulatory pathways. The aim of this study is to highlight challenges, opportunity and impact on patients in glaucoma treatments.

II. DISCUSSION

Aim

To study how Ripasudil eye drops are approved in Japan and India and to see what is similar, different, and challenging in getting regulatory approval for glaucoma treatment.

2.1 Objectives

1. To analyze and compare the regulatory approval requirements of ripasudil ophthalmic solution in Japan and India.
2. To understand the regulatory framework pathways in Japan (PMDA/MHLW).
3. To understand the regulatory framework pathways in India (CDSCO/DCGI).
4. To conduct comparative analysis between Japan and India.
5. To identify the impact of regulatory similarities and differences.

2.2 Methodology

A descriptive, comparative methods regulatory analysis based on documentary review. This study will compare the regulatory approval process in country Japan and India.

2.2.1 Data source

Data collected from the official website of pharmaceutical and medical devices agency (PMDA/MHLW) Japan and central drugs standard control organizers (CDSCO/DCGI) India.

2.2.2 Scientific literature review

Article searched on using different keywords like ripasudil, glaucoma, PMDA/MHLW, CDSCO/DCGI, standard of ophthalmic solution approval process.

2.2.3 Search strategy

Online search on official regulatory agency websites (PMDA, CDSCO), PubMed, google scholar, ResearchGate etc related to ripasudil ophthalmic solution and glaucoma.

III. DRUG PROFILE

- Name of drug: Ripasudil
- IUPAC name: 4-Fluoro-5-{[(2S)-2-methyl-1,4-diazepan-1yl]sulfonyl}isoquinoline
- Molecular formula: C15H18FN3O2S
- Molar mass: 323.39 g•mol−1
- Class of drug: Rho-associated coiled-coil containing protein kinase (ROCK) inhibitor
- Route of administration: Topical (ophthalmic solution)
- Trade name: Glanatec [4]

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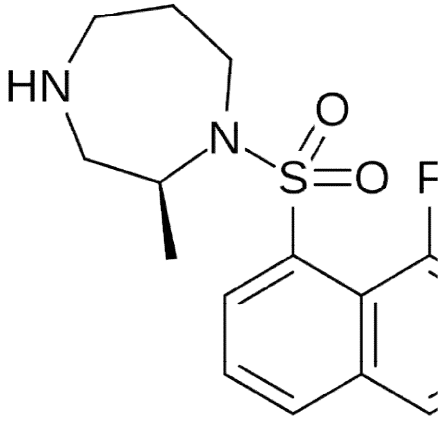

[Figure 1; structure of ripasudil]

IV. CLINICAL DATA OVERVIEW

In phase 1 clinical trial were conducted in healthy volunteer to evaluate safety, tolerability and pharmacokinetics of the ripasudil. These studies were designed Randomized, placebo controlled, double-masked, group comparison phase1 clinical trials involving both single ascending and multiple-dose administrations. Different concentration of ripasudil ophthalmic solution from ranging 0.01% to 0.8% were instilled in either once or multiple times in one or both eyes. 100 healthy volunteers were involved in phase 1 clinical trial. Results showed ripasudil ophthalmic solution was generally well tolerated with the most common adverse effect being transient conjunctival hyperemia which is resolved without intervention. Additionally, rapid onset of intraocular pressure (IOP) lowering effect was observed after instillation, indicating promoting therapeutic potential.[5]

Phase II clinical were conducted to evaluate further safety, efficacy and dose optimization of ripasudil ophthalmic solution in patients diagnosed with primary open angle glaucoma (POAG) and ocular hypertension (OHT). These trials were Multicenter, prospective, randomized, placebo controlled, double-masked, parallel group comparison clinical study. 210 patients were involved across multiple centers in Japan. Study compared different concentration of ripasudil ophthalmic solution, with 0.4% administrated twice daily emerging as an optimal dose. Over a period of 8 weeks to 3 months, patients treated with Ripasudil experienced a clear and meaningful drop in their eye pressure. Remarkably, this effect began within just an hour after applying the drops and continued steadily throughout the study. The safety profile was measurable with adverse effects generally limited to mild and transient ocular reactions such as conjunctival hyperemia.[6]

Phase III clinical trials aimed to confirm safety and efficacy of ripasudil ophthalmic solutions in a larger patient of populations and to collect data for regulatory approval in major different regulatory agency. These studies were carried out at multiple medical centers and involved patients with glaucoma or ocular hypertension whose eye pressure wasn't well managed with their current treatments. Around 400 patients took part in the study, where Ripasudil 0.4% eye drops, given twice a day, were compared with timolol and a placebo for 8 weeks. Some participants continued for up to a year so researchers could closely monitor its long-term safety. The results showed that Ripasudil significantly lowered average eye pressure throughout the day compared to the placebo and worked just as well as timolol. When combined with prostaglandin eye drops, it provided an extra pressure-lowering benefit, making it a strong addition to existing glaucoma treatments. The most common side effect was temporary redness of the eyes, which was generally mild and went away on its own. Importantly, no serious side effects affecting the rest of the body were reported during the trials.

Following the positive results from these trials, Japan's Pharmaceuticals and Medical Devices Agency (PMDA) approved Ripasudil 0.4% eye drops in September 2014 for treating glaucoma and ocular hypertension. This approval

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was a big step forward, as Ripasudil became the first Rho kinase inhibitor available for eye treatment, bringing a fresh and innovative approach to managing glaucoma.[7]

V. REGULATORY FRAMEWORK IN JAPAN

The Pharmaceuticals and Medical Devices Agency (PMDA) is the regulatory body in Japan responsible for reviewing applications for the drug approvals, foreign manufacturer accreditation (FMA), Drug Master File (DMF) registration, and other related submissions including ophthalmic solutions. The Pharmaceuticals and Medical Devices Agency (PMDA) operate under the Ministry of Health, Labour and Welfare (MHLW).

To get a approval of ripasudil ophthalmic solution in Japan, companies submit a New Drug Application (NDA) in the Common Technical Document (CTD) or electronic Common Technical Document (eCTD) format. CTD/eCTD contain detailed information about the drug which need to regulatory agency.[8]

It's divided into five sections:

I. Module 1: Administrative Information and Prescribing Information.
II. Module 2: Summaries.
III. Module 3: Quality.
IV. Module 4: Nonclinical study reports.
V. Module 5: Clinical study reports.

Contents of Dossier for Drug Approval in Japan as per PMDA:

Module 1: Administrative Information and Prescribing Information

1.1 Application Forms & Administrative Data
1.2 Product Information
1.3 CMC Attachments
1.4 Clinical & Non-Clinical Information
1.5 Electronic Submission Information
1.6 Other regional requirements

Module 2: Summarie

2.1 CTD Table of content
2.2 Introduction
2.3 Quality overall summary
2.4 Nonclinical Overview
2.5 Clinical Overview
2.6 Nonclinical Written and Tabulated Summaries
2.7 Clinical summary

Module 3: Quality

3.1 Table of content
3.2 Body of Data
3.2.S Drug Substance
3.2.P Drug Product
3.2.A Appendices
3.2.R Regional Information
3.3 Literature References

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Module 4: Nonclinical study reports

4.1 Table of content
4.2 Study reports
4.2.1 Pharmacology
4.2.2 Pharmacokinetics
4.2.3 Toxicology
4.3 Literature References

Module 5: Clinical study reports

5.1 Table of Contents
5.2 Tabular Listing of all Clinical Studies
5.3 Clinical Study Reports
5.3.1 Reports of Biopharmaceutic Studies
5.3.2 Reports of Studies Pertinent to Pharmacokinetics using Human Biomaterials
5.3.3 Reports of Human Pharmacokinetic (PK) Studies
5.3.4 Reports of Human Pharmacodynamic (PD) Studies
5.3.5 Reports of Efficacy and Safety Studies
5.3.6 Reports of Post-marketing Experience
5.3.7 Case Report Forms and Individual Patient Listings
5.4 Literature References [10]

The application needs to show clear and thorough evidence that the drug is safe, effective, and of high quality, following Japan's regulations. This includes meeting standards from the Japanese Pharmacopoeia for things like sterility, formulation, and container compatibility. For eye drops and other ophthalmic solutions, there's extra focus on how gentle and safe the drug is for the eyes, the safety of preservatives used, and how well the product holds up under Japanese climate conditions. Clinical trials for these drugs often compare them with existing standard treatments to clearly demonstrate that they work as intended.

To make the approval process smoother, the PMDA offers face-to-face consultation services at important stages of drug development. While these consultations are paid, they are highly recommended because they help companies stay on track with regulatory requirements and avoid delays.

There are four stages of the consultation process:

1) before Investigational New Drug Application (INDA)
2) phase II research conclusion
3) before New Drug Application (NDA)
4) for individual study protocols [11]

Ophthalmic solutions are treated as a sterile pharmaceutical product and regulated through PMDA for review and, MHLW for final marketing authorization. If drug is not approved in Japan than applicant need to submit full New Drug Application (NDA) and if drug is approved or generic than applicant need to submit Generic application using BE or clinical endpoint studies per PMDA guidance.

5.1 Steps of approval requirement process in Japan

1. Pre-clinical study
2. Clinical Trial Notification (CTN) submission before human studies
3. Clinical trial phase I to phase III
4. NDA submission to PMDA
5. PMDA scientific review
6. MHLW final approval
7. Post marketing surveillance [17]

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5.2 Timelines for approval requirements in Japan

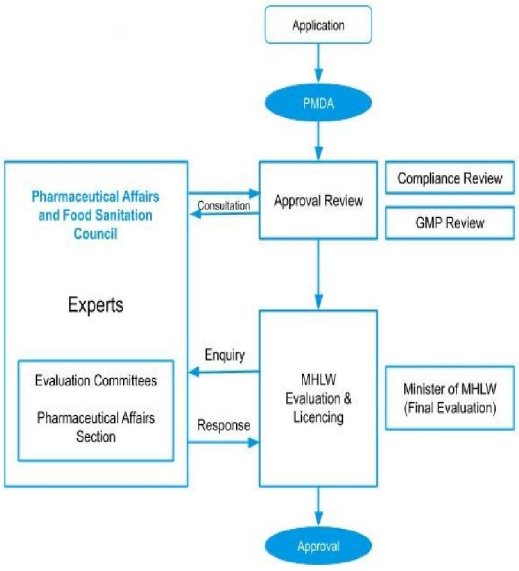
The approval process for an ophthalmic solution in Japan typically begins with an initial consultation with the PMDA, which usually takes around half to slightly more than half a month. This is followed by the expert review, where regulatory specialists carefully examine the submitted data, including clinical trial results and quality information; this stage generally lasts between 5 to 7 months. After the expert review, a compliance review is conducted to ensure that all regulatory requirements and guidelines have been properly met, taking approximately 1 to 2 months. A Good Manufacturing Practice (GMP) inspection may be carried out at the manufacturing site to verify adherence to quality standards, which usually take around 3 weeks to one and a half months. Finally, the application undergoes evaluation by the Pharmaceutical Affairs and Food Safety Committee (PAFSC), a process that typically requires half a month or slightly more. Altogether, the entire approval process in Japan generally ranges from 9 to 12 months, depending on the complexity of the submission and the need for additional clarifications.[12]

5.3 Labeling requirements for Japan

In Japan, Pharmaceuticals and Medical Devices Agency (PMDA) mandates specific labeling requirements, primarily outlined in the Pharmaceuticals and Medical Devices (PMD) Act. Japan has transitioned to a mandatory electronic labeling (e-labeling) system for package inserts, though physical containers still require specific information. package insert (PI) carries legal weight. This means the information provided isn't just guidance—it is legally binding for manufacturers, healthcare providers, and pharmacists. The PI must comprehensively cover the following details:

1) Full Drug Composition
2) Pharmacological Properties
3) Indications
4) Dosage and Administration
5) Adverse Reactions and Precautions
6) Storage Instructions
7) MAH (Marketing Authorization Holder) Information [13]

The Marketing Authorization Holder (MAH) is responsible for affixing the correct labeling and ensuring all information is accurate and up-to-date. Foreign manufacturers must work with a Japanese MAH to meet these strict requirements.



[Figure 2; Drug approval process in Japan]

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VI. REGULATORY FRAMEWORK IN INDIA:

The Drug and Cosmetic 1940 and Rules 1945 were passed by the Indian parliaments to regulates the manufacturing, imports, distribution and sale of the drugs and cosmetics. These rules provide detailed procedures, standards, and requirements to ensure safety, efficacy, and quality of pharmaceutical products and also focus on aspects like drug approvals, labelling, licensing, clinical trial requirements, and penalties for violations. The central drugs standard control organization (CDSCO) and Drugs Controller General of India (DCGI) was established. In 1988, schedule Y is added in the drugs and cosmetics rules 1945 was added by the governments of India. schedule Y is specially deals with the requirements and guidelines for clinical trials and approval of new drugs in India. schedule Y was revised in 2005 to make Indian regulation more like with international standard such as International Council for Harmonization (ICH), Good Clinical Practice (GCP) and WHO guidelines. This change includes, establishing definitions for phase I–IV trials and clear responsibilities for investigators and sponsors. [15]

If any sponsor(country) in India wants to imports or develop a new drug, it must file form 44 and apply for permission from the Drugs Controller General of India (DCGI) issued in schedule Y drugs and cosmetics act 1940 and rules 1945. This application is usually prepared in the Common Technical Document (CTD) or electronic Common Technical Document (eCTD) format, which organizes all the information regulators need in a clear and structured way. Clinical trial has to be performed in accordance to schedule Y. To conduct clinical trials in India, an application must be submitted to the DCGI along with all relevant data on the drug's chemistry, manufacturing, quality control, and animal studies. The submission should also include the trial protocol, investigator's brochure, and informed consent documents. A copy of this application must be shared with the Ethics Committee, and the clinical trials can only begin after receiving approval from both the DCGI and the Ethics Committee. These trials are designed to evaluate important aspects such as the maximum tolerated dose in humans, potential side effects, and overall safety profile. Applicants are also required to submit comprehensive details on the drug's regulatory approval and market presence outside India, along with safety and efficacy information. [15]

As per the law 122A of drugs and cosmetics act 1940 and rules 1945, clinical trial may be waived if new drug are approved and being used for several year in other country. The sponsor needs to provide detailed information to the DCGI for an investigational new drug about:

1. Generic name
2. Patent status
3. Brief description of physico-chemical/biological
4. Technical information

A. Stability
B. Specifications
C. Manufacturing process
D. Worldwide regulatory status
E. Animal pharmacology and toxicity studies

5. Published clinical trial reports
6. Proposed protocol and format
7. Trial duration
8. During master file
9. Undertaking to Report Serious or Life-threatening Adverse Drug Reactions.

The requirement to conduct clinical trials in India mostly depends on the drugs approval status in other countries. If the drug is already approved in other country, generally only Phase III trials need to be conducted in India. Phase I trials are generally not required unless relevant data from other countries is available. However, the DCGI may allow Phase I trials in India if the drug addresses a significant health concern specific to the Indian population, such as malaria or tuberculosis.

Bioavailability and bioequivalence (BABE) studies must be conducted as per the official BABE guidelines. In addition to safety and efficacy data, detailed information about the drugs marketing status in other countries is also required. The submission should include details on prescriptions, sample handling, testing protocols, product monographs, and

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labelling. Mostly it takes around three months to get clinical trial approval in India. Once approved, the clinical trials can be registered in the Clinical Trials Registry–India (CTRI), providing complete information about the trial design and the subjects involved.

The rules to be followed under The Drugs and Cosmetics Rules 1945 are:

1. Rule 122-A: Application for Permission to Import a New Drug
2. Rule 122-B: Application for Permission to Manufacture a New Drug
3. Rule 122-D: Permission to Import or Manufacture Fixed-Dose Combinations (FDCs)
4. Rule 122-DA: Application for Permission to Conduct Clinical Trials
5. Rule 122-DAB: Compensation in Case of Injury or Death During Clinical Trials [8,11]

CTD format as per CDSCO:

1. Module 1: India specific General information
2. Module 2: CTD Summary
3. Module 3: Quality
4. Module 4: Non-clinical study data
5. Module 5: Clinical study data

Contents of Dossier for Drug Approval in India as per CDSCO:

Module 1: India specific General information

1.1 Covering Letter & Comprehensive Table of Contents
1.2 Administrative Information
1.3 General Information on Drug Product
1.4 Summary of Testing Protocol(s) for Quality Control Testing together with a complete impurity profile and release specifications for the product should be submitted.
1.5 Regulatory Status in other countries
1.6 Domestic Price of the Drug followed in the Countries of Origin in INR.
1.7 Manufacturer's Research Activity Profile
1.8 Manufacturer's Business Activity Profile
1.9 Information regarding involvement of Experts
1.10 Samples of Drug Product
1.11 Promotional Materials

Module 2: CTD Summary

2.1 Table of Contents of Module 2
2.2 Introduction
2.3 Quality Overall Summary (QOS)
2.3.P Summary of Drug Product
2.3.A Appendices
2.4 Non-Clinical Overview
2.5 Clinical Overview
2.6 Non-Clinical Written and Tabulated Summaries
2.7 Clinical Summary

Module 3: Quality

3.1 Table of Contents of Module 3
3.2 Body of Data
3.2.S Drug Substance(s)
3.2.P Drug Product (Name, Dosage Form)
3.2.A Appendices
3.3 Literature References

Module 4: Non-clinical study data

4.1 Table of Contents of Module 4

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4.2 Study Reports
4.2.1 Pharmacology
4.2.2 Pharmacokinetics
4.2.3 Toxicology
4.3 Literature References
Module 5: Clinical study data
5.1 Table of Contents of Module 5
5.2 Tabular Listing of All Clinical Studies
5.3 Clinical Study Reports
5.3.1 Reports of Biopharmaceutical Studies
5.3.2 2 Reports of Studies Pertinent to Pharmacokinetics Using Human Biomaterials
5.3.3 Reports of Human Pharmacokinetic (PK) Studies
5.3.4 Reports of Human Pharmacodynamic (PD) Studies
5.3.5 Reports of Efficacy and Safety Studies
5.3.6 Reports of Post-Marketing Experience
5.3.7 Case Report Forms and Individual Patient Listings
5.4 Literature References

6.1 Steps of approval requirement process in India

1. Preclinical study
2. CTA for clinical trial
3. Clinical trial phase I to Phase III
4. NDA submission to CDSCO
5. CDSCO review application
6. Marketing Authorization Approval (MAA)
7. Post marketing surveillance [15]

6.2 Timelines for approval requirements in India

The approval process for an ophthalmic solution in India begins with the application submission, which usually takes about 1 to 2 weeks. Once submitted, the application undergoes screening and acknowledgment, a step that generally requires 2 to 4 weeks to ensure all required documents and forms are in order. After this, the application moves to the technical evaluation stage, where the regulatory authorities carefully review the scientific data, manufacturing details, and quality specifications; this step can take anywhere from 3 to 6 months. Following the technical review, the Expert Committee, also known as the Subject Expert Committee (SEC), examines the application and provides recommendations, a process that typically lasts 1 to 2 months. Once the SEC gives its approval, the final stage is approval and licensing, which may take an additional 1 to 2 months for the issuance of the marketing authorization. Overall, the entire process usually spans 6 to 12 months, depending on the complexity of the application and the completeness of the submitted data. [13]

6.3 Labeling requirements for India

The Drugs and Cosmetics Rules, 1945, framed under the Drugs and Cosmetics Act, 1940, lay down the detailed regulatory framework for the manufacture, import, sale, distribution, labeling, and packaging of pharmaceutical products in India. Among these rules, Rule 96 plays a central role as it specifies the essential information that must appear on the labels of all drugs, ensuring clarity, safety, and accountability. This rule governs labeling on both the immediate container and the outer carton, requiring details such as the drug's proper (generic) name, brand name, active ingredients, batch number, manufacturing and expiry dates, manufacturer's license number, and storage conditions. It also mandates the inclusion of cautionary statements, pharmacopeial standards where applicable, and specific warnings for scheduled drugs. By setting these clear standards, Rule 96 helps ensure that healthcare professionals and patients

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have access to accurate and consistent information, supporting the safe and effective use of medicines across the country.

Rule 96 "Manner of labelling" contain:

1) Name of drug
2) Net content
3) Batch number
4) Active ingredients
5) Manufacturing license number
6) Manufacturing and expiry dates
7) Name and address of manufacturer
8) Storage condition
9) Label language – English is mandatory

For ophthalmic preparations such as Ripasudil eye drops, the provisions of Rule 96 apply in their entirety, ensuring that all essential labeling information is clearly presented. In addition to these general requirements, Schedule F II lays down extra rules that focus specifically on the unique needs of eye products, such as maintaining sterility, declaring preservatives, and including important usage instructions. For example, labels must clearly state "For ophthalmic use only," specify the storage conditions, and mention when the product should be discarded after opening. These added details are crucial because eye preparations require a higher level of safety and precision to prevent contamination and ensure patient well-being.

Typical label includes:

• Proper name + IP/BP if applicable
• Brand name (with generic name equally prominent)
• "Ophthalmic Solution" clearly stated
• Active ingredients per mL
• Preservatives & concentration
• Storage (e.g., "Store between 2–8 °C")
• Batch no., Mfg./Exp. date, License no.
• "For ophthalmic use only"
• "Not for injection", "Discard after 4 weeks of opening"
• Manufacturer name & address
• Schedule warning (e.g., Schedule H: "Rx — To be sold by retail on the prescription of a Registered Medical Practitioner only.") [14]

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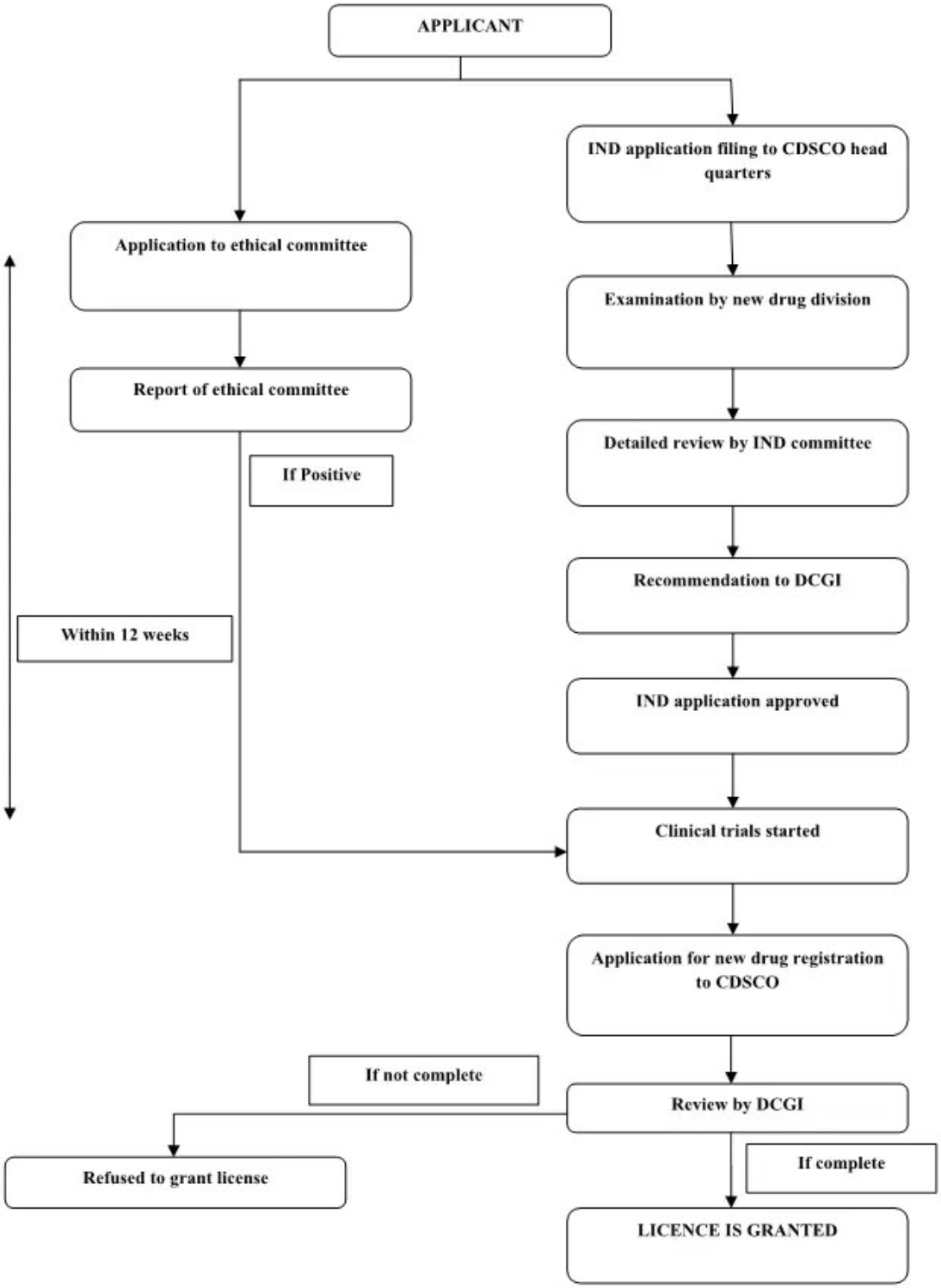

[Figure 3; Drug approval process in India]

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VII. COMPARATIVE ANALYSIS STUDY:

Aspect	Japan (PMDA/MHLW)	India (CDSCO/DCGI)
Act	Pharmaceutical and Medical Device Act (PMD Act)	Drugs and Cosmetics Act, 1940 & Rules, 1945
Regulatory Body	PMDA (reviews & evaluates) + MHLW (approves & authorizes)	CDSCO (reviews) + DCGI (approves)
Submission Format	Common Technical Document (CTD) / eCTD	Common Technical Document (CTD) / eCTD
Modules in CTD	5-module structure with Japan-specific administrative requirements	5-module structure with India-specific administrative requirements
Consultation Process	Mandatory multi-stage PMDA consultation (pre-IND, pre-NDA, protocol-level)	Optional but encouraged pre-submission meetings with CDSCO/SEC
Clinical Trial	PMDA approval after Clinical Trial Notification (CTN)	DCGI approval after submission in Form 44 under Schedule Y
Ethics Oversight	Institutional Review Boards (IRBs)	Ethics Committee + Clinical Trials Registry – India (CTRI) registration
Clinical Trial Phases	Phase I–III in Japanese population mandatory	Phase I may be waived if drug approved abroad; Phase III mandatory
Time to Approval	9 to 12 months	6 to12 months
Post-marketing Surveillance	Conducted under PMDA with re-examination after 8 years	PVPI (Pharmacovigilance Programme of India) + post-marketing surveillance under Rule 122DAB
Language	Japanese	English (mandatory)
Mandatory Information	Product name, dosage, MAH, storage, lot no., sterility, “For ophthalmic use only”	Generic name, brand name, strength, batch, expiry, manufacturer, “For ophthalmic use only”, Schedule H warning

Table 1; comparative analysis between PMDA and CDSCO

Ripasudil ophthalmic solutions approval process in Japan are managed by pharmaceutical and medical devices agency (PMDA) under Ministry of Health, Labour and Welfare (MHLW) and in India managed by central drug standard Control Organization (CDSCO) under Drugs Controller General of India (DCGI). [14,16]

There is a table of comparative analysis study on both Japan and India:

VIII. KEY SIMILARITIES

Table 2; key similarities between PMDA and CDSCO

Aspect	Similarity
Regulatory Role	Both Japan (PMDA/MHLW) and India (CDSCO/MoHFW) are national authorities responsible for drug approval, safety, efficacy, and quality.
Application Format	Both PMDA and CDSCO follow the Common Technical Document (CTD/eCTD) format (Modules 1–5).
Clinical Trial Process	Both require preclinical studies and Phase I–III clinical trials before approval.
Quality Standards	Both PMDA (JP) and CDSCO (IP) follow national pharmacopoeial standards ensuring product quality and sterility.
Labeling Rules	Both have detailed, mandatory labeling requirements for ophthalmic products (e.g., “For ophthalmic use only”).
Post-Marketing Surveillance	Both require continuous monitoring of drug safety after approval.
Review Process	Both involve expert evaluation and committee review before marketing authorization.

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IX. MAJOR DIFFERENCES

Here's table contain major differences between PMDA and CDSCO

Table 3; Major differences between PMDA and CDSCO

Aspect	Japan (PMDA/MHLW)	India (CDSCO/DCGI)
Regulatory Authority	Pharmaceuticals and Medical Devices Agency (PMDA), under Ministry of Health, Labour and Welfare (MHLW)	Central Drugs Standard Control Organization (CDSCO), under Ministry of Health & Family Welfare (MoHFW)
Act	Pharmaceuticals and Medical Devices Act (PMD Act)	Drugs & Cosmetics Act, 1940 and Rules, 1945 (Schedule Y)
Application Type	New Drug Application (NDA)	New Drug Application (Form 44)
Clinical Trial Submission	Clinical Trial Notification (CTN)	Clinical Trial Application (CTA) with DCGI & Ethics Committee approval
Clinical Trial Phases	Phase I–III conducted as per ICH-GCP guidelines	Phase I–III as per Schedule Y; Phase I may be waived if approved abroad
Final Approval Authority	Ministry of Health, Labour and Welfare (MHLW)	Drugs Controller General of India (DCGI)
Labeling Regulation	Mandatory electronic labeling (e-labeling) system	Rule 96 of Drugs and Cosmetics Rules, 1945
Key Labeling Requirement for Ophthalmic Products	"For ophthalmic use only", sterility & dropper instructions, PI legally binding	"For ophthalmic use only", sterility, preservatives, discard period, Schedule H warning
Labeling Language	Japanese	English
Post-Marketing Surveillance	Mandatory PMS under PMDA	PvPI & PSUR reporting required under CDSCO

X. CONCLUSION

The comparison of regulatory requirements for Ripasudil Ophthalmic Solution in Japan and India highlights how differences in approval pathways reflect each country's healthcare priorities and regulatory maturity. Japan's well-established framework emphasizes innovation and safety through rigorous clinical evaluation, while India's evolving system aims to balance accessibility and affordability for patients. Understanding these contrasts not only deepens appreciation for each country's approach but also underscores the shared goal of ensuring safe, effective, and timely treatments for those living with glaucoma worldwide.

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