

Generic Drug Development and Current Scenario

Pandhare Shubham¹, Wamane Vikas B²

¹Student, Pratibhatai Pawar College of Pharmacy

²Assistant Professor, Pratibhatai Pawar College of Pharmacy

Abstract:

Drugs or medicines are those which are used for treatment, diagnosis, mitigation and prevention of diseases. But it's very expensive. Not or all but for lower- and middle-class people taking treatment is very difficult because of the cost of the medicines. Many deaths are caused because the patient cannot afford the cost of the medicines. The entry of generic medicines in market brought a revolutionary change in healthcare system and the market share is continuously increasing. In the present scenario generic drugs have an important role in pharmaceutical market. Generic drugs are bioequivalent to brand drugs and are much cheaper as compared to brand drugs because of no R&D cost and minimum marketing expenses. This review presents considerations which can be employed during the development of a semisolid topical generic product. This includes a discussion on the implementation of quality by design concepts during development to ensure the generic drug product has similar desired quality attributes to the reference-listed drug (RLD) and ensure batch to batch consistency through commercial production.

Keywords: generic medicines, scenario, brand drugs, expensive, quality by design

Introduction:

Generic drugs have become an essential part of modern healthcare systems, providing patients with more affordable and accessible treatment options. Generic drugs are copies of branded drugs that have already been approved by regulatory authorities and have shown to be safe and effective in treating certain conditions. They offer the same quality, safety, and efficacy as the original drug, but at a lower cost, making them accessible to a larger patient population. Generic drugs have played a crucial role in reducing healthcare costs, increasing patient access to treatment, and improving the overall efficiency of healthcare systems. According to the definition given by the World Health Organization (WHO), generic medicines or generics are pharmaceutical products usually intended to be interchangeable with the innovator product, marketed when period of patent is over or other exclusivity rights. Generic or branded medicines are not clearly defined under the Drugs & Cosmetics Act, 1940 and Rules, 1945. However, generic medicines are those which contain same active ingredient with same amount in same dosage form, administered by the same route of administration and equivalent safety and efficacy as that of branded medicines [1].

A generic drug is simply a copy of innovator/brand name drug and is bioequivalent to a brand name drug with respect to pharmacokinetic and pharmacodynamic properties. Generic medicines must contain the same active ingredient at the same strength as the innovator drug product and are required to meet the same pharmacopoeia standards, but often have different inactive ingredients. Therefore, generics are assumed be identical in dose, strength, route of administration, safety, efficacy and intended use. Trademark laws prohibit a generic drug from looking exactly like other drugs on the market. After all;

brand-name companies have made distinctive colors, shapes, and sizes part of their sales strategy. Generic drugs usually cheaper than the innovator drug because of the following reasons: -

- 1). No cost of identification and isolation of New Chemical Entity (NCE),
- 2). No cost of research and development,
- 3). Minimum marketing cost because Branded drug is already approved as safe and effective. A generic drug can be produced for the Drugs:
 - Where the patent has expired;
 - Which have never held patent?
 - In countries where a patent(s) is/are not in force; [2]

The pharmacists were given right to substitute to generic drugs. In this prescription format, a space was provided for signature in case all prescription drugs cannot be changed to generic drugs. With the signature of physicians, all prescription drugs could not be substituted. In 2012, the Prescription format was modified to one that allowed generic substitution for individual drug, making it easier to substitute to generic drugs. Many actions including the prescription format Change is carried out in Japan to promote the generic drugs usage. Additionally, in 2013, the MHLW announced a 5-year plan to expand the use of generic drugs to over 60% by 2018. In order to promote the use of generic drugs, accelerated approval review for generic drugs is indispensable. [3]

In Japan, the drug product containing an API that has the different hydrate form or crystalline form from the original drug can essentially apply for as a generic drug, because they have basically the same chemical structure. The drug product containing an API that has different salts, esters, and ethers from the original drug can apply for as a new drug, not a generic drug. The original drugs are given the reexamination period of 8 years at the time of approval. The applicant can apply for the generic drugs after the reexamination period of original drugs. Because generic drugs are approved after the patent expiration of the original drugs and a reexamination period in Japan, the generic drugs have a reduced development cost, as compared to the original drugs. Therefore, the generic drug price is cheaper than the original drug. For example, in Japan, the price of a generic drug is usually 60% of the original drug price. Recently, demand has increased for reduced medical expenses in many countries including Japan, the USA, and Europe. Over 20% of Japan's population is over the age of 65 years, and it is estimated that it will reach nearly 40% by 2050. This is a key factor for healthcare cost expansion in Japan. The Ministry of Health, Labor, and Welfare (MHLW) proposed the use of generic drugs to reduce healthcare costs in 2007. In particular, the generic drug market share in Japan was lower than in other developed countries, as the market share of generic drugs in Japan was 18.7% in 2007. In contrast, the market share of generic drugs was 72% in the USA, 65% in England, and 63% in Germany. One of the reasons for the low generic drug market share in Japan is that there was no substitution right for the pharmacists. The physicians had the decision right of the generic drug substitution before 2006. In 2006, one important change of public health insurance was that the pharmacists were given right to substitute generic drugs for original drugs if the physicians explicitly allow substitution on their prescription format. The prescription format before 2008 was the format that the pharmacists could not change to generic drugs unless the physicians signed in the space on the prescription. The change of the prescription format was carried out in 2008.

A generic drug is a pharmaceutical drug that is equivalent to a brand-name product in dosage, strength, route of administration, quality, performance, and intended use. The term may also refer to any drug marketed under its chemical name without advertising, or to the chemical makeup of a drug rather than the brand name under which the drug is sold. Original Brand or the Innovators Brand is supposed to be the

branded version of the generics, which is patented and priced higher as the addition of the Research and Development (R&D) cost is added to the drug. There is a lot of confusion surrounding the nomenclature in India as we see the terms Branded generics, most commonly sold generics and low-cost generics in the literature. The reason for this is the patent act 1970 which removed product patent for 15 years as in the west and allowed process patent for 5-7 years. This allowed the Indian pharmaceutical companies to reverse engineer the drugs changing the process of making the drug and produce low cost generics. The process helped the Indian Pharmaceutical industry growth in making it among the top exporter of the generic drugs worldwide. [4]

Innovator and Generic Drug Products

Innovator products are also called “Reference Listed Drug” or “Patent Drug”. Innovator company or organization develop the medicinal product by trial and error and must have to conduct human trial or bio-availability study. As mentioned earlier, the generic drug product has to be bioequivalent to the innovator product and ensure the same biological effect with proper safety and efficacy. For example, “Zentiva Pharma UK Limited” invented an active, named “Dicycloverine Hydrochloride” and the marketed products was “Dicycloverine Hydrochloride 20 mg and 10 mg Tablets”. Another pharmaceutical industry “Teva UK Limited” developed bio-equivalent product by conducting bioequivalence study against the innovator product. So, the product of Zentiva is innovator and the product of Teva is generic product

Basic Requirement of Generic Medicines

There are some mandatory rules to develop a generic product and the following parameters should be same as the innovator for developing any generic:

1. The Active Pharmaceutical Ingredient and use.
2. Dose and strength.
3. The route of administration [4]

Generic Drug Approval

The generic drug approval process has evolved over the past 35 years. In 1970 FDA established the Abbreviated New Drug Application (ANDA) as a mechanism for the review and approval of generic versions of drug products that had been approved between 1938 and 1962. For drugs approved after 1962, manufacturers of generic products were required to submit complete safety and efficacy through clinical trials. After 1978, however, manufacturers were required to cite published reports of such trials documenting safety and efficacy. Neither of these approaches was considered satisfactory, as the former was quite expensive and the latter required evidence that was usually unavailable, i.e., data that had not been published. In 1984 the Drug Price Competition and Patent Term Restoration Act (Hatch-Waxman Amendments) focused on modifying and accelerating the ANDA procedure and gave FDA statutory authority to approve generic versions of innovator products approved after 1962 as safe and effective. Generic drug applications are termed “abbreviated” because they are generally not required to include preclinical and clinical data to establish safety and effectiveness. Instead, generic applicants must scientifically demonstrate that their product is bioequivalent to innovator product. Because the generic product must be pharmaceutically equivalent and bioequivalent to the innovator product, it is expected that the two products will also be therapeutically equivalent. [11]

Beginning of Generics: -

On September 24, 1984, in the 98th United States Congress, the act named The Drug Price Competition and Patent Term Restoration Act was passed, informally known as the Hatch-Waxman Act, encouraging the manufacture of generic drugs by the pharmaceutical industry and established the modern system of

government generic drug regulation in the United States.[5] The requirement was an abbreviated new drug application (ANDA) to be submitted by the pharmaceutical companies to the regulatory authorities for getting the approval to market a generic drug. ANDA process does not require the manufacturer to carry out repeat testing of generics in animals which is often time-consuming, as their branded versions have already been tested and approved for the safety and effectiveness. They are formulated when patent and other exclusivity rights of the innovator have expired. Generic drug manufacturers do not have to spend extra money for drug discovery and preclinical and clinical trials. Generics are available at a lower cost; they provide an opportunity for savings in drug expenditure in a country. [6]

Regulatory Landscape: -

The regulatory framework for generic drug development is complex, involving a range of regulatory agencies and guidelines. In the United States, generic drugs are regulated by the U.S. Food and Drug Administration (FDA) under the Hatch-Waxman Act, which provides a pathway for generic drug manufacturers to seek approval for their products. Under this act, generic drugs must be shown to be bioequivalent to the reference listed drug (RLD) and meet the same safety, efficacy, and quality standards as the RLD. The FDA requires that generic drugs be manufactured according to Current Good Manufacturing Practices (CGMPs), which ensure the quality and consistency of the manufacturing process. [7]

Name of Country/ Group	Regulatory authority
USA	FDA
EU	EMA
Canada	HPFB
Japan	PMDA
Australia	TGA
South Africa	MCC
AFRICA (Tanzania)	Independent regulatory agencies/TFDA
LATAM (Brazil)	Independent regulatory agencies/ANVISA
CIS (Russia)	Independent regulatory agencies/ ROSZDRAVNADZOR
ASIAN (Hong Kong)	Independent regulatory agencies/DOH
GCC	Independent regulatory agencies/National filling

Fig 1. Regulatory authorities of various countries

Formulation Development: -

Formulation development is a critical step in the development of generic drugs, as it involves the creation of a drug product that is equivalent to the reference listed drug (RLD) in terms of safety, efficacy, and quality. The goal of formulation development is to create a drug product that has the same active pharmaceutical ingredient (API), dosage form, strength, route of administration, and labeling as the RLD. The formulation development process begins with the selection of the API and the excipients that will be used to create the drug product. Excipients are the inactive ingredients that are added to the drug product to help it maintain its stability, solubility, and bioavailability. Excipients must be carefully selected to ensure that they do not interact with the API and do not impact the safety or efficacy of the drug product. [8]

Once the API and Excipients have been selected, the next step is to develop a formulation that meets the required specifications. This involves the optimization of the formulation to ensure that it provides the appropriate release of the API, has the desired stability and shelf life, and meets the required pharmacokinetic and pharmacodynamic properties. The formulation must also be designed to be manufacturable at a commercial scale.

1. Pre-Formulation Study:

Before starting the lab-based formulation, extensive documentation and study is carried out to assess the API, e.g., appearance, solubility, salt form, pKa, assay, residual solvent, loss on drying, water content. Even bulk density and tapped density are analyzed. For specific molecule additional test may need to carry, e.g., “specific surface area” has to determine for “Nitrofurantoin Macrocrystal”. The following Figure 1 shows different parameters to be considered during preformulation studies [9].

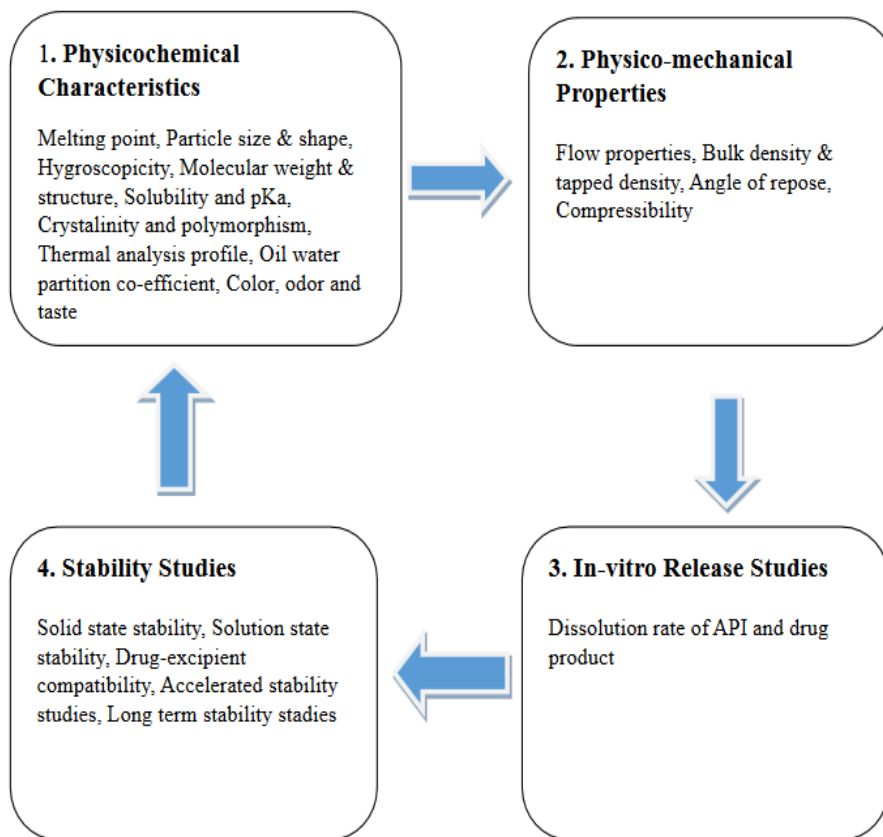


Figure 2. Parameters to be considered during a Preformulation Study

In preformulation study, drug-excipient compatibility has to be determined because it affect the final dosage form and stability of the drug and can modify the pharmacological effect as well “Pre-formulation” work must be reviewed prior to preparing actual trial formulations to achieve as much information related to the drug substance & reference product as possible [10].

2. Excipient Selection and Designing of Formulation Method

There are some basic requirements of pharmaceutical excipients:

- Chemically inert
- Cheap and available
- Exert the desired response for which they are used

From development point of view, nature of API, excipient used in reference product helps to design the formulation and selection of proper excipient. If any API is moisture sensitive, anhydrous lactose and cross povidone as filler and disintegrating agent will be right option rather than lactose monohydrate (filler) and maize starch (disintegrating agent). Formulation scientist has to assess such critical things during selection of proper excipient for formulation development [11].

3. Selection of Manufacturing Method:

Manufacturing method is the most critical decision for a formulation development, e.g., for solid dosage form manufacturing method can be Granulation or Direct compression. Again, granulation can be wet or dry. The method to be followed depends on the many things, like the characteristics of API; if API is heat and moisture sensitive, then wet granulation is not possible, similarly if particle size of API is larger, then the distribution of API may be ununiform in final products [6]. During the development a product by direct compression someone may find good physical and chemical result initially with small size batch. But in case of larger batch size, it may fail to comply uniformity of dosage unit by content. Then formulator may think about different approaches, like wet granulation if API is not heat and moisture sensitive and then product may comply with all specification. The scale-up plan must take into account the manufacturing technique used in smaller batch manufacturing, and the equipment employed in the development process frequently imposes many limits during scale-up operations. In the production of solid dosage forms, the following pharmaceutical unit procedures are used: [12]

- Wet granulation
- Compression
- Extrusion
- Drying
- Dry blending
- Roller compaction
- Encapsulation
- Coating [13]

4. Lead Formula Identification:

When pre-formulation, excipient selection and manufacturing method has been designed, then trial is planned to execute. The batch size should be as small as possible considering the expense of the industry. The prime objective is to match the dissolution profile with the reference. So, formulation scientist designs a unit formula composition considering the percentage of excipient. The formulation scientist will take suitable percentage of all excipient and will decide for target weight that allow for manufacturing [7].

Initially a small batch, e.g., 200 - 300 units are planned to manufacture and for that formula and method of manufacturing; steps in detail are documented and checked. Then materials are dispensed and manufactured up to final dosage form with proper documentation. Analytical method is also designed to carry on analysis simultaneously with formulation development. For first 2 - 3 small trial are done to just check the physical parameter like, weight variation, hardness, thickness, disintegration time and mainly to check the similarity with the dissolution profile with reference. If dissolution profile of test product matches with RLD and physical parameter are good enough, then formulator decides to scale up the formulation. The initial trial batches are called pilot batch or lab-based batch. The number of scales up batches may have to be taken depending upon the physical and chemical assessment of the finished products e.g., formulator brought a successful trial batch initially, but complicity may arise in the pilot batches. Then the formulation scientist has to rethink about the composition of the formulation and the method of manufacturing

considering the complicity arises during the pilot batches. The formulation scientists may have to take new trial batch after taking multiple scale-up batches, even after a validation or optimization batch at GMP facility. The formula that passes the trial batch and scale up trial and passes to comply at least 3-month stability according to the ICH guideline can be called a lead formula. But it can be or need to change depending upon the situation arise as explained already [14].

Increase in batch size or scale-up are obtained by using larger, high-speed machinery that may necessitate co-relation to the process parameters determined using small scale equipment. Then the end goods must meet all predefined specifications, and the products from scaled-up batches must be physically and chemically identical, notably the dissolving profile [15]. Large scale batches or scale-up batches using modern technology has become essential in minimizing manufacturing costs in today's competitive market [16]. The finished products must meet all predetermined specifications, and the products from scaled-up batches must be physically and chemically equivalent, specially the dissolution profile. "Informal stability" should be carried out under accelerated, long term and intermediate conditions as well for 2 - 3 months to ensure the stability of the product. But this stability data cannot be submitted as document, stability data can only be submitted from commercial site, not from R&D facility. The generic product is analyzed at monthly intervals mainly potency, dissolution, related substances. Stability of RLD should be carried as well for information only, mainly to assess the related substances [11]. This is important for the formulation scientist to validate and characterize the critical parameters and set specification during the initial formulation process. Critical parameters are as follow [17]:

- Milling rate
- Drying method
- Rate of addition of the granulating vehicle
- Screen size for initial sieving, during drymilling, during wet milling
- Milling rates during wet granulation
- Hardness of tablets
- Screen-sizes
- Shell size of capsule
- Granulating time
- Mixing order
- LOD of granule
- Blender type and blending time
- Drying time
- Lubrication time
- Drying condition
- Machine speed during compression and encapsulation
- Speed of chopper and agitator during granulation
- Feeder speed

The formulation scientist is responsible to manufacture of the exhibit batch. Batch can be manufactured as a sub-batch using similar equipment as the scale-up equipment and using the same raw materials. As for example, using a 30 kg capacity granulator can be used to manufacture 60 kg batch-size. In this case, granulation sub-lots would be required (30×2) to complete the batch manufacture. During each granulation, drying, milling, and blending operations need be optimized according to protocol. Manufacturing of tech transfer or submission batches should be carried out under

GMP facility by maintaining the cGMP regulations. Samples from the executed batches must be tested to the laboratory under cGMP facility with validated method. Proper documentation needs to be prepared which describes the whole process, termed as Batch Manufacturing Record and for packaging, batch packaging record. Stability must be conducted as per requirements [18]. A proper and documented validation protocol ensures the above. A validation master plan should include the following:

- Personnel Responsibilities
- Sampling plan
- Critical process and product parameters
- Critical process steps
- Testing plan
- Purpose of the study
- Acceptance criteria

During the manufacturing process, extensive samples are collected and tested to validate the process the samples are tested to appropriate testing using validated analytical methods. The validation report should include the following:

- Critical process steps studied
- Attachments of copies of the executed batch records
- Aim of the validation study • List of raw materials used in the manufacturing process
- List of manufacturing equipment
- Product and process acceptance criteria evaluation
- Recommendations by the validation department
- Data collected and their analysis
- Statistical analysis of results

After careful evaluation of the validation documentation the manufacturing process is released for regular production

5 Bioequivalence Studies: -

Bioequivalence studies are essential in establishing the safety and efficacy of generic drugs. Bioequivalence refers to the comparison of the rate and extent of drug absorption from the generic drug product to that of the RLD. These studies are designed to demonstrate that the generic drug is pharmaceutically equivalent to the RLD and has the same pharmacokinetic properties. Bioequivalence studies are typically conducted in healthy volunteers, and the endpoints measured include the maximum concentration of the drug (C_{max}), the time to reach maximum concentration (T_{max}), and the area under the concentration-time curve (AUC). The results of bioequivalence studies are used by regulatory agencies to determine whether a generic drug can be approved for use. Bioequivalence studies are a critical component of the development of generic drugs, as they provide evidence that the generic drug is equivalent to the RLD in terms of its safety, efficacy, and quality. Bioequivalence studies are conducted to demonstrate that the generic drug has the same rate and extent of absorption as the RLD when administered at the same dose and under the same conditions. [19]

The goal of a bioequivalence study is to compare the pharmacokinetic properties of the generic drug and the RLD in healthy volunteers. The study typically involves the administration of a single dose of the drug to each volunteer, followed by the collection of blood samples over a specified period. The blood samples are analyzed to determine the concentration of the API in the bloodstream at various time points. The results of the bioequivalence study are typically expressed in terms of the area under the curve (AUC)

and the maximum concentration (C_{max}) of the API in the bloodstream. The AUC reflects the total exposure of the body to the API, while the C_{max} reflects the maximum concentration of the API in the bloodstream. [20]

The regulatory requirements for bioequivalence studies vary by region and by drug product. In the United States, bioequivalence studies are required for generic drugs that are intended to be administered orally, while in the European Union, bioequivalence studies are required for all generic drugs, regardless of the route of administration. In conclusion, formulation development and bioequivalence studies are critical components of the development of generic drugs. Formulation development involves the creation of a drug product that is equivalent to the RLD in terms of safety, efficacy, and quality, while bioequivalence studies are conducted to demonstrate that the generic drug is equivalent to the RLD in terms of its pharmacokinetic properties. The successful completion of these steps is necessary for regulatory approval and the commercialization of generic drugs. [16]

6 Clinical Trials:

Clinical trials are an essential part of the drug development process, and generic drugs are no exception. Clinical trials are designed to test the safety and efficacy of a drug in a specific patient population. The clinical trial process for generic drugs is similar to that of branded drugs, and includes four phases of clinical development. Phase I clinical trials are conducted in healthy volunteers and are designed to establish the safety of the drug. Phase II trials are conducted in a small number of patients with the disease of interest and are designed to establish the efficacy of the drug. Phase III trials are conducted in a larger patient population and are designed to confirm the safety and efficacy of the drug. Phase IV trials are conducted after the drug has been approved and are designed to monitor the long-term safety and efficacy of the drug in the real world. [21]

Quality Control:

Quality control is a critical aspect of generic drug development, ensuring that the drug is safe, effective, and of high quality. The quality control process involves the testing and validation of analytical methods, in-process controls, and finished product testing. Analytical methods are used to test the purity, identity, and potency of the API and other components of the drug. In-process controls are used to monitor the manufacturing process and ensure that the drug is being produced consistently and meets the required specifications. Finished product testing is used to test the final product and ensure that it meets the required quality standards. [22]

Patent Law and Litigation:

Patent law plays a critical role in the development of generic drugs, and the potential for litigation can create significant challenges for generic drug manufacturers. Patents are granted to inventors and provide them with the exclusive right to manufacture, use, and sell their invention for a certain period. Generic drug manufacturers must navigate a complex web of patent laws and regulations to bring their products to market. In some cases, branded drug manufacturers may file lawsuits against generic drug manufacturers to protect their patents and prevent them from entering the market. These lawsuits can be costly and time-consuming and can delay the availability of generic drugs. [23]

Current Scenario of Generic Drugs:

The current scenario of generic drugs is one of growth and opportunity, as the demand for affordable medications continues to increase. Generic drugs play an important role in providing patients with access to safe and effective treatments at a lower cost than their brand-name counterparts. In this section, we will

discuss the current state of the generic drug industry, including the challenges and opportunities facing the industry today.

Indian Scenario

As India is one of the highest per capita out-of-pocket expenditures’ countries, such generics will save a lot of money which can be used for other health issues. [4] In all the countries, use of generic drugs has increased significantly in recent years. The regulations governing the approval of generic drugs are somewhat the same world over, with very few differences in developing countries, as in this part of the world it is not mandatory to undergo bioequivalence (BE) studies for getting approval for generics, and the gold standard considered for regulation in this field is United States. In 2008, the Government of India, through the Department of Pharmaceuticals, started a new initiative “Jan Aushadhi” (a Hindi word literally translated as “Medicine for People”). This program envisaged making unbranded quality medicines available to poor people in the country at a reasonable and affordable price through retail outlets’ setup with the help of the government. It has taken ownership of setting up Jan Aushadhi stores, which are pharmacies selling only generic name medicines to the extent possible, giving preference to pharmaceutical public sector undertakings too. Until March 15, 2018, 3200 Jan Aushadhi stores were operating in more than 33 states/union territories across India. [8] There are not enough Jan Aushadhi stores, possibly 3200 against more than 8 lakh retail pharmacies in existence, with many rural areas still underserved. [8]

The Medical Council of India, in an amendment to the code of conduct for doctors in October 2016, has recommended that every physician should prescribe drugs with generic names legible and he or she shall ensure that there is a rational prescription which promotes the use of generic drugs. In future, the Government of India may bring a legal framework under which doctors will have to prescribe generic medicines to patients. [15]

Market Size and Growth:

The generic drug industry has experienced significant growth in recent years, driven by factors such as the expiration of patents on many brand-name drugs and the increasing emphasis on cost containment in healthcare. According to a report by IQVIA, the global market for generic drugs is expected to reach \$380 billion by 2022, up from \$269 billion in 2017.

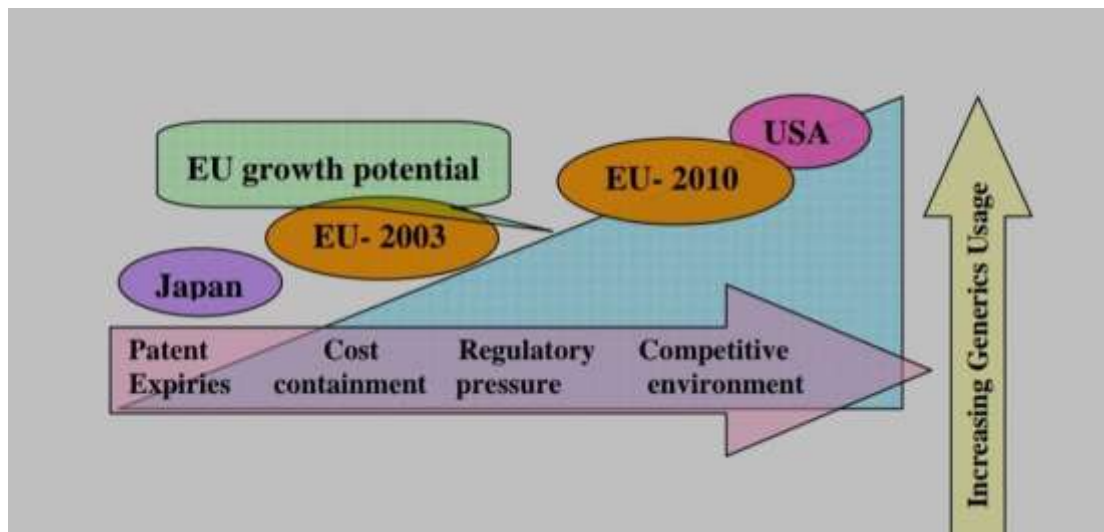


Fig 3: US/Europe generics market growth opportunities

The United States is the largest market for generic drugs, accounting for over half of global sales. The European Union and Japan are also significant markets for generic drugs. In the United States, generic drugs account for over 80% of all prescriptions filled, and the use of generic drugs has saved the healthcare system an estimated \$1.7 trillion over the past decade. [24]

Challenges Facing the Industry:

Despite the growth and success of the generic drug industry, there are several challenges facing the industry today. One of the biggest challenges is the increasing competition within the industry, which has led to a decline in prices and profit margins. As more companies enter the market and the number of generic drugs increases, companies must compete on price and efficiency to remain profitable. Another challenge facing the industry is the increasing regulatory scrutiny of generic drugs. Regulatory authorities are placing greater emphasis on the quality and safety of generic drugs, and companies must meet increasingly stringent standards to obtain approval for their products. [22] This has led to increased costs and longer development timelines for generic drugs.

Opportunities for Growth:

Despite the challenges facing the industry, there are also significant opportunities for growth in the generic drug market. One of the biggest opportunities is the increasing demand for generic drugs in emerging markets such as China and India. As these markets continue to grow and mature, the demand for affordable medications is expected to increase, creating new opportunities for generic drug manufacturers. Another opportunity for growth in the generic drug market is the development of complex generics. Complex generics are drugs that are difficult to develop and manufacture, such as injectable drugs, inhalers, and biosimilars. Developing these products requires specialized expertise and technology, which can create a barrier to entry for competitors. Companies that can successfully develop and manufacture complex generics have the potential to capture a significant share of the market and achieve higher profit margins.

In addition, the increasing emphasis on personalized medicine and the development of targeted therapies is creating new opportunities for generic drug manufacturers. As more targeted therapies are developed, there is a growing need for generic versions of these drugs to increase access and affordability.

Market Competition:

Market competition is a crucial factor in the development and availability of generic drugs. The availability of generic drugs creates competition in the market, which can lead to lower prices and increased access to treatment. The pricing of generic drugs is typically lower than that of branded drugs, making them more affordable and accessible to patients. Generic drugs also provide an opportunity for new entrants to the market, which can stimulate innovation and promote competition. [25]

Future Perspectives: -

The future of generic drug development is influenced by a range of factors, including emerging technologies, regulatory changes, and healthcare trends. Emerging technologies, such as gene therapy and cell therapy, have the potential to revolutionize the treatment of many diseases and may create new opportunities for generic drug manufacturers. Regulatory changes, such as the introduction of new guidelines for the development and approval of generic drugs, may impact the development process and require generic drug manufacturers to adapt their strategies. Healthcare trends, such as the shift towards value-based care and personalized medicine, may also impact the development of generic drugs. [16]

Quality of Generic medicines:

Generic or branded drugs which are manufactured in the country are required to comply with the same standards as prescribed in the Drugs and Cosmetics Act, 1940 and Rules, 1945 for their quality and efficacy. Both are expected to have similar effects.

The Advantages of Generic Medicines: -

1. It usually costs 80% to 85% less than the price of branded drugs.
2. Considered effective and safe as like branded medicines.
3. Both generic and branded drugs come under the same governance and adhere to the same quality standards.
4. After the expiration of patent period of branded drugs, they come to public domain i.e. anyone can manufacture their generic versions.
5. Because of the fewer prices of generic medicines and rising competition, pharmaceutical companies come under pressure to reduce the price of their branded versions. [1]

Conclusion: -

In conclusion, generic drug development plays a vital role in providing affordable and accessible healthcare options to patients around the world. The current scenario of generic drug development is characterized by increasing regulatory scrutiny, evolving market dynamics, and rapid technological advancements. Despite challenges such as patent litigation, quality concerns, and market competition, generic drugs continue to gain popularity due to their cost-effectiveness and potential to increase patient access to essential medications. The generic drug development landscape is constantly evolving, with regulatory reforms, technological advancements, and market forces shaping the industry. While there are challenges to overcome, the continued growth of the generic drug market is expected to provide patients with more affordable healthcare options and contribute to the overall sustainability of healthcare systems worldwide.

References:

1. Tapan Kumar Mahato, and Durgeshwari Raulji, Present scenario of generic medicines in India: A comparative study, *World Journal of Biology Pharmacy and Health Sciences*, 2021, 07(02), 053–059.
2. Devendra Pratap Singh, Generic Drug Access In Global Scenario. *J. Pharm. Sci. & Res.* Vol.2 (2), 2010, 90-98.
3. Ryosuke Kuribayashi, Maki Matsuhama, and Kenichi Mikami, Regulation of Generic Drugs in Japan: the Current Situation and Future Prospects. *The AAPS Journal*, Vol. 17, No. 5, September 2015 Page no 1312-1316.
4. Phani Prasant Mulakaluri, Generic medicines in the Indian scenario – What are we expecting? *Telangana Journal of Psychiatry*, January-June 2017:3(1):1-3.
5. Kelly C. The balance between innovation and competition: The Hatch-Waxman act, the 2003 amendments, and beyond. *Food Drug Law J.* 2011; 66:417–78.
6. Swain S, Dey A, Patra CN, Bhanoji Rao ME. Pharmaregulations for generic drug products in India and US: Case studies and future prospective. *Pharmaceut Reg Affairs.* 2014; 3:2.
7. Chourasia, G. (2016) A Review on Pharmaceutical Preformulation Studies in Formulation and Development of New Drug Molecules. *International Journal of Pharmaceutical Sciences and Research*, 7, 2313-2320.

8. Chaudhari, S.P. and Patil, P.S. (2012) Pharmaceutical Excipient: An Overview. *International Journal of Advances in Pharmacy, Biology and Chemistry*, 1, 21-32.
9. Terblanche, N.S. (2008) New Pharmaceutical Product Development: Barriers to Overcome and Opportunities to Exploit. *Journal of Commercial Biotechnology*, 14, 201-212.
10. Pramod, K., Tahir, M.A., Charoo, N.A., Shahid, H., Ansari, S.H. and Ali, J. (2016) Pharmaceutical Product Development: A Quality by Design Approach. *International Journal of Pharmaceutical Investigation*, 6, 129-138. <https://doi.org/10.4103/2230-973X.187350>
11. Sravika, S., Bhavana, R., Sharmila, V., Anusha, S., Mounica, N.V.N. and Nagabhushanam, M.V. (2017) A Comprehensive Study on Regulatory Requirements for Development and Filing of Generic Drugs Globally. *Journal of Pharmaceutical Innovation*, 6, 153-158. <https://doi.org/10.5530/ijper.52.4.63>
12. Sravika, S., Bhavana, R., Sharmila, V., Anusha, S., Mounica, N.V.N., Reddy, D.N. and Nagabhushanam, M.V., 2017. A comprehensive study on regulatory requirements for development and filing of generic drugs globally. *The Pharma Innovation*, 6(4, Part C), p.153.
13. Grabowski, H.G., 2002. Patents and new product development in the pharmaceutical and biotechnology industries. *Science and Cents: Exploring the Economics of Biotechnology*, pp.95-96.
14. Hamrell, M.R., 1997. An update on the generic drug approval process. *Clinical Research and Regulatory Affairs*, 14(2), pp.139-154.
15. Handoo, S., Arora, V., Khera, D., Nandi, P.K. and Sahu, S.K., 2012. A comprehensive study on regulatory requirements for development and filing of generic drugs globally. *International journal of pharmaceutical investigation*, 2(3), p.99.
16. Yousefi N et al. / *IJPR* (2017), 16 (2): 834-846.
17. Kirtikumar, N. and Maheshwari, D., 2014. Documentation requirements for generic drug application to be marketed in india-a review. *Journal of pharmaceutical science and bioscientific research*, 4(4), pp.237-42.
18. Kovaleski, J., Kraut, B., Mattiuz, A., Giangiulio, M., Brobst, G., Cagno, W., Kulkarni, P. and Rauch, T., 2007. Impurities in generic pharmaceutical development. *Advanced drug delivery reviews*, 59(1), pp.56-63.
19. Lionberger, R.A., 2019. Innovation for generic drugs: science and research under the generic drug user fee amendments of 2012. *Clinical Pharmacology & Therapeutics*, 105(4), pp.878-885.
20. Grabowski, H., Long, G. and Mortimer, R., 2014. Recent trends in brand-name and generic drug competition. *Journal of medical economics*, 17(3), pp.207-214.
21. Chongprasert, S., 2016. Successful generic drug product development: From research to marketing approval. *Asian Journal of Pharmaceutical Sciences*, 1(11), pp.35-36.
22. Pharm, B. and Pharm, M., 2013. Quality by design (QbD): manufacturing and product quality of Generics drugs perspective. *Journal of Global Trends in Pharmaceutical Sciences*, 4(4), pp.1257-62.
23. Leon S, Kanfer I. Introduction to Generic drug product development. In: *Generic drug product development Solid Oral Dosage forms*. New York: Marcel Dekker Inc; 2005. p. 8.
24. Hamrell MR. An Update on the Generic Drug Approval Process. California: ON Clinical Research and Regulatory Affairs; 1997. Vol. 14, No. 2. p. 139-54.
25. Graner M and Mißler-Behr M. Key determinants of the successful adoption of new product development methods. *Eur. J. Innov. Manag.* (2013) 16: 301-16.