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A Quality Assessment of Generic Drugs: A Review

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Abstract

Among the developing countries of the world India has made its own identity in the health care department or in the pharmaceutical department. Currently India is considered to be a world of pharmacy of generic medicines. Generic drugs are those drugs which are same as the branded one. This is mandatory that generic drugs only manufactures after expiry of innovative drug's patent. Generics have an important role to play in public health as they are well known for their affordable prices. After expiry of the patent it is open to manufacture and marketing generic by everyone. According to WHO there is no precise legal definition for widely available worldwide, generic drugs play an efficient role in pharmaceutical expenditures. Generic medicines stay in trend because these are available on a reasonable price in the market which is easy to grab for the Indian market. The healthcare system of India offer generic drugs 20-90% cheaper than original branded drugs. Objective of this study is to provide a high description of what generic drugs are and how these drugs are different from branded or innovative drugs, and what the regulatory and legislative levels of generic drugs are, here we initiate the study from the historical and current regulation of the generic medicines.

History of generic drugs

The Drug Price Competition and Patent Term Restoration Act, known as the Hatch-Waxman Act, it is a 1984 United States Federal law which initiates the manufacture of Generic drugs by the pharmaceutical industry and it also initiates the government generic drug regulation in the US FDA. It introduced a new market when the FDA approves the marketing of a newer entity drug a five year period of data exclusivity awarded, during that five year period the FDA cannot approve a generic version of that particular entity. On this period market exclusivity for that innovator drug has no limit for the patent right.

This act provides the facility of filling the ANDAs by generic companies, this provide the information regarding the manufacturing of drug with high and assure quality. When any company is ready to file its ANDA, then this act requires it to declare the activity when it begins to market.

Introduction

(What are generic drugs?) (Mosab Arafat et al.)

Generic drugs are those which are came in the market after expiring of patent, and which are same in terms of active pharmaceutical ingredients, activity, safety, efficacy, potency, toxicity, and route of administration. Other than active pharmaceutical ingredient in any formulation is can be same or different with innovative or branded drug.

Generic medicines in Iraq

In Iraq, the Ministry of Health (MOH) is responsible for all importing medicines from companies registered with KIMADIA (this is the state company for importation and distribution of drugs and medical appliances). Currently, there is no social health insurance system exist in Iraq. Prescribing drugs by generic name and encouraging pharmacists to dispense prescriptions with generic medicines is one frequently suggested means for lowering the costs of healthcare.

(USAID, Pharmaceutical and Medical products in Iraq)

In Iraq, some physicians were against prescribing generic medicines, whereas others were open-minded.

"I don't prescribing generic medicines because I do not have confidence in the therapeutic effect of this type of medicine"

In order to prevent substitution of the medicines in the pharmacy, physicians said that they write trade names and do not use generic names in their prescription.

"I write trade name to prevent the substitution in the pharmacy and to stop them from giving any medicine that does not work".

Disease severity is a factor that inhibitors physicians from prescribing generic medicines. In severe cases, physicians tend to use innovative medicines.

"In chronic cases, I don't prescribe any generic medicines".

Generic medicines in the UK (Schacht W R Thomas J R, Karki L, Richard G. Frank)

The UK has one of the lowest pricing levels for generic medicines in Europe. The UK exhibits one of the highest prices for branded products and the lowest prices for generics in Europe. UK generics pricing levels have long been admired by many other European countries. Apart from Denmark, which uses the blunt instrument of mandatory generic substitution, the UK having the highest generics penetration levels in Europe?

The generic drugs are meant to be safe and effective as these are bioequivalent to the branded drugs. *Bioequivalence* means when two products are pharmaceutically equivalent and the bioavailability after administration of those products are the same; the efficacy and safety parameters are similar to each other with the same route of administration.

There is no question that branded medicines have tremendous influence in medicines utilization, but as we mentioned that generic drugs are bioequivalent to their brand name counterparts, generic usually considered safe as well as cost-effective medicines. Globally, the use of generic drugs has increased steadily as a result of economic pressure on drug budgets. Generic medicines provide major opportunities for savings in health care expenditures.

The Hatch Waxman Act grants for the manufacturing of generic drugs, the ability to mount a challenge without increasing the cost. In addition, the Hatch Waxman Act requires the FDA, among other things, the want to makes publicly available a list of approved generic drugs with the same therapeutic equivalence or effect evaluations with monthly supplements, known as Orange Book. Patent and exclusive listing for patent are also included in this.

The Hatch Waxman Act amended the Federal Food, Drug and Cosmetic Act (FDCA) and the Patent Act, established an abbreviated

new drug application 60 days later, and so created the modern US generic industry. Although the Hatch Waxman Act was passed with overwhelming support in the US congress, it was, and remains, an uneasy compromise and a delicate balance between the interests of the brand name drug industry and the generic drug industry.

Now a day generic drugs cover 60-63% prescriptions of all U.S. since generic drugs available at a lower prices than their brand name drugs, they save consumers and purchasers of prescription drugs tens of billions of dollars per year. During 2007-2010, approx. 110 drugs lose their patent protection including well-known drugs like *Amlodipine (Norvasc), Sumatriptan (Imitrex), Alendronate (Fosamax) and Riseperidone (Risperdal)*.

Competition from generic drugs could generate large additional savings. Economic benefits are widely viewed by the Drug Price Competition and Patent Restoration Act of 1984, or the Hatch Waxman Act, which set the rule for the generic drugs so that they can compete with the brand name drugs. During 1984, only 18.6% prescription was written for generic products. The main aim of manufacturing generic drugs is to control price competition into the prescription drug market or branded markets, because higher the cost, higher the economy and higher the budget, but after introducing Hatch Waxman Act or generic drugs in the market they control the price of branded drugs as well, because prescription are covered with generic drugs and they are less in price and bioequivalent to their brand name drugs. Before 1984 this was not a rule to perform safety and efficacy tests that had been required for the brand name manufacturers to receive approval for the market from the FDA, but after Hatch Waxman Act changed all that, it contained 3 features that compete between brand name drugs and generic drugs. This law set an abbreviated process to receive FDA approval for generic drugs.

Most of the time in some cases brand name companies find that their own patented drugs competing with generic versions of rival drugs in the same class. These have powerful incentives to devise ways to revenue losses long before their patent expires.

Pradhanmantri Bhartiya Jan Aushdhi Pariyojana Kendra in India

Over the last few years, our country has developed a scheme for quality generic drugs in most of the therapeutic categories. These generic drugs are available at reasonable prices but still most of the population of our country is still unaware of these stores. Pradhanmantri Bhartiya Jan Aushdhi Pariyojana Kendra is a campaign, launched by the department of pharmaceutical, the government of India to provide quality and effective medicine which available at a lesser price in every store.

With the help of these stores Indian people almost save 2000 cr. in the year of 2018. Here are few rate lists which show a huge difference.

Generic drug	***Price (rs)***	***Brand name***	***Price (rs)***
Amlodipine	2.90	Mankind	11.83
Amlodipine	2.90	Cipla	41.18
Telmisartan	6.75	Glenmark	57.44
Telmisartan	6.75	Mankind	20.16
Allopurinol	15	GSK	19.26
Allopurinol	15	Cipla	25
Etoricoxib	25	Sun pharma	109
Etoricoxib	25	Magnet labs	87.84
Metformin HCL	8	Lupin	29
Metformin HCL	8	Macleods	18.93
Glimepiride	25	Dr. Reddy	83
Glimepiride	25	Micro labs	89.5

Table 1

Result and Discussion

Formulation	*Generic*	*Brand 1st*	*Purity*	*Brand 2nd*	*Purity*
Amlodipine Besylate	102.0	Mankind	99.70	Cipla	101.6
Telmisartan	99.77	Mankind	99.18	Cipla	101.03
Allopurinol	97.3	GSK	101.3	Cipla	99.67
Etoricoxib	94.1	Sun pharma	100.9	Magnet lab	99.4
Metformin Hcl	102.1	Macleods	102.5	Macleods Lupin	99.1
Glimepiride	98.98	Dr. Reddy	99.7	Micro lab	100.4

Table 2: Percent purity (Assay) in formulation.

Drug name	*Initial wt. (mg)*	*Final wt. (mg)*	*% friability*
Amlodipine	875.7	870.2	0.632
Telmisartan	1594.1	1579.1	0.940
Allopurinol	3055.6	3048.3	0.238
Etoricoxib	3121.4	3120.4	0.0320
Metformin Hcl	7745.1	7721.3	0.307
Glimepiride	1996.6	1989.7	0.3455

Table 3: Friability Test.

Drug name	*Brand 1st*	*Initial wt. (mg)*	*Final wt. (mg)*	*% Friability*
Amlodipine	Mankind	985.12	985.10	0.0020
Telmisartan	Mankind	1023.89	1023.88	0.00097
Allopurinol	GSK	1759.4	1758.0	0.079
Etoricoxib	Sun pharma	2365.1	2365.1	0
Metformin HCL	Lupin	6993.3	6979.3	0.200
Glimepiride	Dr. Reddy	1394.8	1394.6	0.014

Table 4: Friability Test.

Drug name	*Brand 2nd*	*Initial wt. (mg)*	*Final wt. (mg)*	*% Friability*
Amlodipine	Cipla	1200.2	1200.0	0.0166
Telmisartan	Glenmark	854.9	854.7	0.0233
Allopurinol	Cipla	2008.7	2008.5	0.0099
Etoricoxib	Magnet labs	2655.2	2655.0	0.0075
Metformin HCL	Macleods	7595.4	7588.5	0.0908
Glimepiride	Micro labs	1200.2	1200.2	0

Table 5: Friability Test.

Drug name	*Brand 1st*	*Disintegration time (min)*	*Brand 2nd*	*Disintegration time (min)*
Amlodipine	Mankind	3min 26 sec	Cipla	3min 49 sec
Telmisartan	Mankind	4min 2sec	Glenmark	3 min 19 sec
Allopurinol	GSK	3 min	Cipla	3min 47sec
Etoricoxib	Sun pharma	4mim 7sec	Magnet labs	3min 54sec
Metformin Hcl	Lupin	-	Macleods	-
Glimepiride	Dr. Reddy's	3min 37 sec	Micro labs	3min 49 sec

Table 6: Disintegration Time.

Release Rate of Drugs

S. No.	*Brand*	*In vitro drug release (%)*
1.	Cipla	100.87±0.7730
2.	Mankind	99.214±0.1735
3.	Generic	100.87±0.1980

(P value-0.0079).

Table 7: Amlodipine Besylate.

S. No.	*Brand*	*In vitro drug release (%)*
1.	Mankind	98.24±1.101
2.	Glenmark	103.22±1.802
3.	Generic	102.80±1.712

(P value-0.0194).

Table 8: Telmisartan.

S. No.	*Brand*	*In vitro drug release (%)*
1.	Sun pharma	101.04±0.83
2.	Magnet lab	99.32±0.422
3.	Generic	98.54±7.511

(P value- not significant).

Table 9: Etoricoxib.

S. No.	Brand	In vitro drug release (%)
1.	Glaxo Smith Klein	102.84±1.063
2.	Cipla	102.17±1.108
3.	Generic	98.92±1.77

(P value-0.0258).

Table 10: Allopurinol.

S. No.	Brand	In vitro drug release (%)
1.	Dr. Reddy	101.74±1.688
2.	Micro lab	103.22±1.802
3.	Generic	99.08±6.6

(P value- not significant).

Table 11: Glimepiride.

S. no.	Macleods (% drug release)	Lupin (% drug release)	Generic (%drug release)
1.	38.83±2.0	29.58±2.0	35.11±0.4
2.	47.96±2.2	41.77±1.2	49.40±1.4
3.	59.29±2.8	51.34±0.7	58.29±4.1
4.	78.90±2.3	65.47±1.8	67.38±1.3
5.	85.01±2.2	82.97±2.2	77.20±3.4
6.	95.64±1.3	92.03±3.0	86.95±1.3
7.	98.71±1.1	97.40±2.2	96.69±1.5

(P value- 0.0137).

Table 12: Metformin HCL.

In-vitro cumulative drug release of Metformin HCl

Percent Drug Content

S no.	Brand	% drug content
1.	Mankind	99.18±0.66
2.	Glenmark	100.03±0.492
3.	Generic	100.93±0.159

(P value- 0.0057).

Table 13: Telmisartan.

S. no.	Brand	% drug content
1.	Mankind	99.37±0.3
2.	Cipla	101.6±0.4
3.	Generic	102.03±1.2

(P value-0.011).

Table 14: Amlodipine Besylate.

S. no.	*Brand*	*% drug content*
1.	Dr. Reddy	100.9±0.4
2.	Magnet lab	99.42±0.3
3.	Generic	92.6±2.30

(P value- 0.0007).

Table 15: Etoricoxib.

S. no.	*Brand*	*% drug content*
1.	Glaxo Smith Klein	101.3±0.30
2.	Cipla	99.66±0.416
3.	Generic	97.65±1.86

(P value-0.0199).

Table 16: Allopurinol.

S. no.	*Brand*	*% drug content*
1.	Dr. Reddy	99.75±0.08
2.	Micro lab	100.42±0.54
3.	Generic	98.92±5.4

(P value- not significant).

Table 17: Glimepiride.

S. no.	*Brand*	*% drug content*
1.	Macleods	102.55±0.56
2.	Lupin	99.1±0.69
3.	Generic	102.1±1.6

(P value- 0.015).

Table 18: Metformin Hcl.

Result and Discussion

Pradhanmantri Bhartiya Jan Aushdhi Pariyojana launched by the Department of Pharmaceuticals, Government of India is aimed to provide quality medicines at affordable prices. The stores under the scheme are selling generic medicines which are equivalent in quality and efficacy as expensive branded drugs. But as per the survey we found that these drugs were not pharmacologically active as per the branded quality so the quality assessment was required for the benefit of healthcare department.

Quality of product refers to its confining to the standards preset to assure the desired purpose. A quality product gives not only better therapeutic effect but also gives satisfaction to the patient and increases its market value. The reason behind declination of this market value might be due to lack of awareness among the public, placebo effects of cheaper medication, poor supply chain management and these generic drugs have been found to contain less than the required amount of active ingredient (API), rendering them ineffective. To check this issue the drug controller general of India has issued an order to standardize the quality of generic drug to be bioequivalent to standard branded drug. In current the comparison of the generic drugs with multi branded molecules gives a major feedback about the therapeutic activity of the dosage form in-vitro evaluation parameters play a significant role.

The price of the branded drugs was compared with the generic drugs. The maximum difference was found to be 94.2% during observation. That was the highest difference between prices; while in case of Insulin the difference was significantly lower that was 16.02%. In case of weight variation parameter all the drugs were passed but Etoricoxib and Glimepiride from the generic category

showed high extent of excipients as compared to standard formulations, due to which the P value of release rate of these formulations was affected and showed higher P value than the standard limits. P value of Etoricoxib and Glimepiride was not significant. P value of Etoricoxib was 0.7821 and of glimepiride was 0.7612. The friability test of each formulation showed similar result with standard limits. The weight variation limit of each formulation showed significant result, limits of weight variation for 80mg or less was 10% and the observed results were in Amlodipine (Mankind) higher value was 1.614%, (Cipla) higher value was 4.52% but the generic formulation of Amlodipine was near about the highest variation limit which was 9.61%. For Telmisartan the highest variation in weight in brand (Mankind) was 1.29%, for 2nd brand (Glenmark) the highest variation limit in weight was 2.33% and for generic the value was acceptable, which was higher from branded formulation but under the IP limit that was 5.18%. The weight variation limits of Glimepiride brand (Dr.Redddy) was 1.07%, for 2nd brand (Microlab) the weight variation percent was 1.03%, and for generic formulation it was under the limit of IP that was 1.066%. For more than 80mg or less than 250 mg formulations the weight variation limits were 7.5%. The weight variation percent of brand 1st Etoricoxib (Sun pharma) was 2.10%, for 2nd brand (Magnet lab) the percent weight variation was 1.96%, and for generic formulation the percent of weight variation was under the acceptance criteria that was 1.55%. Weight variation percent in branded allopurinol (GSK) was 1.91%, for 2nd brand (Cipla) was 2.73% and for generic formulation the weight variation percent limit was 2.56% that was equivalent to branded formulations. For more than 250 mg formulation the weight variation limit percent was for Metformin HCl generic formulation was 1.17%, for brand (Lupin) the weight variation percent was 1.05% and for (Macleods) the percent was 1.05%. In terms of assay of Etoricoxib showed less than standard limit, according to the Indian Pharmacopoeia the standard limit were (95-115%), and observed limit was 94.00%.

The disintegration time of formulation is dependent upon its excipients (diluent, disintegrating agent, lubricant, glidant, and binder) because the amount of excipients allow the formulation to disintegrate in appropriate medium, all the formulation either they are generic or branded disintegrate in appropriate given time. Other formulation showed the result within the limit but Metformin HCl was a sustained release formulation, so did not require passing disintegration.

Conclusion

Though they were created to adhere to official criteria and had quality on par with that of branded formulations, several generic formulations just barely fell short of those requirements. Additionally, a few customers stated that these generic medications did not have the anticipated outcome. This suggests that the generic formulation's quality needs to be carefully monitored. This will guarantee a high-quality product at a fair price and the success of the PMBJP.

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