E. R. Zakharochkina et al /J. Pharm. Sci. & Res. Vol. 10(10), 2018, 2651-2652

ISSN:0975-1459
Journal of Pharmaceutical Sciences and Research
www.jpsr.pharmainfo.in

Analysis of Measures to Establish the Institution of Medications' Interchangeability

E. R. Zakharochkina, R. Y. Garankina, N. Bekhorashvili, S.B. Lisovskaya, A.A. Bashilov, N.V. Petrushina

Sechenov First Moscow State Medical University, Bolshaya Pirogovskaya Street, 19/1, Moscow, Russia, 119146

Abstract

The national legislation of Russia first introduced the interchangeability standards for medications in late 2014. The interchangeability is defined for the purpose of using it in procurement of medications for state and municipal needs and medication supply programs financed from state and municipal budgets and state off-budget funds. The norms on regulation of interchangeability issues were established in 2016 as part of forming the common market of medications in the Eurasian Economic Union. The Russian government adopted a roadmap for promoting competition in healthcare in early 2018, which provided for a set of measures to ensure the functioning of the interchangeability institution for the market for medications. The implementation of system analysis of regulatory documents provides information on the current state and trends in the regulation of interchangeability of medications to the market stakeholders.

Keywords: interchangeability of medications, common market for medications in the Eurasian Economic Union, development of competition in healthcare.

INTRODUCTION

The issue of interchangeability of medications has been widely debated and important for the professional community for a few years since the introduction of new standards in 2014-2015 until the prospects of the establishment of the interchangeability institute as part of the competition development in healthcare in 2018-2019 [1-4].

RESULTS AND DISCUSSION

National regulation of interchangeability of medications is established by the following basic documents:

• Federal Law "On the circulation of medications", Article 27.1,

• Government Decree No. 1154 dated 28.10.2015.

According to national standards, an interchangeable medication is the one that has proven therapeutic equivalence or bioequivalence with respect to the reference medication, as well as the qualitative and quantitative composition of the active and auxiliary substances, the dosage form and the mode of administration equivalent to the reference medication.

The most important issue in case of the unavailability of reference medication in circulation is the standard on equating the medication registered in Russia for the first time on the basis of independent preclinical and clinical studies to the latter.

The definition of interchangeability does not apply to reference medications, herbal medications, homeopathic medications, as well as the medications permitted for their medical use in Russia for more than 20 years and for which a study of their bioequivalence cannot be conducted.

Interchangeability is defined during the state registration based on the comparison with reference medication in accordance with the established parameters:

1) Equivalence of the qualitative and quantitative characteristics of pharmaceutical substances (comparability – for biological analogues);
2) Equivalence of the medicinal form;
3) Equivalence or comparability of the composition of excipients;
4) Identity of the mode of administration and use;
5) Absence of clinically significant differences in the study of the medication bioequivalence; in the case of impossibility to conduct a bioequivalence study– the absence of clinically significant differences in the safety and efficacy of the medication in the study of therapeutic equivalence; for biological analogues – the data on the absence of clinically significant differences in safety, efficacy and immunogenicity in comparison with the reference medication according to the results of clinical trials; and
6) Conformity of the medication manufacturer to the requirements of due Good Manufacturing Practice (GMP).

The initial stage in regulation process can be taken as a period until December 31, 2017, when the interchangeability was defined for:

- medications registered before 01.07.2015;and
- medications registered after 01.07.2015 in cases of filing applications for state registration or the renewal of state registration, the examination of the quality, and the examination of the relationship of expected benefits to the possible risk of using medication before 01.07.2015.

Since early 2018, information on interchangeability has to be included in the state register of medications, and the use of the results of defining the interchangeability is allowed.

The basis for determining interchangeability as part of the creation of a common market for medications of the Eurasian Economic Union is established by the Decision of the Council of the Eurasian Economic Commission dated 03.11.2016 No. 92 "On Individual Issues of Medicines Circulation".

The authorized bodies of the Member State have the right to carry out the procedure for determining the interchangeability in accordance with the national legislation of their state, and the decision will be effective only on the territory of the respective Member State. The decision of the authorized body of the Member State to issue a registration certificate valid on the entire territory of the Eurasian Economic Union. The decision is adopted without taking the results of the definition of interchangeability into account.

The definition of interchangeability does not affect the further circulation of medications within the Eurasian Economic Union.

The authorized bodies of the Member States can maintain a register (list) of interchangeable medications circulating in the territory of the Member State in accordance with the procedure established by national legislation, using the information from the unified register of registered medications in the Eurasian Economic Union – in particular, for informing the subjects of circulation.

The newest stage of state regulation on the issues of interchangeability is made by adopting a roadmap for promoting competition in healthcare. Order of the Government of Russia No. 9-r dated January 12, 2018 contains a plan of measures regarding the market for medications.

The analysis of the roadmap allowed to identify the main stages, expected regulatory documents, and the goals of the regulatory bodies to secure the operation of the institution of medications' interchangeability.

A set of measures was adopted for the formation of the interchangeability institution in 2018.

Creation of the list of reference medications has two purposes: providing developers with public information on reference medications for state registration of the reproduced medications and reducing the time for consideration of manufacturers' applications for registering the maximum selling prices for vital and essential medications.

Improving the order of creating the lists of medications assumes the exclusion of medicinal forms from them and the inclusion of modes of administration. This measure will promote the creation of equal conditions of circulation for equivalent medicinal forms.

When considering the inclusion of a medication in the list of vital and essential medications, it is proposed to establish a requirement for the commission of the Ministry of Health of Russia to provide information on all medications in the list that have equivalent indications for use. This will allow to create equal conditions for manufacturers of interchangeable medications, as well as exclude unreasonable inclusion of vital and essential medications in the list.

The issue of establishing professional responsibility of healthcare workers is being considered in order to eliminate the disproportionate responsibility of (to ?) the degree of public danger of violations in the field of medications' circulation and healthcare, as well as to remove restrictions on competition in the use of interchangeable medications and to increase the availability of medications for patients.

Explanation of the availability of cheaper equivalents of expensive medications to population and healthcare workers, establishment of a stable demand for the lower middle price segment, and prevention of low-price medication being "washed away" from sale require elaboration of the measures to inform the medical community and patients about interchangeable medications.

Imposition of administrative responsibility of manufacturers for the inclusion of irrelevant information or noninclusion of actual information about the properties and characteristics of a medication in the instruction for medical use will create competitive conditions and ensure the safety of use.

The most important innovation is related to the elimination of unjustified differences in the instructions for the medical use of medications with the same international nonproprietary name (INN). Improvement of the procedure for introducing changes in the instructions for medications with the same INN includes the imposition of the requirement to amend all instructions when changing data on contraindications and side effects of one of the medications. It is proposed to impose administrative responsibility for holders or owners of registration certificates for noncompliance with these requirements.

Pharmacies will also actively participate in the establishment of the interchangeability institution. Two requirements for pharmacies will be introduced: first offering the cheapest interchangeable medication to buyers and informing customers about the availability of cheaper equivalents of purchased medications and prices for them. These requirements will increase the price-specific and range-specific availability by preventing low-price medication from being "washed away" from sale.

The issue of making appropriate amendments to the Federal Law "On the circulation of medications" is under consideration in order to eliminate the possibility of state registration of medications with therapeutically unreasonable dosages, as well as the termination of the practice of dishonest use of instructions in procurement. These changes will relate to the imposition of a ban on the registration of reproduced medications in dosages different from the reference medications. It is also proposed to prohibit state registration of reproduced medications with instructions different from the reference medications.

The establishment of equivalence of medicinal forms will help prevent restriction of competition among medications' manufacturers registered before the adoption of the list of medicinal forms by the Ministry of Health of Russia (Order of the Ministry of Health of Russia No. 538n dated July 27, 2016).

There are plans to implement two measures to form an interchangeability institution in 2019.

Creation of a register of standard instructions for the use of interchangeable medications will eliminate the unjustified differences in instructions for medications with the same INN and create conditions for competition among manufacturers.

The measure of interchangeability is to be finalized in the second half of 2019 as part of the roadmap for the competition development. The plans are to check the registration dossier documents for imported medications for compliance with the registration dossiers for the same medications registered abroad. There are also plans to check the compliance of registration dossiers for with? reference and reproduced medications registered in Russia.

CONCLUSION

The roadmap for the competition development in healthcare is the most important document to ensure the operation of the institution of medications' interchangeability and to determine the pool of regulatory documents adopted in 2018-2019, which will have great impact on the development of the pharmaceutical market in Russia in the short term.

ACKNOWLEDGEMENTS

The work was supported by the "Russian Academic Excellence Project 5-100".

REFERENCES

1. Zakharochkina, E.R., Pravovoye pole po formirovaniyu obshchego rynka lekarstvennykh sredstv Yevraziyskogo ekonomicheskogo soyuza [Legal field for the formation of the common market of medicinal products of the Eurasian Economic Union], in *Collection of materials of the Days of Belarusian Science in Moscow: Scientific achievements of the Republic of Belarus*, Moscow 2017, pp.81-84.
2. Zakharochkina, E.R., Maksimkina, E.A., Normativnyy pul dokumentov po formirovaniyu obshchego rynka lekarstvennykh sredstvYevraziyskogo ekonomicheskogo soyuza [Normative pool of documents on the formation of the common market of medicinal products of the Eurasian Economic Union], *Bulletin of Roszdravnadzor* 2017, 5, 63-70.
3. Zakharochkina, E.R., Raisian, M.G., Behorashvili, N.Yu., Voprosy vzaimozamenyayemosti lekarstvennykh preparatov v ramkakh Yevraziyskogo ekonomicheskogo soyuza [Interchangeability of medicinal products in the Eurasian Economic Union], *Medicine: Science and Education* 2017, *23*, 106-110.
4. Zakharochkina, E.R., Rayisyan, M.G., Bekhorashvili, N., Garankina, R.Y., Ryajemov, V.V., Simonyan, M., Uniform Rules for Registering Medicinal Products in the Eurasian Economic Union, *Journal of Pharmaceutical Sciences and Research* 2018, *10(5)*, pp. 1045-1047.