Real World Evidence (RWE) and Orphan drug policies in selected Central and Eastern European (CEE) Countries

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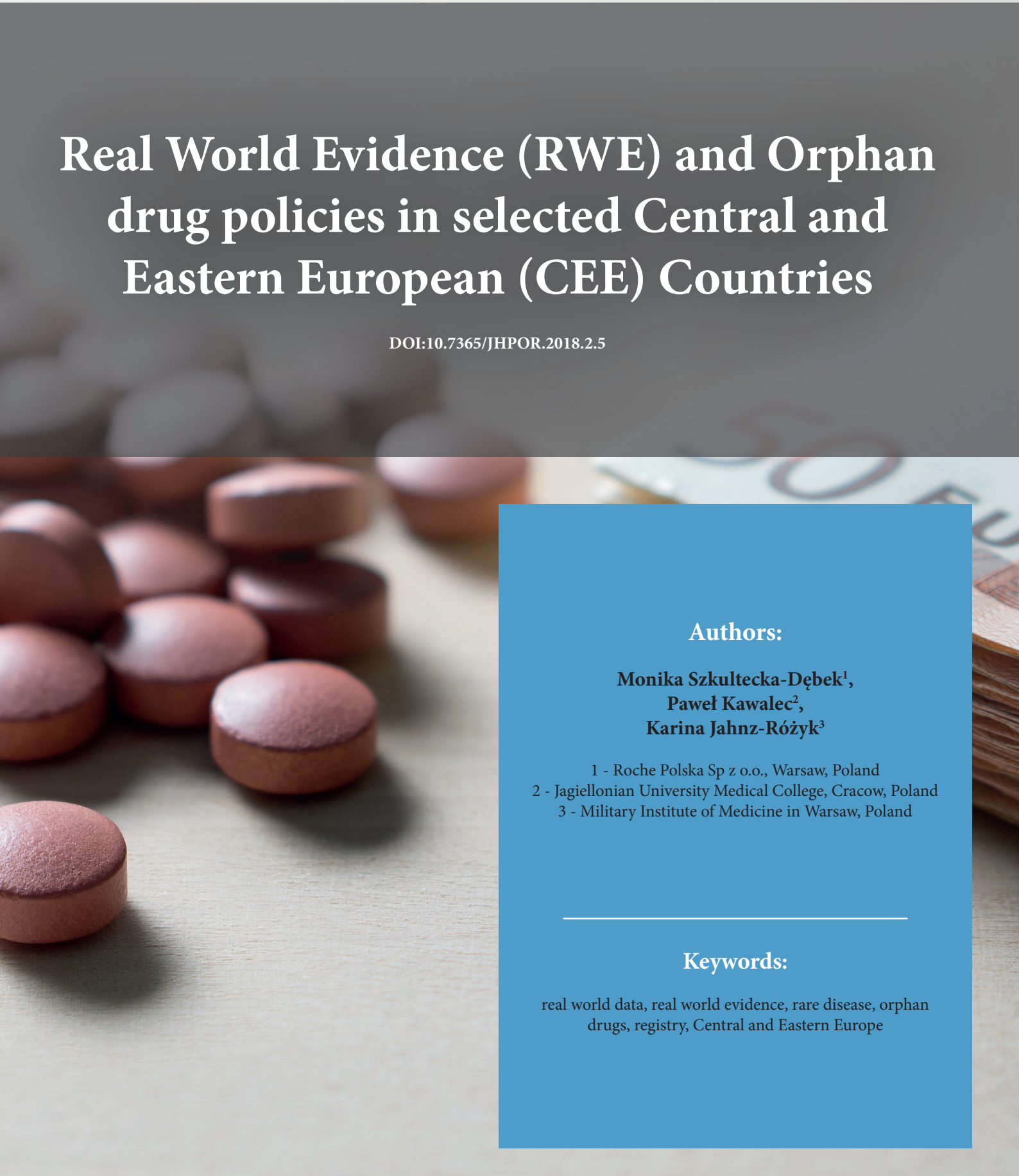

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Abstract

The rationale for the initial project performed in the Central and Eastern European countries (CEE) was to assess and to share information from the region regarding drug policies. With this special cross countries comparison we aimed to analyze the significance of real world data (RWD) and real world evidence (RWE) for access to new therapies decisions and orphan drugs policies. We focused our comparison on the selected CEE countries (Poland, Estonia, Latvia, Croatia, Czech Republic and Hungary). It shows that although all of those countries are using HTA during reimbursement process, the approach towards RWD is different. In most of the cases RWD are not mandatory for reimbursement decisions, however in all the countries RWD can be submitted as supportive information for the decision making process.

Introduction

Nowadays more and more often medicinal products are granted marketing authorization based on evidence generated e.g. from phase 2 clinical trials. The reason for that maybe that when the evidence is strong, demonstrates efficacy and provides great value to the patients in consequence it might be unethical to continue phase 3 trials and not provide the treatment to patients. However, it is must be said that even if the marketing authorization is granted, it does not have to mean that patients have access to the treatment in every European country.

Access to treatment is strongly correlated with reimbursement decisions issued by individual European member states. The reimbursement process differs across the region and there are different key elements which are taken into account by the decision-makers. Real world data are the source of evidence which could support the decision-making process, by providing additional valuable information in case where randomized clinical trials cannot be implemented or when more evidence e.g. to prove long term effects and/or safety is required.

According to our knowledge there was no such research done until now with focus on CEE. That was the reason why within an ISPOR CEE Publication Network we decided to work with several Central and Eastern European countries and to summarize key issues related to their relevant drug policies. We included the analysis of the importance of RWD for decision-making in our research. Within the project we also collected information related to the existence of special regulations facilitating access to medicines in case of rare and/or orphan diseases.[1]

The rationale for the project was to assess and share information from the region regarding drug policies, to improve understanding of pharmaceutical systems with special focus on the pricing and reimbursement system throughout the CEE countries and its use in healthcare decisions. With this special cross countries comparison we aim to analyze the significance of RWD for access to new therapies decisions and orphan drugs policies.

Methods

The comparison of RWD and orphan drugs policies as a component of drug policy in CEE countries was performed on the basis of the information collected between November 2015 – September 2016.

For the project purpose in all the countries participating in the study we used the same, especially designed questionnaire. We designed the questionnaire taking into account different aspects of drug policy and with the aim to collect information in a structured way from different countries.

With the questionnaire distributed through the ISPOR CEE publication network members we collected information about the health care systems, paying special attention to the decision making process, HTA, RWD, reimbursement decision criteria and their revisions, orphan drugs policies, patients' co-payments and cost containment measures.[1]

The countries we selected for the specific comparison of the RWD significance in the reimbursement process and the policy for rare and/or orphan diseases were Poland, Estonia, Latvia, Croatia, Czech Republic and Hungary.

Results

The comparison of the approach towards the role of RWD in the reimbursement process proves the situation to be ambiguous (table 1).

Table 1. Summary of RWD requirements for reimbursement and pricing in different CEE countries (source: prepared by the authors)

Country	RWD required	RWD not required
Poland	√	
Estonia		√
Latvia		√
Croatia		√
Czech Republic	√*	
Hungary	√**	

** for highly innovative drugs temporary reimbursement*
*** for risk sharing agreements for new products*

In Poland the access to real-world data is limited and the only registry data available are for the drugs which are used within the special drug programs.[2]

The Polish HTA guidelines however define certain requirements for RWD to be fulfilled for reimbursement dossiers preparation and submission.[3] The guidelines introduce a definition for RWD and RWE. According to the current guidelines the data which are related to practical effectiveness should be collected through reliable studies carried out under a real clinical practice conditions (real world data, RWD; real world evidence, RWE). These data source can be either a prospective or retrospective research (e.g. pragmatic clinical trials with randomization, observational studies, databases, registries, payer or other entities databases).[3]

We found out that in Estonia there is a number of registries with RWD available, however such type of data is not mandatory to be used during reimbursement process. There is no formal requirement to submit RWD for decision making process, even when reimbursement the HTA analysis is required for the new drugs. It is worth mentioning that in Estonia the RWD are collected on regular basis through the registries. There are two types of registries: national and institution based. Data about birth, abortions and death are collected in a national registry. There are also national registries for tuberculosis, myocardial infarcts and drugs. The institution-based registries are the rheumatology registry and the breast cancer registry.

The Estonian National Cancer Registry is where all the information about tumor type, incidence and gender is collected and published on annual basis. In addition the prevalence data can be available upon request.[4]

In Latvia no formal requirement for RWD submission within the reimbursement dossier exists.

The evidence required for the decision making process should be collected through randomized controlled clinical trials and it is considered for decisions only when the results are published. RWD can be a supportive argument for decision makers.[5]

Even though it is not mandatory for reimbursement process, the RWD are still collected in Latvia. The main institution responsible for collecting and summarizing all health-related data is the Center of Disease Prevention and Control (CDPC) and they can share externally the information upon special request.

The CDPC is maintaining the Cancer Registry, Registry of Tuberculosis, Registry of Sexually Transmitted Infections, Registry of Mental Disorders, Registry of Drug Abuse, Registry of Occupational Diseases, Registry of Chernobyl-Related Diseases, Registry of Diabetes Mellitus, Registry of Injuries, Registry of Congenital Abnormalities, and Multiple Sclerosis Registry.

In addition to the information collected by CDPC the NHS is collecting all data related to the use of NHS paid health services.[5]

Croatia is another country where RWE can be used only as supportive information. Local data from real world for the analysis required for reimbursement dossier could be valuable and the source for such information could be the registries owned by the Croatian Institute of Public Health. However currently only limited data are collected and that information is not published on an on-going basis and thus being available with some delay. When real world data are needed for pharmacoeconomic analysis usually those are captured through surveys.[6]

Czech Republic is an experienced country in working with registries and using RWD by payers in the decision making process. There are many registries in place and there are two types of registries: mandatory and voluntary. In the Czech Republic the requirement to provide real practice data exists for highly innovative products when reimbursement decisions are temporary (3 years) and during this period there is an obligation to collect additional data through a registry.[7]

Czech National Cancer Registry (CNCR) is an important registry where all cases of cancer are registered and their evolution is monitored on periodical basis. The information is widely used among others for incidence and prevalence assessment.[8]

The voluntary registries are usually dedicated to collect information e.g. about diagnosis or treatment and they are dedicated to disease areas.[9]

In Hungary the insurer requires RWD and analyzes it in relation to risk-sharing agreements which are mandatory for new active ingredients and the RWD are used for high-priced medicine during the central tendering process.[10] The real world data are also used to inform the government when defining the annual health insurance fund and also with the purpose of ensuring better funds allocation within the healthcare budget and for monitoring healthcare spending. The National Cancer Registry is in place since 2000. Also the NIHIF owns a database where some statistical data are collected and data about drug utilization, some medical devices as well as registered drug prices are published. The more detailed data are not published and can be obtained for research purposes upon special request.[10]

Our research confirmed that in all the compared countries there is no special orphan drugs policy in place (table 2).

Table 2. Orphan drugs policy comparison

Country	Special regulation	No special regulation
Poland		√
Estonia		√
Latvia		√
Croatia		√
Czech Republic		√
Hungary		√

In Poland orphan drugs are usually funded by NHF within the Drug Programs and there is no separate budget or specific reimbursement procedure dedicated.

Croatia is following the Article 18 of the Ordinance of Ministry of Health for reimbursement decisions and there are no exceptions for orphan drugs.

The similar situation is in Estonia where there is no special pricing policy in place for orphan drugs and during the reimbursement decision making process they are evaluated using the same criteria as the other products. There is no special program existing which would facilitate access to the treatment for patients with rare diseases. Latvia has no special policy for orphan drugs in place. In case of orphan drugs, the reimbursement can be obtained either through the reimbursement system being included into the positive list of reimbursed drugs, or upon individual request by each patient. In case of children rare diseases there is a special program for their treatment funded by the State: "Medicinal treatment for children with rare diseases".

Hungary is another CEE country where a special policy for orphan drugs reimbursement does not exist . However patients can be treated with drugs obtained upon individual request or purchased through tenders.

Czech Republic also has no special differentiation for orphan products during the reimbursement process and during drugs assessment.

Discussion

All the selected compared countries although all using HTA during reimbursement process, they differ in terms of the approach towards RWD. In most of the cases, RWD are not mandatory for reimbursement decisions, however they can be submitted as supportive data for the decision making process in all those countries.

The discussion related to RWD in Europe is ongoing and there have been roundtable discussions organised around this subject with different stakeholders from several European countries involved. During the four roundtable discussions which took place in 2016 and 2017 the international experts group discussed how to improve the understanding of the use of RWE across Europe. Together they developed a three – year roadmap for the RWE increased use and recognized RWD as a valuable source of information for market access and reimbursement decisions.[11] However the situation is still evolving and in view of the rapidly changing environment the group agreed that still significant work is required for RWD. Especially the areas of data generation, interpretation and use need more work in order to include RWD in the decision-making process.[11]

Independently from the ISPOR CEE project J. Gill et al. performed a survey related to RWD which was presented as a poster during European ISPOR meeting in 2017. There were 22 countries involved, mostly from Europe, and 40 respondents answered the LSE survey.[12]

One of the questions asked to the countries was about acceptability of lower level of evidence.

The countries like Austria, Bulgaria, Czech Republic, Slovenia, and Spain mentioned that lower evidence is considered for orphan diseases. While European countries like UK, Germany, Poland, Italy mentioned such acceptability in the case of rare diseases.[12]

From our research complemented with the results of the LSE survey we can see that even if there is no special policy for orphan drugs, in some countries the level of accepted evidence during the reimbursement process is lower

and this is the case when RWD can provide the information needed for decision making.

However there is still need for improvement of the data availability and quality. This is especially important in view of the expected increase of RWD use in economic evaluations and reimbursement decisions reviews in the following years.

Conclusions

RWD can be a valuable source of information for market access and reimbursement decisions however more work is required in the areas of data generation, interpretation and use. There is also a need for improvement in terms of the access to data and data quality.

The compared CEE countries have no special policy for orphan drugs however rare diseases are the special case when RWD can be supportive during the decision making process.

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