PASS information

Title	**Evaluation of the Effectiveness of Risk Minimization Measures: Trimetazidine Drug Utilization Study in European Countries using databases – analysis for France, Hungary, Romania and Spain**
Version identifier of the final study report	20 January 2016 (Version 2.0)
Date of last version of the final study report	16 September 2015 (Version 1.0)
EU PAS register number	ENCEPP/SDPP/9871
Active substance	Trimetazidine dihydrochloride (ATC code: C01EB15)
Medicinal product	Please refer to Annex 1 for a List of products for which this study is applicable
Product reference	Lupamadazine 35mg Retardtabletten, Znr 80108.00.00
Procedure number	DE/H/2652/01/DC as per C(2012)6196 Final
Marketing authorisation holder(s)	Consortium of companies represented by Lupin (Europe) Limited. Please refer to Annex 1 for a List of Companies (and/or their Affiliates and licensors) that are part of the consortium and for the complete list of marketing authorizations of TMZ containing products which are represented by this study.
Joint PASS	Yes
Research question and objectives	The research question is whether the risk minimization measures (DHPC and updated SmPC) were effective in influencing the prescribing behaviour of physicians for TMZ in indications no longer supported. <u>Primary objective</u>: • To assess, per country, the proportion of prescriptions of TMZ for ophthalmological or ENT diagnoses (within the scope of its past indications) among the total prescriptions of TMZ after the restriction of its indications. <u>Secondary objectives:</u> • To assess, per country, the extent of prescriptions of TMZ for ophthalmological or ENT diagnoses (within the scope of its past indications) by GPs, ophthalmologists and ENT specialists before and after the restriction of its indications. • To assess, per country, the extent of prescriptions of TMZ for ophthalmological or ENT diagnoses (within the scope of its past indications) with regards to specialists' characteristics before and after the restriction of its indications. • To illustrate, per country, the trends of prescription of TMZ for ophthalmological or ENT diagnoses (within the scope of its past indications) over time before and after its restriction of indications. • Assess, per country, the extent of prescriptions of TMZ in the cardiovascular indication before and after the restriction of its indications (amongst cardiologists and GPs). • To assess, in countries where it is feasible (France and Spain), the extent of prescriptions of TMZ for angina pectoris without other concomitant prescriptions for angina pectoris after the restriction of its indications (only amongst cardiologists and GPs).
Country(-ies) of study	*France, Hungary, Romania, and Spain*

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Marketing authorisation holder(s)

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1. Abstract

Title

Evaluation of the Effectiveness of Risk Minimization Measures: Trimetazidine Drug Utilization Study in European Countries using databases – analysis for France, Hungary, Romania and Spain – Version: 2.0, 18 January 2016

Keywords

Trimetazidine, drug utilisation study, evaluation of risk minimization measures, withdrawn indications, cohort study using existing databases

Rationale and background

Following the restriction of use by the EMA in September 2012 the MAHs are required to conduct a study to monitor the effectiveness of the DHPC in order to strengthen risk minimization measures (RMM) for TMZ.

Research question and objectives

The research question is whether the risk minimization measures (DHPC and updated SmPC) were effective in influencing the prescribing behaviour of physicians for TMZ in indications no longer approved by the Competent Authorities.

The primary objective was to

- Assess, per country, the proportion of prescriptions of TMZ for ophthalmological or ENT diagnoses (within the scope of its past indications) among the total prescriptions of TMZ after the restriction of its indications.

The secondary objectives were to

- Assess, per country, the extent of prescriptions of TMZ for ophthalmological or ENT diagnoses (within the scope of its past indications) by GPs, ophthalmologists and ENT specialists before and after the restriction of its indications.
- Assess, per country, the extent of prescriptions of TMZ for ophthalmological or ENT diagnoses (within the scope of its past indications) with regards to specialists' characteristics before and after the restriction of its indications.
- Illustrate, per country, the trends of prescription of TMZ for ophthalmological or ENT diagnoses (within the scope of its past indications) over time before and after its restriction of indications.
- Assess, per country, the extent of prescriptions of TMZ in the cardiovascular indication before and after the restriction of its indications (among cardiologists and GPs).
- Assess, in countries where it is feasible (France and Spain), the extent of prescriptions of TMZ for stable angina pectoris without other concomitant prescriptions for angina pectoris after the restriction of its indications (among cardiologists and GPs).

Study design

This was a multi-national, cross-sectional, non-interventional study using prescription or delivery databases (secondary use of data already collected by GPs, cardiologists, ophthalmologists and ENT specialists, or pharmacists) in each participating country.

Setting

The study was conducted in the outpatient setting in Hungary, Romania, Spain and France.

Subjects and study size, including dropouts

All calculations were made for TMZ prescriptions or deliveries by ENT specialists, ophthalmologists, cardiologist and GPs/other that were recorded in the country-specific databases during the 24-month reference period (July 2010 - June 2012) and the 24-month assessment period (April 2013 - March 2015) and met the selection criteria of the study.

Variables and data sources

For the analysis, variables regarding prescriptions (drug name, quarter of prescription, ICD-10 code and label of the diagnosis related to the prescription, specialty of prescriber, information on whether the prescription was an initiation or renewal) and prescribers (physician's specialty, age, gender and region of practice within the country) were considered.

The following cross-sectional databases were considered: IMS Prescribing Insights (PI) for France and Spain, National Diagnostic Index (NDI) for Romania and National Prescription Audit (NPA) for Hungary.

Results

Over all specialties, 775,859 prescriptions were evaluated in Hungary in the reference period and 849,855 in the assessment period. In Romania, 5,105,121 prescriptions in the reference period and 10,440,159 in the assessment period were analysed. For France, 1,936 (reference period) and 371 (assessment period) prescriptions were included in the study. In Spain, 713 (reference period) and 535 (assessment period) prescriptions were evaluated.

After the restriction of use (assessment period) the following proportions of TMZ use in ophthalmological and ENT indications were observed in the target countries. In Hungary, the past ophthalmological and ENT indications represent a marginal share of all TMZ prescriptions (reference period: 0.9%; assessment period: 0.6%). In Romania, the past ophthalmological and ENT indications represent a marginal share of all TMZ prescriptions in Romania (reference period: 0.1%; assessment period: 0.1%). In France, half of all TMZ prescriptions (reference period: 49.1%; assessment period: 52.8%) reported by physicians in the assessment period were for ophthalmological or ENT indications. A similar pattern of use can be observed in Spain, where about two-thirds (reference period: 78.1%; assessment period: 66.4%) of prescriptions were for ophthalmological or ENT indications. In comparison to the reference period a decrease of TMZ use in past ophthalmological and ENT indications was observed in Hungary (absolute difference: -0.4% / relative difference: -38.4%), Romania (abs. diff.: -0.0% / rel. diff.: -20.1%) and Spain (abs. diff.: -11.8%), but not in France (abs. diff.: +3.7%).

Discussion

In Hungary and Romania, the proportion of prescriptions for the past ENT and ophthalmological indications was already very low before the restriction of use and it remained low after. In France and Spain, more than half of the prescriptions were issued for the past ophthalmological and ENT indications after the restriction of TMZ use. However, these proportions must be interpreted in the context of a decrease in total number of TMZ prescriptions between the reference and the assessment period in these both countries. This corresponds to the overall decrease in TMZ sales units observed in France and Spain suggesting a reduction of the absolute risk..

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Names and affiliations of principal investigators

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