

Consultation with target patient groups: User (Readability) testing/bridging procedure Regulatory experience with Agency for medicinal products and medical devices of Bosnia and Herzegovina (ALMBiH)

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Introduction

All medicinal products placed on the market in the European Union are required by EU law to be accompanied by labeling and package leaflet which provide a set of comprehensible information for appropriate and safe use of the product.

European Commission's "Guideline on the readability of the labeling and package leaflet of medicinal products for human use", Revision 1, 12 January 2009, and "Guidance concerning consultations with target patient groups for the package leaflet Article 59(3), Article 61(1) and 63(2) of Directive 2001/83/EC as amended by Directive 2004/27/EC" require that the package information leaflet (PIL) reflects the results of consultations with target patient groups to ensure that it is legible, clear and easy to use, that these results are provided to the competent authority, and that the package leaflet must be written and designed to be clear and understandable, enabling the users to act appropriately, when necessary with the help of health professionals.

In addition, CMDh guidance "Consultation with target patient groups -meeting the requirements of article 59(3) without the need for a full test -recommendations for bridging" (CMDh/100/2007, Revision 3, December 2017), indicates that not every leaflet needs to be subject to a full test. Applicants and marketing authorisation holders (MAH) may be able to rely on testing applied to PILs for similar products. Bridging is used when leaflets are sufficiently similar in both content and layout and successful user consultation on one leaflet can be used to demonstrate that another leaflet meets the requirements of article 59(3) of Council Directive 2001/83/EC. Evidence of successful user test on the PILs used for bridging

purpose (e.g. a copy of the relevant Public Assessment Report (PAR) or European Public Assessment Report.

The aim of this paper is to present the regulatory outcome for the User testing/ Bridging procedures submitted to ALMBiH in module 1 (section 1.3.4) of the application for obtaining or renewal of marketing authorization (MA) for medicinal products manufactured by Replek Farm Ltd. Skopje in the period 2019-2022.

Material and methods

User (Readability) testing was performed as one to one, face to face interviews with selected participants using structured Questionnaire 30 up to 45 minutes. Interviews were divided in the following stages: preliminary test (pilot test) for identification of major changes to the leaflet; 1st and 2nd round of testing that involved 25 participants; revision of PIL after 1st and 2nd round of testing if necessary, in order to achieve better understanding and 3th round of testing that was to be performed, if necessary. Interviews were conducted with healthy volunteers that could be potential users of the medicinal products subject of user testing, recruited by placing an announcement in pharmacy shops by marketing team of Replek Farm Ltd. Skopje) who have signed Informed Consent Form. Total number of 25 participants was tested for each User testing. Five participants were tested in the preliminary stage, 10 participants were tested in the 1st round, and 10 participants in the 2nd round. Interviews were conducted in accordance with protocols for conducting studies during COVID-19. Interviewers were previously informed for performing of Readability testing with Instructions for the Interviewer and obtained structured

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Questionnaire based on prioritized data from final revised version of PIL. The Questionnaire was developed to include 15 questions specific to the medicine, 3 specific to the layout and 3 for overall feedback regarding the PIL. The questions addressed key safety issues and concerns of the medicine.

Results and discussion

Six User (Readability) testing were performed by REPLEK FARM Ltd Skopje, for these medicinal products: NEURO-VIT, film coated tablets 100mg/200mg/50mcg submitted for first registration; Paracetamol Syrup 100mg/5ml; Paracetamol Tablets 500mg; REKONAZOL Shampoo 2%; NORFLOKSACIN Film-coated tablets 400mg and VENTOR tablets 100mg submitted for renewal of marketing authorization to ALMBiH. Revision of PIL between two rounds of testing was assessed as necessary for NEURO-VIT, film coated tablets to achieve better understanding.

According to "Guideline on the readability of the labeling and package leaflet of medicinal products for human use", Revision 1, 12 January 2009, a satisfactory test outcome is when, for each question, 90% of all participants are able to find the information requested within the PIL and 90% can show that they understand and can act upon it. All six User (Readability) testing met these criteria and were accepted as satisfactory by ALMBiH with subsequent granting of MA or renewals of existing MA for all submissions until 2021. Submissions in 2022 are under review.

Nine Bridging User (Readability) testing were performed by REPLEK FARM Ltd Skopje, for these medicinal products: Karvedilol Replek Farm Tablets 6.25mg; 12.5mg; MHRA Public Assessment Report: Procedure No: UK/H/1170/001-4/DC; UK Licence No: PL 32256/0004-7). Ibuprofen Replek Farm Cream 100mg/g; MHRA/UKPAR /PL 10972/0089. IBUPROFEN REPLEK FARM Syrup 100mg/5ml; MHRA Public Assessment Report/UK Licence No. : PL 00037/0677. Ibuprofen Replek Farm Film-coated tablets 400mg; MHRA Public Assessment Report/UK Licence No. : PL 00037/0674. Klaritromicin Replek Farm Film-coated tablets 500 mg; Public Assessment Report (Scientific discussion) Procedure No NL/H/3682/001-002/DC). REFALGIN Tablets 500 mg; Public Assessment Report: (Decentralised Procedure No. DE/H/5204/001/DC, 03.09.2018). Atorvastatin Replek Farm Film-coated tablets 10mg; 20mg; Public Assessment Report (BASG - Public Assessment Report and Scientific discussion. Procedure No. AT/H/0667/001-004/DC). Folic acid Replek Farm Tablets 5mg; Public Assessment Report (Public Assessment Report Scientific discussion. Procedure No. SE/H/1793/01-02/DC). Olanzapin Replek Farm Film coated tablets 5 mg, 10mg; Public Assessment Report and Scientific discussion. Procedure No. IS/H/0140/001/DC; IS/H/0143/001/DC.

All nine Bridging user testing were submitted for renewal of Marketing Authorisation and were accepted as satisfactory by ALMBiH with subsequent renewal of MA.

Conclusion

User consultation and user testing is the most applied form mostly valued type of consultation with target patient groups. At the same time this procedure is time and resources consuming, usually takes 1,5 month, that may be challenging when several studies need to be performed in short period of time. Recruitment of participants may also be challenging taking into consideration voluntarily participation as well as inclusion of children. Regarding the questions, profound analysis of key safety issues and careful choice should be done, as well as suitable questionnaire. If preliminary results are not satisfactory, revision of PIL might be necessary with accompanying variation of existing PIL.

The most challenging part of this procedure is obtaining available PAR/EPAR (user consultation included) on official website of HMA or EU Medicinal Agency and even more, obtaining Parent PIL that is updated and in English. Translating Parent PIL from one of the languages used in EU to English may sometimes substantially change the context of the key safety information; hence the whole procedure may be invalid. Additionally Parent PIL may not be updated and accompanying variation of existing Daughter PIL might be necessary.

References

- CMDh Consultation with target patient groups -meeting the requirements of Article 59(3) without the need for full test-recommendations for bridging. CMDh/100/2007, Rev. 3 December 2017.
- DIRECTIVE 2001/83/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 6 November 2001 on the Community code relating to medicinal products for human use.
- EUROPEAN COMMISSION GUIDELINE ON THE READABILITY OF THE LABELLING AND PACKAGE LEAFLET OF MEDICINAL PRODUCTS FOR HUMAN USE Revision 1, 12 January 2009.
- EUROPEAN COMMISSION Guidance concerning consultations with target patient groups for the package leaflet Article 59(3) and 61(1) of Directive 2001/83/EC as amended by Directive 2004/27/EC, May 2006