

References:

[1] Nationale VersorgungsLeitlinie. Unipolare Depression. Place of Publication: AWMF online. 2022 [cited 2024.04.29]. Available from: https://register.awmf.org/assets/guidelines/nvl-005k_S3_Unipolare-Depression_2023-01.pdf; DOI: 10.6101/AZQ/000498 [2] de Aguiar Neto FS, Rosa JLG. Depression biomarkers using non-invasive EEG: A review. *Neuroscience & Biobehavioral Reviews*. 2019; 105:83–93. DOI: 10.1016/j.neubiorev.2019.07.021. [3] Hollenbenders Y, Maier C, Reichenbach A. Multiverse Analysis for Robust Depression Biomarkers Based on Electroencephalography. *GMDs*; 2023 [cited 2024.04.29]. Available from: <https://www.egms.de/static/de/meetings/gmds2023/23gmds125.shtml>; DOI: 10.3205/23gmds125. [4] Xie YH, Zhang YM, Fan FF, Song XY, Liu L. Functional role of frontal electroencephalogram alpha asymmetry in the resting state in patients with depression: A review. *World J Clin Cases* 2023; 11(9): 1903-1917. DOI: 10.12998/wjcc.v11.i9.1903. No conflict of interest

<https://doi.org/10.1016/j.nsa.2025.106086>

PS03-2052

NEUROSCIENCE APPLIED 5 (2026) 106085

EVALUATION OF PHARMACOGENOMIC INFORMATION IN PACKAGE LEAFLETS AND SUMMARIES OF PRODUCT CHARACTERISTICS FOR CNS-ACTING DRUGS IN PORTUGAL

A.R. Ferreira¹, M. Santos¹

¹ REQUIMTE/LAQV, Escola Superior de Saúde- Instituto Politécnico do Porto, Porto, Portugal

Background: Pharmacogenomics (PGx), the field that studies the influence of genetic variation on drug response, has emerged as a cornerstone of precision medicine (1). In the context of central nervous system (CNS) disorders, where therapeutic efficacy and tolerability often vary significantly between individuals, the integration of PGx into clinical practice is particularly relevant. By identifying genetic biomarkers associated with drug metabolism, efficacy, or toxicity, pharmacogenomic approaches enable tailored treatment strategies that improve outcomes and minimize adverse drug reactions (1,2). However, the implementation of PGx in routine care depends heavily on the availability and accessibility of relevant information (2), especially in regulatory documents such as Package Leaflets (PLs) and Summaries of Product Characteristics (SmPCs). These documents serve as primary sources of drug-related information for healthcare professionals and patients alike. Despite their importance, the degree to which PGx information is included, standardized, and aligned with clinical guidelines in these materials remains underexplored, particularly within the Portuguese pharmaceutical context.

Objective: This study aimed to systematically assess the prevalence, quality, and standardization of pharmacogenomic information in PLs and SmPCs for CNS-acting drugs authorized in Portugal. A secondary objective was to evaluate the degree of alignment between the PGx content identified and established international recommendations, particularly from the Clinical Pharmacogenetics Implementation Consortium (CPIC®) (3) and the Pharmacogenomics Knowledge Base (PharmGKB®).

Methods: A comprehensive content analysis was conducted on 1,136 PLs and 1,135 SmPCs for CNS-active medications listed in the national regulatory database. Each document was manually reviewed to identify any references to pharmacogenomic testing, specific genetic polymorphisms, genotype-related dosage adjustments, or contraindications based on genetic markers. Identified data were compared against CPIC® guidelines and PharmGKB® annotations to determine clinical relevance and guideline concordance. Additionally, the specific sections of the documents where PGx information was presented were recorded to assess consistency in structure and clarity of communication.

Results: Pharmacogenomic information was present in 12.0% of PLs (n=136) and 64.8% of SmPCs (n=736). In PLs, most PGx references appeared in the "Before taking the medicine" section, typically alerting patients to inform healthcare providers of known genetic conditions or testing. In SmPCs, information was most commonly found in the "Interactions with other medicinal products and other forms of interaction" section, although notable variation in terminology and presentation was observed. While a majority of the PGx references aligned with CPIC® and PharmGKB® recommendations, many lacked detail regarding clinical implications or specific guidance for healthcare decision-making.

Conclusion: The findings underscore significant variability in how pharmacogenomic information is presented across regulatory documents for CNS drugs in

Portugal. Despite relatively high representation in SmPCs, inconsistent structure and limited actionable content may hinder clinical utility. Its inconsistent structure, variability in depth, and limited actionability reduce its practical value for clinical decision-making. Moreover, the low prevalence of PGx data in PLs may hinder patient engagement and informed discussions with healthcare professionals. To ensure that pharmacogenomic knowledge translates into meaningful clinical practice, there is a pressing need for regulatory authorities to adopt harmonized guidelines that mandate the clear, concise, and actionable integration of PGx information into both PLs and SmPCs.

References:

(1) Ingelman-Sundberg M. Pharmacogenomic Biomarkers for Prediction of Severe Adverse Drug Reactions. *N Engl J Med*. 2008;358(6):637–639. (2) Whirl-Carrillo M, et al. Pharmacogenomics Knowledge for Personalized Medicine. *Clin Pharmacol Ther*. 2012;92(4):414–417. (3) Relling MV, Klein TE. CPIC: Clinical Pharmacogenetics Implementation Consortium of the Pharmacogenomics Research Network. *Clin Pharmacol Ther*. 2011;89(3):464–467. No conflict of interest

<https://doi.org/10.1016/j.nsa.2025.106085>

PS03-2053

NEUROSCIENCE APPLIED 5 (2026) 106086

PROTEOMIC INSIGHTS INTO IMMUNE MARKERS AND TREATMENT OUTCOMES IN MAJOR MENTAL HEALTH DISORDERS: A SYSTEMATIC REVIEW AND META-ANALYSIS

A. Biancalani¹, C. Possidente¹, B.T. Baune², A. Serretti³, C. Fabbri¹

¹ University of Bologna, Department of Biomedical and Neuromotor Sciences, Bologna, Italy; ² University of Münster, Department of Psychiatry and Psychotherapy, Münster, Germany; ³ Kore University of Enna, Department of Medicine and Surgery, Enna, Italy

Background: Poor treatment response and treatment resistance (TR) are well-established contributors to worsened prognosis in schizophrenia (SCZ), bipolar disorder (BD), and major depressive disorder (MDD). TR may involve shared biological mechanisms across SCZ, BD, and MDD, supporting the transdiagnostic study of biomarkers of non-response/TR to aid the early identification of individuals at risk. Peripheral blood proteins represent easily accessible biomarkers, which have been previously studied with particular focus on cytokines and other inflammatory markers, as these are involved in all major psychoses [1]. A relationship between the levels of these markers and treatment outcomes has been hypothesised [2].

Aim: We aimed to perform a systematic review and meta-analysis (SRMA) on the potential association between inflammatory protein markers and treatment outcomes across SCZ, BD, and MDD.

Methods: This SRMA was conducted by searching PsycInfo, PubMed/ MEDLINE, Scopus, and Web of Science from inception to October 25th, 2024. Original studies providing quantitative data on the association between serum and/or plasma protein markers of inflammation and psychopharmacological treatment outcomes in people with SCZ spectrum disorders, BD and related disorders, and depressive disorders were included. To infer potential causal association, only studies with a prospective design were included. No language restriction was imposed. Heterogeneity was assessed using the I² statistic (I²>50% was considered high). Global inconsistency was evaluated using the Q statistics with the corresponding p-value (no inconsistency for p-value>0.1). The study protocol followed the PRISMA guideline and was preregistered on the OSF platform.

Results: The initial search yielded 4,072 unique abstracts, 499 of these were included in the full-text screening. A hundred and fifty studies met the inclusion criteria. Due to the high heterogeneity across reported effect sizes, we included only studies reporting either the correlation between changes in biomarker levels and changes in symptom scales at follow-up, or comparisons of baseline blood biomarker levels between treatment outcomes groups. Among the 87 records entering the MA, depressive disorders were the most represented diagnoses (55 studies), followed by SCZ (21 studies), and BD (7 studies). Interleukin-6 (IL-6) was the most tested biomarker (over 50 studies), followed by tumor necrosis factor-α (TNF-α), C-reactive protein (CRP), IL-1, IL-8, IL-2, IL-10, interferon-γ. The reduction in symptom severity scores after treatment was positively correlated with the reduction in IL-6 levels (k=20, r=0.193, p<0.01, I²=78.6%, Qpvalue<0.0001), while no significant correlation was found between change in symptomatology and change of blood levels of CRP, IL-2 and TNF-α. No significant differences were found in the levels of the other biomarkers (IL-6, CRP and TNF-α) when considering response to treatment.