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36 **Letter to the Editor**
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40 Short running title: pharmacokinetics of zolpidem and sex
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To the Editor:

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4 We read with interest the paper by Polasek et al. on the evaluation of zolpidem as a mechanism-
5 based inactivator of human CYP3A in vitro with the assessment of its metabolic interaction potential with
6 CYP3A drugs [1]. The paper clearly points out the mechanism of inactivation of human CYP3A in vitro
7 along with its implications for the in vivo metabolic interactions involving CYP3A. The issue is of vital
8 importance due to the prescription rate of zolpidem with regard to efficacy and patients' safety.
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14 However, the discussion of that interesting paper left unaddressed an issue of patients' sex with
15 its endocrine specificity as if zolpidem pharmacokinetics were independent of the one. The
16 pharmacokinetics of zolpidem seems to be related to the endocrine factors associated with CYP3A4
17 metabolism. Low plasma concentrations of free testosterone may contribute to lower CYP3A activity and
18 women achieve up to 50% higher zolpidem plasma levels while the exposure to testosterone activates the
19 biotransformation via CYP3A [2]. That effect is conspicuous in the relative higher incidence of ADR with
20 zolpidem in women [3].
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28 The conclusions of the paper are true for the model study on male subjects. The discussion,
29 however, might include the exciting element of endocrine-related differences in zolpidem action.
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34 **Conflict of interest statement**

35 The authors declare that they have no conflict of interest.
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40 **References**

- 41
42 1/ Polasek TM, Sadagopal JS, Elliot DJ, Miners JO (2010) In vitro-in vivo extrapolation of zolpidem as a
43 perpetrator of metabolic interactions involving CYP3A. *Eur J Clin Pharmacol* 66: 275-283
44
45 2/ Olubodun JO, Ochs HR, von Moltke LL, Roubenoff R, Hesse LM, Harmatz JS, Shader RI, Greenblatt
46 DJ (2003) Pharmacokinetic properties of zolpidem in elderly and young adults: possible modulation by
47 testosterone in men. *Br J Clin Pharmacol* 56: 297-304
48
49 3/ Cubala WJ, Landowski J, Wichowicz HM (2008) Zolpidem abuse, dependence and withdrawal
50 syndrome: sex as susceptibility factor for adverse effects. *Br J Clin Pharmacol* 65: 444-445
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