

viduals with gender dysphoria pre- and post puberty when informing the patients themselves and their family members, as well as when carrying out the diagnostic process and favouring the proper psycho-social development of the minor. We would like to underline that in spite of the fact that gender dysphoria usually manifests from the first stages of infancy, it is indispensable to consider that the younger the individual with gender dysphoria is, the more important it is to monitor the case and be conservative with medical treatments. This is because the said condition is unstable over time. We consider it to be fundamental to evaluate whether the said dysphoria consolidates and increases in the stages after puberty, to achieve a maximum degree of certainty before starting irreversible medical treatments.

## References

1. Sánchez Lorenzo I, Mora Mesa JJ, Oviedo de Lucas O. Atención psicomédica en la disforia de identidad de género durante la adolescencia. *Rev Psiquiatr Salud Ment (Barc)*. 2015.
2. Wallien MS, Cohen-Kettenis PT. Psychosexual outcome of gender-dysphoric children. *J Am Acad Child*. 2008;47:1413–23.
3. Drummond KD, Bradley SJ, Peterson-Badali M, Zucker KJ. A follow-up study of girls with gender identity disorder. *Dev Psychol*. 2008;44:34–45.
4. De Vries AL, Cohen-Kettenis PT. Clinical management of gender dysphoria in children and adolescents: the Dutch approach. *J Homosex*. 2012;59:301–20.
5. Spack NP, Edwards-Leeper L, Feldman HA, Leibowitz S, Mandel F, Diamond DA, et al. Children and adolescents with gender identity disorder referred to a pediatric medical center. *Pediatrics*. 2012;129:418–25.
6. De Vries AL, Steensma TD, Doreleijers TA, Cohen-Kettenis PT. Puberty suppression in adolescents with gender identity disorder: a prospective follow-up study. *J Sex Med*. 2011;8:2276–83.
7. Steensma TD, Biemond R, de Boer F, Cohen-Kettenis PT. Desisting and persisting gender dysphoria after childhood: a qualitative follow-up study. *Clin Child Psychol Psychiatry*. 2011;16:499–516.
8. Zucker KJ. Gender identity development and issues. *Child Adolesc Psychiatr Clin N Am*. 2004;13:551–68.
9. Cohen-Kettenis PT, Pfäfflin F. *Transgenderism and intersexuality in childhood and adolescence: making choices*. Thousand Oaks, CA: Sage; 2003.

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## Tianeptine, antidepressant with positive benefit/risk<sup>☆</sup>



## Tianeptina, antidepresivo con perfil beneficio/riesgo positivo

Dear Editor,

In reply to the letter published in the *Rev Psiquiatr Salud Ment (Barc)*. 2016;9:176–177 by Calabozo et al.,<sup>1</sup> under the title “Tianeptine: why has it not been classified as a narcotic in Spain?”, here in *Juste SAQF* we would like to express certain considerations. Firstly, *Juste SAQF* is a pharmaceutical company which commenced the commercialisation of medicines in the Spanish market in the year 1922, and since its origins it has always been characterised by strict compliance with the parameters that guarantee patient safety and well-being. Health is the chief objective of *Juste*, and therefore, according to the pharmacovigilance regulations in force, it monitors medicines and continuously and permanently evaluates their safety profile.

Tianeptina (Zinosal<sup>®</sup>) is a generic medicine which was authorised in Spain on 13/08/2014, and it is currently commercialised by our company. Tianeptine has been com-

mercialised in France since 1988, and it is authorised in 15 European countries and in 66 countries around the world. The safety profile of Tianeptine is still monitored in the countries where it is authorised, and additionally, it is included in the EURD-list of the EMA for single evaluation of the Periodical Safety Report (PSUSA/00002943/201806; updated DLP: 04/03/2016).

This pharmacovigilance is fundamental given that, as with all medicines, adverse effects may arise which permit the evaluation of each drug in terms of its benefits and risks for each specific disease. In this respect, it is necessary to underline that the last revision undertaken by the French authorities on 5 December 2012, on Tianeptine, concluded that its benefit/risk ratio is still positive.<sup>2</sup> Based on this evaluation, in the section of adverse reactions of the technical data sheet of Zinosal<sup>®</sup>, it is said that it may be involved in “*substance abuse and dependency*”, although it states that this basically involves a specific type of patient: “*above all in patients under 50 years old with a history of drug or alcohol abuse*”, while this adverse reaction is classified under the heading of “*Rare*” (>1/10,000 to >1/1000).

Two years later, in 2014, the French National Medicine and Health Products Safety Agency re-evaluated the information from 2012 to 2013, concluding that the number cases of abuse involving Tianeptine had fallen, given that only 7 cases<sup>3</sup> had been described (ANSM, 2014).

Moreover, it is important to emphasise that Tianeptine has a different pharmacodynamic profile from those of current antidepressants,<sup>4,5</sup> and that it has been proven in

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comparative studies to be more effective than a placebo and not inferior to tricyclic antidepressants or SSRI, with a more favourable tolerability profile.<sup>5-11</sup>

As the French public health authority (HAS) points out, Tianeptine<sup>2</sup> has a positive benefit/risk ratio. Given that not all patients respond to existing antidepressant treatments, and given the clearly different action of Tianeptine on possible mechanisms that lead to an antidepressant effect, approval of its use in Spain represents a broadening of the spectrum of antidepressant treatment that has duly been authorised by the AEMPS for commercialisation under the commercial name of Zinosal<sup>®</sup>. Juste guarantees the pharmacovigilance of this drug in the same way that it does for all those within its catalogue.

## References

1. Calabozo B, Molina V, Uribe F. Tianeptina: ¿por qué en España no ha sido catalogada como estupefaciente? *Rev Psiquiatr Salud Ment (Barc)*. 2016;9:174-7.
2. Haute Autorité de Santé (HAS). Commission de la transparence. Avis, 5 December 2012. Available at: [http://www.has-sante.fr/portail/upload/docs/evamed/CT2029\\_STABLON\\_ReevalSMR\\_avis2\\_CT10411\\_CT12029.pdf](http://www.has-sante.fr/portail/upload/docs/evamed/CT2029_STABLON_ReevalSMR_avis2_CT10411_CT12029.pdf) [accessed 04.07.16].
3. ANSM. Comité technique des Centres d'Évaluation et d'Information sur la Pharmacodépendance-CT022013043 Zolad; 2014.
4. McEwen BS, Chattarji S, Diamond DM, Jay TM, Reagan LP, Svenningsson P, et al. The neurobiological properties of tianeptine (Stablon): from monoamine hypothesis to glutamatergic modulation. *Mol Psychiatry*. 2010;15:237-49.
5. Yoo I, Woo JM, Lee SH, Fava M, Mischoulon D, Papakostas GI, et al. Influence of anxiety symptoms on improvement of neurocognitive functions in patients with major depressive disorder: a 12-week, multicenter, randomized trial of tianeptine versus escitalopram, the CAMPION study. *J Affect Disord*. 2015;185:24-30.
6. Lõo H, Ganry H, Dufour H, Guelfi JD, Malka R, Olié JP, et al. Long-term use of tianeptine in 380 depressed patients. *Br J Psychiatry Suppl*. 1992;15:61-5.
7. Guelfi JD. Efficacy of tianeptine in comparative trials versus reference antidepressants. An overview. *Br J Psychiatry Suppl*. 1992;72-5.
8. Costa e Silva JA, Ruschel SI, Caetano D, Rocha FL, da Silva Lippi JR, Arruda S, et al. Placebo-controlled study of tianeptine in major depressive episodes. *Neuropsychobiology*. 1997;35:24-9.
9. Bonierbale M, Lancon C, Tignol J. The ELIXIR study: evaluation of sexual dysfunction in 4557 depressed patients in France. *Curr Med Res Opin*. 2003;19:114-24.
10. Kasper S, McEwen BS. Neurobiological and clinical effects of the antidepressant tianeptine. *CNS Drugs*. 2008;22:15-26.
11. Jeon HJ, Woo JM, Lee SH, Kim EJ, Chung S, Ha JH, et al. Improvement in subjective and objective neurocognitive functions in patients with major depressive disorder: a 12-week, multicenter, randomized trial of tianeptine versus escitalopram, the CAMPION study. *J Clin Psychopharmacol*. 2014;34:218-25.

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