



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

6 May 2010
EMA/HMPC/216362/2008
Committee on Herbal Medicinal Products (HMPC)

List of references supporting the assessment of *Valeriana*

This document was valid from 6 May 2010 until September 2019. It is now superseded by a [new version](#) adopted by the HMPC on 25 September 2019 and published on the EMA website.

Final

The Agency acknowledges that copies of the underlying works used to produce this monograph were provided for research only with exclusion of any commercial purpose.

Abourashed EA, Koetter U, Brattström A. *In vitro* binding experiments with a valerian, hops and their fixed combination extract (Ze91019) to selected central nervous system receptors. *Phytomedicine* 2004; 11: 633-638

Balduini W, Cattabeni F. Displacement of [³H]N⁶-cyclohexyladenosine binding to rat cortical membranes by an hydroalcoholic extract of *Valeriana officinalis*. *Med Sci Res* 1989; 17: 639-640

Bos R, Woerdenbag HJ, De Smet PAGM et al. *Valeriana* species. In: De Smet PGMA, Keller K, Haensel R, Chandler RD (eds.): *Adverse effects of herbal drugs*. Vol 3, Springer-Verlag Berlin, 1998; 165-180

Brattström A. Wirksamkeitsnachweis von Phytopharmaka am Beispiel einer Hopfen-Baldrian-Kombination. *Forsch Komplementärmed* 1996; 3: 188-195

Brattström A. Scientific evidence for a fixed extract combination (Ze 91019) from valerian and hops traditionally used as a sleep-induced aid. *Wien Med Wochenschr* 2007; 157 (13-14): 367-370

Butterweck V, Brattstroem A, Grundmann O, Koetter U. Hypothermic effects of hops are antagonized with the competitive melatonin receptor antagonist luzindole in mice. *J Pharm Pharmacol* 2007; 59: 549-552

Cavadas C, Araújo I, Cotrim MD, Amaral T, Cunha AP, Macedo T, Fontes Ribeiro C. *In vitro* study on the interaction of *Valeriana officinalis* L. extracts and their amino acids on GABA-A receptor in rat brain. *Arzneim.-Forsch./Drug Res* 1995; 45/II (7): 753-755



Coxeter PD, Schluter PJ, Eastwood HL, et al. Valerian does not appear to reduce symptoms for patients with chronic insomnia in general practice using a series of randomised n-of-1 trials. *Complementary Therapies in Medicine* 2003; 11: 215-222

Dorn M. Efficacy and tolerability of valerian versus oxazepam in non-organic and non-psychiatric insomnias: a randomized, double-blind, clinical, comparative study. *Komplementärmedizin und Klassische Naturheilkunde* 2000; 7: 79-84

Estrada J, Gozala F, Cecchini L, Casquette E. Contact urticaria from hops (*Humulus lupulus*) in a patient with previous urticaria-angioedema from peanut, chestnut, and banana. *Contact Dermat* 2002; 46: 127

Flesch P. Hopfen-Baldrian-Kombination als Benzodiazepin-Ersatz? *Geriatric Praxis* 1, 1997 (suppl.) 21-23

Füssel A, Wulf A, Brattström A. Effect of a fixed valerian-hop extract combination (ZE91019) on sleep polygraphy in patients with non-organic insomnia: a pilot study. *Eur J Med Res* 2000; 18 (5): 385-390

Gerhauser C, Frank N. Xanthohumol, a new all-rounder? *Molec Nutr & Food Res* 2005; 49 (9): 821-823

Göggelmann W, Schimmer O. Mutagenic activity of phytotherapeutic drugs. In: Knudsen I, editor. *Genetic Toxicology of the Diet*. New York, Alan R. Liss, 1986; 63-72

Grundmann O, Brattström A, Koetzer U, Butterweck V. Hypothermic effects of hops could antagonise with the competitive melatonin receptor antagonist luzindole. *Planta Medica* 2006; 72 (11): 1065, 281

Hendriks H, Bos R, Woerdenbag HJ, Joster AS. Central nervous depressant activity of valerenic acid in the mouse. *Planta Med* 1985; 51: 28-31

Jacobs BP, Bent S, Tice JA, et al. An internet-based randomized, placebo-controlled trial of kava and valerian for anxiety and insomnia. *Medicine* 2005; 84: 197-207

Kamm-Kohl AV, Jansen W, Brockmann P. Moderne Baldriantherapie gegen nervöse Störungen im Senium. *Med Welt* 1984; 35: 1450-1454

Koetter U, Schrader E, Käufeler R, Brattström A. A randomized, double-blind, placebo-controlled, prospective clinical study to demonstrate clinical efficacy of a fixed valerian hops extract combination (Ze 91019) in patients suffering from non-organic sleep disorder. *Phytother Res* 2007; 21: 847-851

Lataster MJ, Brattström A. Die Behandlung von Patienten mit Schlafstörungen. Wirksamkeit und Verträglichkeit von Baldrian-Hopfen-Dragees. *Notabene Medici* 1996; 4: 182-185

Leathwood PD, Chauffard F, Heck E, Munoz-Box R. Aqueous extracts of valerian root (*Valeriana officinalis* L.) improves sleep quality in man. *Pharmacol Biochem Behav* 1982; 17: 65-71

Mennini T, Bernasconi P, Bombardelli E, Morazzoni P: *In vitro* study on the interactions of extracts and pure compounds from *Valeriana officinalis* roots with GABA, benzodiazepine and barbiturate receptors in rat brain. *Fitoterapia* 1993; 64 (4): 291-300

Milligan S, Kalita J, Pocock V, Heyerick A, De Cooman L, Rong H, De Keukeleire D. Oestrogenic activity of the hop phyto-oestrogen, 8-prenylnaringenin. *Reproduction* 2002; 123: 235-242

Morin CM, Koetter U, Bastien C, Wane JC, Wootter V. Valerian-hops combination and diphenhydramine for treating insomnia: a randomised placebo-controlled clinical trial. *Sleep* 2005; 28 (11): 1465-1471

Mueller-Limmroth W, Ehrenstein W. Experimental studies of the effects of Seda-Kneipp on the sleep of sleep disturbed subjects: implications of the treatment of different sleep disturbances. *Med Klin* 1977; 72: 1119-1125

- Mueller CE, Schumacher R, Brattström A, Abourashed EA, Koetter E. Interactions of valerian extracts and a fixed valerian-hop extract combination with adenosine receptors. *Life Sciences* 2002; 71 (16): 1939-1949
- Notter D, Brattström A, Morandell D, Polasek W. Wirksamkeit und Sicherheit eines Baldrian-Hopfen-Kombinationspräparates bei verschiedenen Schlafstörungen. *Phytotherapie* 2003; 3: 9-12
- Ortiz JG, Nieves-Natal J, Chavez P. Effects of *Valeriana officinalis* extracts on [³H]flunitrazepam binding, synaptosomal [³H]GABA uptake and hippocampal [³H]GABA release. *Neurochem Res* 1999; 24: 1373-1378
- Rodenbeck A, Hajek G. Polysomnographische Pilotstudie zur Wirkung von Hopfen/Baldrian auf den Schlaf von Patienten mit primärer Insomnie. Eine doppelblinde, randomisierte, placebokontrollierte Studie im Schlaflabor 1998, Study Report MI 9221
- Romero-Jimenez M. et al. Genotoxicity and antigenotoxicity of some traditional medicinal herbs. *Mut Res* 2005; 147-155.
- Rücker G, Tautges J, Sieck A, Wenzl H., Graf E. Untersuchungen zur Isolierung und pharmakodynamischen Aktivität des Sesquiterpens Valeranon aus *Nardostachys jatamansi* DC. *Arzneim.-Forsch./Drug Res* 1978; 28/I (1): 7-13
- Schellenberg A, Sauer S, Abourashed EA, Koetter U, Brattström A. The fixed combination of valerian and hops (Ze91019) acts via a central adenosine mechanism. *Planta Med* 2004; 70: 694-697
- Schmitz M, Jäckel M. Comparative study for assessing quality of life of patients with exogenous sleep disorders (temporary sleep onset and sleep interruption disorders) treated with a hops-valerian preparation and a benzodiazepine drug. *Wien Med Wochenschr* 1998; 148: 291-298
- Stevens JF, Page JE. Xanthohumol and related prenylflavonoids from hops and beer: to your good health! *Phytochem* 2004; 65: 1317-1330
- Vonderheid-Guth B, Iodora A, Brattström A, Dimpfel W. Pharmacodynamic effects of valerian and hops extract combination (Ze 91019) on the quantitative-topographical EEG in healthy volunteers. *Eur J Med Res* 2000; 5: 139-144
- Von Skramlik E. Über die Giftigkeit und Verträglichkeit von ätherischen Ölen. *Pharmazie* 1959; 14: 435-445
- Vorbach EU, Goertelmeyer R, Brüning J. Therapie von Insomnien. Wirksamkeit und Verträglichkeit eines Baldrianpräparates. *Psychopharmakontherapie* 1996; 3: 109-115
- Wegener T. Phytopharmaka zur Anxiolyse. Zur Wirkung einer Kombination von Baldrian und Hopfen bei Angstzuständen. *Dt Apoth Ztg* 2003; 143: 618-625
- Yuan CH, Mehendale S, Yiao Y, et al: The gamma-aminobutyric acidergic effects of valerian and valerenic acid on rat brainstem neuronal activity. *Anesth Anal* 2004; 98: 353-358
- Ziegler G, Ploch, Miettinen-Baumann A, Colle W. Efficacy and tolerability of valerian extract LI 156 compared with oxazepam in the treatment of non-organic insomnia – a randomized, double-blind, comparative clinical study. *Eur J Med Res* 2002; 7: 480-486