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Benzodiazepines for the long-term treatment of anxiety disorders? – Authors' reply

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We thank Prashant Tibrewal and colleagues for their Correspondence, in which they argue that benzodiazepines are an important medication for refractory anxiety disorders. We agree. We wrote our Seminar[1] for a broad clinical readership, and we were particularly careful about treatment recommendations that would apply for general care. Although benzodiazepines might be an option in specialised settings, the risk of inappropriate over-medication potentially leading to long-term use is considerable in primary care, leading to substantial public health problems.

We do not question the overall efficacy of benzodiazepines for reducing anxiety symptoms.[1] Large-scale (network) meta-analyses[2,3] show that benzodiazepines reduce anxiety symptoms significantly more than placebo in, for example, patients with generalised anxiety disorder or panic disorder. The efficacy of benzodiazepines was similar to that of antidepressants, but the acceptability of benzodiazepines was comparatively poor.[2,3] Also, on benzodiazepine withdrawal, anxiety symptoms often recur, leading to long-term benzodiazepine use. In line with pertinent guidelines by the National Institute for Health and Care Excellence,[4] we therefore do not consider benzodiazepines to be a first-line treatment option due to poor acceptability, their potential for adverse interactions with alcohol and opioids, the potential for addiction and dependence in groups at high risk, and increased risk for falls and cognitive impairment. Our views also consider the announcement from the US Food and Drug Administration in September, 2020, concerning an update to the boxed warning on all benzodiazepines to explicitly "address the serious risks of abuse, addiction, physical dependence, and withdrawal reactions"[5] among this class of medications. The new

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prescribing information advises clinicians to warn patients of the risks of benzodiazepines, assess patients' risk of abuse, misuse, and addiction, use caution when coprescribing benzodiazepines with opioids, and consider alternate therapies first. These were all leading arguments for us to indicate that benzodiazepines should be given cautiously and only after failure of first-line treatments.

We agree with Tibrewal and colleagues that benzodiazepines can be useful treatments in specialised settings, in which more patients might suffer from refractory anxiety disorders. However, detailed psychopharmacological knowledge, highfrequency monitoring to avoid long-term use, and careful assessment of their risk–benefit ratio, including screening for risk factors, are prerequisites for prescription. For patients already prescribed a benzodiazepine, clinicians should regularly re-evaluate the use of benzodiazepines, aiming for the lowest effective dose for the shortest treatment duration possible, and gradually taper off benzodiazepines after adequate remission. Under these specialised conditions, benzodiazepines are clearly valuable in the hands of the expert.

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