

PEER-REVIEW REPORT

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Title: Recent Advances in the treatment of opioid use disorders – focus on long-acting buprenorphine formulations

Reviewer's code: 00505042

Position: Editorial Board

Academic degree: PhD

Professional title: Professor

Reviewer's Country/Territory: United States

Author's Country/Territory: Germany

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Reviewer chosen by: AI Technique

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The author presents a comprehensive review of buprenorphine and its slow-release formulations. References are up to date, and the relative advantages of these formulations are covered in detail. Thereby, the review will be useful to clinicians and patients as well. A few relatively minor issues need to be addressed. Page 5. 'The overall findings indicate a 1-year retention rate of 57% and a 3-year retention rate of 38.4%. A number of factors modify the retention rate: age, (additional) substance use, dose of the maintenance drug, legal issues and attitudes towards OMT predict outcome.' It would be helpful to provide a comparison between methadone and buprenorphine gleaned from this or other studies. page 7. '13.2% of OUD patients had injection-site adverse events' This is also the case for the other formulations. It would be helpful to discuss whether this is a substantial issue, in view of the long duration of the treatment at the local site. Page 7. 'Usually, treatment with CAM 2038 is initiated with weekly injections. Later on the patient can be transferred from sublingual to monthly depot injections.' This does not make sense. Page 10. 'The FDA had require (spelling) a special risk management for this treatment. The „Probuphine Risk Evaluation and Mitigation Strategy“ (REMS) program was initiated (<https://probuphinerems.com>). Meanwhile Titan Pharmaceuticals on oct 15, 2020 announced to discontinue its US propupine implant sales.' This requires further discussion; why did Titan discontinue the drug? Page 23>. Is morphine a full agonist? Typically it is viewed as partial agonist with relatively high efficacy. A number typos and phrases need correcting: 'there is now doubt about the efficacy of these compounds'. Supposedly, 'no doubt' is meant. 'The adherence to treatment depends on adequate dosing and retention can be improved by adequate dosage' 'were given in patients with opioid dependent.'" With respect to the injection sites mild local reactions were reported by 18.-22 % of the participants.'



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‘Overall these data indicate that RBP-6000 is effective.’ ‘The efficacy of buvidal has also studied demonstrated in several clinical trials.’ ‘The dose of the buprenorphine implant released’ ‘Steady state conditions were noted recorded after 3-4 weeks’ ‘In addition, the utilization of health care resources will be reduced.’ ‘Depot formulations are already used in prisons’ ‘will probably be no major problem introducing’