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Dear Healthcare Provider,

Thank you for your inquiry regarding IGALMI™ (dexmedetomidine) sublingual film and somnolence.

IGALMI is an alpha-2 adrenergic receptor agonist indicated in adults for the acute treatment of agitation associated with schizophrenia or bipolar I or II disorder.

IGALMI is an orally dissolving film formulation for sublingual or buccal use under the supervision of a health care provider.

Limitations of Use: The safety and effectiveness of IGALMI has not been established beyond 24 hours from the first dose.

The approved IGALMI package insert/prescribing information contains the following information:

- IGALMI can cause somnolence. In placebo-controlled clinical studies in adults with agitation associated with schizophrenia or bipolar I or II disorder, somnolence (including fatigue and sluggishness) was reported in 23% and 22% of patients treated with IGALMI 180 mcg and 120 mcg, respectively, compared to 6% of placebo-treated patients. Patients should not perform activities requiring mental alertness, such as operating a motor vehicle or operating hazardous machinery, for at least eight hours after taking IGALMI.

Additional published information may be available for intravenous (IV) dexmedetomidine. Please refer to the bibliography below. This bibliography is not comprehensive but may provide additional information relevant to your query. These references were identified from the National Library of Medicine (PubMed) on 22 June 2023 using search terms [dexmedetomidine] and [somnolence] and may include information outside the FDA approved indication for IGALMI. They are included as a professional courtesy and are not intended to recommend use of IGALMI outside the FDA approved indication.

Important Information
BioXcel Therapeutics does not recommend the use of IGALMI outside of the FDA approved prescribing information. Please refer to the IGALMI FDA approved package insert for important safety information and full prescribing information at https://www.igalmihcp.com/igalmi-pi.pdf

If you have any additional questions and would like to speak with our Medical Affairs team, please contact medicalaffairs@bioxceltherapeutics.com.

Reference: IGALMI [Prescribing Information]. New Haven, CT: BioXcel Therapeutics, Inc; April 2022

Selected Dexmedetomidine Bibliography:

1. Preskorn SH, Zeller S, Citrome L, et al. Effect of Sublingual Dexmedetomidine vs Placebo on Acute Agitation Associated With Bipolar Disorder: A Randomized Clinical Trial. *JAMA*. 2022;327(8):727-736. doi:10.1001/jama.2022.0799

2. Citrome L, Preskorn SH, Lauriello J, et al. Sublingual Dexmedetomidine for the Treatment of Acute Agitation in Adults With Schizophrenia or Schizoaffective Disorder: A Randomized Placebo-Controlled Trial. *J Clin Psychiatry*. 2022;83(6):22m14447. Published 2022 Oct 3. doi:10.4088/JCP.22m14447
3. Karlin DM, Nelson LA, Campbell AR. Dexmedetomidine Sublingual Film: A New Treatment to Reduce Agitation in Schizophrenia and Bipolar Disorders [published online ahead of print, 2023 Apr 29]. *Ann Pharmacother*. 2023;10600280231171179. doi:10.1177/10600280231171179

For U.S. Healthcare Professionals Use Only

This information is provided as a professional courtesy in response to your unsolicited request for information and may contain information that is not part of the FDA-approved labeling. This information is intended to provide pertinent data that may assist you in forming your own conclusions and making your own decisions. It is not intended to recommend any use of IGALMI other than recommended in the FDA-approved prescribing information.

The information contained in this letter is for the sole use of the intended recipient(s). It is for informational purposes only and not intended for publication or distribution.

To report SUSPECTED ADVERSE REACTIONS, contact BioXcel Therapeutics, Inc. at 1-833-201-1088 or medinfo@bioxceltherapeutics.com or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch