555 Long Wharf Drive
12th Floor
New Haven, CT 06511 USA

medicalaffairs@bioxceltherapeutics.com

www.bioxceltherapeutics.com

Dear Healthcare Provider,

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

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 self administration 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.

As of June 2023, there have been no reports of Igalmi overdose. In the event of Igalmi overdose, consider contacting Poison Control Center (1-800-222-1222).

The approved IGALMI package insert/prescribing information contains the following information from experience with intravenous dexmedetomidine (IGALMI is not approved for intravenous use):

- In a tolerability study of intravenous dexmedetomidine in which healthy adult subjects were administered doses at and above the recommended dose of 0.2 to 0.7 mcg/kg/hour, the maximum blood concentration was approximately 13 times the upper boundary of the therapeutic range for the intravenous dexmedetomidine (IGALMI is not approved for intravenous use). The most notable effects observed in two subjects who achieved the highest doses were first degree atrioventricular block and second-degree heart block.

- Five adult patients received an overdose of intravenous dexmedetomidine in intensive care unit sedation studies. Two patients who received a 2 mcg/kg loading dose (twice the recommended loading dose) over 10 minutes, experienced bradycardia and/or hypotension.

- One patient who received a loading intravenous bolus dose of undiluted dexmedetomidine (19.4 mcg/kg), had cardiac arrest from which he was successfully resuscitated.

- Consider contacting Poison Control Center (1-800-222-1222) or a medical toxicologist for overdosage management recommendations for IGALMI.

Additional published information may be available for intravenous (IV) or intrathecal 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 [overdose] 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 Inc; 2022

Selected References Relevant to Dexmedetomidine and Overdose:

1. Jorden VS, Pousman RM, Sanford MM, Thorborg PA, Hutchens MP. Dexmedetomidine overdose in the perioperative setting. *Ann Pharmacother*. 2004;38(5):803-807. doi:10.1345/aph.1D376

2. Bernard PA, Makin CE, Werner HA. Hypoglycemia associated with dexmedetomidine overdose in a child? J Clin Anesth. 2009;21(1):50-53.

3. Li C, Clifford M. Dexmedetomidine infusion overdose during anesthesia: A case report. Pediatr Anesth. 2020;30(2):191-193.

4. Nath SS, Singh S, Pawar ST. Dexmedetomidine overdosage: An unusual presentation. Indian J Anesth. 2013;57(3):289-291.

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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