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Dear Healthcare Provider,

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

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:

- The recommended initial dose of IGALMI for patients 65 years and older for mild, moderate, or severe agitation is 120 mcg with an optional 2nd or 3rd dose of 60 mcg. The maximum recommended total daily dosage for patients 65 years and older is 240 mcg.
- In BioXcel Therapeutics clinical studies for the acute treatment of agitation associated with schizophrenia or bipolar I or II disorder, fifteen patients ≥ 65 years of age were enrolled; no patients were 75 years of age or older. Of the total number of IGALMI-treated patients in these clinical studies, 11/507 (2.2%) were 65 years of age and older.
- Clinical studies of IGALMI did not include sufficient numbers of patients 65 years of age and older to determine whether there were differences in the effectiveness of IGALMI in the acute treatment of agitation associated with schizophrenia or bipolar I or II disorder compared to younger adult patients.
- The pharmacokinetic profile of intravenous dexmedetomidine was not altered by age. There were no differences in the pharmacokinetics of dexmedetomidine in young (18-40), middle age (41-65 years), or older (>65 years) subjects. The pharmacokinetic profile of intravenous dexmedetomidine was not altered in geriatric subjects.
- Data from an intravenous dexmedetomidine product demonstrated a higher incidence of bradycardia and hypotension in geriatric patients compared to younger adult patients.
- Avoid use of IGALMI in patients with hypotension, orthostatic hypotension, advanced heart block, severe ventricular dysfunction, or history of syncope. After IGALMI administration, patients should be adequately hydrated and should sit or lie down until vital signs are within normal range. If a patient is unable to remain seated or lying down, precautions should be taken to reduce the risk of falls. Ensure that a patient is alert and not experiencing orthostatic hypotension or symptomatic hypotension prior to allowing them to resume ambulation.

Additional published data 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.

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 concerns 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 Dexmedetomidine Bibliography

1. Weerink MAS, Struys MMRF, Hannivoort LN, Barends CRM, Absalom AR, Colin P. Clinical Pharmacokinetics and Pharmacodynamics of Dexmedetomidine. *Clin Pharmacokinet*. 2017;56(8):893-913. doi:10.1007/s40262-017-0507-7

2. Janssen TL, Alberts AR, Hooft L, Mattace-Raso F, Mosk CA, van der Laan L. Prevention of postoperative delirium in elderly patients planned for elective surgery: systematic review and meta-analysis. *Clin Interv Aging*. 2019;14:1095-1117. Published 2019 Jun 19. doi:10.2147/CIA.S201323

3. Mart MF, Williams Roberson S, Salas B, Pandharipande PP, Ely EW. Prevention and Management of Delirium in the Intensive Care Unit. *Semin Respir Crit Care Med*. 2021;42(1):112-126. doi:10.1055/s-0040-1710572

4. Deiner S, Luo X, Lin HM, et al. Intraoperative Infusion of Dexmedetomidine for Prevention of Postoperative Delirium and Cognitive Dysfunction in Elderly Patients Undergoing Major Elective Noncardiac Surgery: A Randomized Clinical Trial. *JAMA Surg*. 2017;152(8):e171505. doi:10.1001/jamasurg.2017.1505

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.