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Dear Healthcare Provider,

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

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 have not been established beyond 24 hours from the first dose.

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

> Available published literature reports the presence of dexmedetomidine in human milk following intravenous administration. There is no information regarding the effects of dexmedetomidine on the breastfed child or the effects on milk production. Advise women to monitor the breastfed infant for irritability. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for IGALMI and any potential adverse effects on the breastfed child from IGALMI or from the underlying maternal condition.

The information below is from the *Drugs and Lactation Database (LactMed®)*[1]*:*

> Limited data indicate that very small amounts of dexmedetomidine are excreted into breastmilk for 4 to 6 hours after the end of an intravenous infusion. The drug is absent from breastmilk by 24 hours after the end of an infusion. The amounts in milk after sublingual use are expected to be less than after intravenous infusion. Because of the low dose in milk and its poor oral bioavailability, dexmedetomidine would not be expected to cause adverse effects in breastfed infants or neonates. Monitor the breastfed infant for irritability during sublingual use.

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 10 June 2023 using search terms [dexmedetomidine] and [lactation] 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 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

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Selected Dexmedetomidine Bibliography

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3. Nakanishi R, Yoshimura M, SunOS M, et al. Detection of dexmedetomidine in human breast milk using liquid chromatography-tandem mass spectrometry: Application to a study of drug safety in breastfeeding after Cesarean section. *J Chromatogram B Analyt Technol Biomed Life Sci*. 2017;1040:208-213. doi:10.1016/j.jchromb.2016.11.015
4. Wang Y, Fang X, Liu C, Ma X, Song Y, Yan M. Impact of Intraoperative Infusion and Postoperative PCIA of Dexmedetomidine on Early Breastfeeding After Elective Cesarean Section: A Randomized Double-Blind Controlled Trial. *Drug Des Devel Ther*. 2020;14:1083-1093. Published 2020 Mar 11. doi:10.2147/DDDT.S241153
5. Yoshimura M, Kunisawa T, Suno M, et al. Intravenous dexmedetomidine for cesarean delivery and its concentration in colostrum. *Int J Obstet Anesth*. 2017;32:28-32. doi:10.1016/j.ijoa.2017.05.002

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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. Please see accompanying full Prescribing Information.

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.