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Dear Healthcare Provider,

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

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:

> There are no available data on IGALMI use in pregnant women to evaluate for a drug-associated risk of major birth defects, miscarriage or other adverse maternal or fetal effects. Available data from published randomized controlled trials and case reports over several decades of use with intravenously administered dexmedetomidine during pregnancy have not identified a drug-associated risk of major birth defects or miscarriage; however, the reported exposures occurred after the first trimester. Most of the available data are based on studies with exposures that occurred at the time of cesarean-section delivery, and these studies have not identified an adverse effect on maternal outcomes or infant Apgar scores. Available data indicate that dexmedetomidine crosses the placenta.

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 24 May 2023 using search terms [dexmedetomidine] and [pregnancy] 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

Selected Dexmedetomidine Bibliography

1. Ala-Kokko TI, Pienimäki P, Lampela E, Hollmén AI, Pelkonen O, Vähäkangas K. Transfer of clonidine and dexmedetomidine across the isolated perfused human placenta. *Acta Anaesthesiol Scand*. 1997;41(2):313-319. doi:10.1111/j.1399-6576.1997.tb04685.x

2. Sun S, Wang J, Wang J, Wang F, Xia H, Yao S. Fetal and Maternal Responses to Dexmedetomidine Intrathecal Application During Cesarean Section: A Meta-Analysis. *Med Sci Monit*. 2020;26:e918523. Published 2020 Jan 29. doi:10.12659/MSM.918523
3. Wang C, Liu S, Han C, Yu M, Hu Y, Liu C. Effect and placental transfer of dexmedetomidine during caesarean section under epidural anaesthesia. *J Int Med Res*. 2017;45(3):964-972. doi:10.1177/0300060517698330
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5. Zhang J, Zhou H, Sheng K, Tian T, Wu A. Foetal responses to dexmedetomidine in parturients undergoing caesarean section: a systematic review and meta-analysis. *J Int Med Res*. 2017;45(5):1613-1625. doi:10.1177/0300060517707113

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.