Department of Health and Human Services
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Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology
Office of Pharmacovigilance and Epidemiology

Pediatric Postmarketing Pharmacovigilance Review

Date:	September 3, 2025
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Product Name:	Lymphoseek (technetium Tc 99m tilmanocept)
Pediatric Labeling Approval Date:	May 19, 2021
Application Type/Number:	NDA 202207
Applicant:	Cardinal Health 414, LLC
TTT Record ID:	2025-13763

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EXECUTIVE SUMMARY

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Lymphoseek (technetium Tc 99m tilmanocept) in pediatric patients less than 18 years of age. The Division of Pharmacovigilance (DPV) conducted this review in accordance with Pediatric Research Equity Act (PREA). This review focuses on United States (U.S.) serious unlabeled adverse events associated with Lymphoseek in pediatric patients.

Lymphoseek (technetium Tc 99m tilmanocept) is a radioactive diagnostic agent and was initially approved in the U.S. on March 13, 2013. Lymphoseek is currently indicated with or without scintigraphic imaging for:

- Lymphatic mapping using a handheld gamma counter to locate lymph nodes draining a primary tumor site in adult and pediatric patients aged one month and older with solid tumors for which this procedure is a component of intraoperative management.
- Guiding sentinel lymph node biopsy using a handheld gamma counter in patients with clinically node negative squamous cell carcinoma of the oral cavity, breast cancer or melanoma.

This pediatric postmarketing safety review was prompted by pediatric labeling on May 19, 2021, that expanded the indication to include use in pediatric patients aged 1 month and older. The safety and effectiveness of Lymphoseek have not been established in pediatric patients less than 1 month of age.

A pediatric safety review for Lymphoseek has not previously been presented to the Pediatric Advisory Committee.

DPV searched FAERS for all U.S. serious reports with Lymphoseek in pediatric patients less than 18 years of age from March 13, 2013, through June 24, 2025, and identified no reports.

DPV did not identify any new pediatric safety concerns for Lymphoseek at this time and will continue routine pharmacovigilance monitoring for Lymphoseek.

1 INTRODUCTION

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Lymphoseek (technetium Tc 99m tilmanocept) in pediatric patients less than 18 years of age. The Division of Pharmacovigilance (DPV) conducted this review in accordance with Pediatric Research Equity Act (PREA). This review focuses on United States (U.S.) serious unlabeled adverse events associated with Lymphoseek in pediatric patients.

1.1 PEDIATRIC REGULATORY HISTORY

Lymphoseek (technetium Tc 99m tilmanocept) is a radioactive diagnostic agent and was initially approved in the U.S. on March 13, 2013. Lymphoseek is currently indicated with or without scintigraphic imaging for:[1]

- Lymphatic mapping using a handheld gamma counter to locate lymph nodes draining a primary tumor site in adult and pediatric patients aged one month and older with solid tumors for which this procedure is a component of intraoperative management.
- Guiding sentinel lymph node biopsy using a handheld gamma counter in patients with clinically node negative squamous cell carcinoma of the oral cavity, breast cancer or melanoma.

This pediatric postmarketing safety review was prompted by pediatric labeling on May 19, 2021, that expanded the indication to include use in pediatric patients aged 1 month and older. The safety and effectiveness of Lymphoseek have not been established in pediatric patients less than 1 month of age.[2]

A pediatric safety review for Lymphoseek has not previously been presented to the Pediatric Advisory Committee.

1.2 RELEVANT LABELED SAFETY INFORMATION

The Lymphoseek labeling contains the following safety information excerpted from the Highlights of Prescribing Information and the *Pediatric Use* subsection. For additional Lymphoseek labeling information, please refer to the full prescribing information.[1]

> **----------CONTRAINDICATIONS----------**
> None.(4)
>
> **----------WARNINGS AND PRECAUTIONS----------**
> Hypersensitivity: Ask patients about prior reactions to drugs, especially dextran or modified forms of dextran. Observe for hypersensitivity signs and symptoms following Lymphoseek injection. Have resuscitation equipment and trained personnel immediately available. (5.1)
>
> **----------ADVERSE REACTIONS----------**
> The most common adverse reactions (incidence < 1%) are injection site irritation and/or pain.(6.1)
>
> **8.4 Pediatric Use**
> The safety and effectiveness of Lymphoseek have been established in pediatric patients 1 month of age and older. Use of Lymphoseek for this population is supported by evidence from adequate and well-controlled studies in adults with additional safety and diagnostic data from an open-label, single-arm trial in 23 pediatric patients with either melanoma (5), rhabdomyosarcoma (4), or other solid tumors (14) who received Lymphoseek (18.5 MBq and 50 mcg) and underwent

intraoperative lymphatic mapping, with or without additional use of preoperative scintigraphic imaging and/or blue dye [see Clinical Studies (14.1)].

Review of the clinical data, including evaluation of the frequency of adverse reactions and localization of lymph nodes, has not identified differences in safety or efficacy between pediatric patients and older patients.

2 METHODS AND MATERIALS

DPV searched the FAERS database with the strategy described in Table 1.

Table 1. FAERS Search Strategy*

Date of search	June 25, 2025
Time period of search	March 13, 2013† - June 24, 2025
Search type	RxLogix Pediatric Focused Review Alert – DPV
Product term	Product active ingredient: Technetium Tc-99m tilmanocept
MedDRA search terms (Version 28.0)	All Preferred Terms

* See Appendix A for a description of the FAERS database.
† U.S. approval date of Lymphoseek
Abbreviation: MedDRA=Medical Dictionary for Regulatory Activities

3 RESULTS

3.1 SELECTION OF U.S. SERIOUS PEDIATRIC CASES IN FAERS

Our FAERS search retrieved zero U.S. serious[1] pediatric reports for patients less than 18 years old from March 13, 2013, through June 24, 2025.

3.2 SUMMARY OF U.S. FATAL PEDIATRIC CASES (N=0)

There are no fatal pediatric adverse event cases for discussion.

3.3 SUMMARY OF U.S. SERIOUS NON-FATAL PEDIATRIC CASES (N=0)

There are no non-fatal pediatric adverse event cases for discussion.

4 DISCUSSION

DPV searched FAERS for all U.S. serious reports with Lymphoseek in pediatric patients less than 18 years of age from March 13, 2013, through June 24, 2025, and did not identify any reports.

5 CONCLUSION

DPV did not identify any new pediatric safety concerns for Lymphoseek at this time and will continue routine pharmacovigilance monitoring for Lymphoseek.

[1] For the purposes of this review, the following outcomes qualify as serious: death, life-threatening, hospitalization (initial or prolonged), disability, congenital anomaly, required intervention, or other serious important medical events.

6 REFERENCES

1. Lymphoseek (technetium Tc 99m tilmanocept) injection, for subcutaneous, intradermal, subareolar, or peritumoral use [Prescribing Information]. Dublin, OH: Cardinal Health 414 LLC; May 2021.
2. Feng Q. NDA/BLA Multidisciplinary Review and Evaluation of Technetium 99m Tilmanocept (Lymphoseek) NDA 202207/S012. July 2020. https://www.fda.gov/media/150329/download?attachment.

7 APPENDICES

7.1 APPENDIX A. FDA ADVERSE EVENT REPORTING SYSTEM (FAERS)

The FDA Adverse Event Reporting System (FAERS) is a database that contains information on adverse event and medication error reports submitted to FDA. The database is designed to support FDA's postmarketing safety surveillance program for drug and therapeutic biological products. The informatic structure of the database adheres to the international safety reporting guidance issued by the International Council on Harmonisation. Adverse events and medication errors are coded to terms in the Medical Dictionary for Regulatory Activities terminology. The suspect products are coded to valid tradenames or active ingredients in the FAERS Product Dictionary.

FAERS data have limitations. First, there is no certainty that the reported event was actually due to the product. FDA does not require that a causal relationship between a product and event be proven, and reports do not always contain enough detail to properly evaluate an event. Further, FDA does not receive reports for every adverse event or medication error that occurs with a product. Many factors can influence whether an event will be reported, such as the time a product has been marketed and publicity about an event. Therefore, FAERS data cannot be used to calculate the incidence of an adverse event or medication error in the U.S. population.