FILSPARI® (sparsentan) Risk Evaluation and Mitigation Strategy (REMS)

Summary

Prescribing Information

- Because of the risks for hepatotoxicity and birth defects, FILSPARI is available only through a restricted program called the FILSPARI REMS[1]
- Under the FILSPARI REMS, prescribers, patients, and pharmacies must enroll in the program[1]

Background

- A REMS drug safety program may be required by the FDA for certain medications with serious safety concerns to ensure that a drug's benefits outweigh its risks[2]

Prescribing Information

Elevations in ALT or AST of at least 3-fold ULN have been observed in up to 3.5% of FILSPARI-treated patients, including cases confirmed with rechallenge. While no concurrent elevations in bilirubin >2-times ULN or cases of liver failure were observed in FILSPARI-treated patients in clinical trials, some endothelin receptor antagonists have caused elevations of aminotransferases, hepatotoxicity, and liver failure. To reduce the risk of potential serious hepatotoxicity, measure serum aminotransferase levels and total bilirubin prior to initiation of treatment and monthly for the first 12 months, then every 3 months during treatment.[1]

Based on data from animal reproductive toxicity studies, FILSPARI can cause fetal harm, including birth defects and fetal death, when administered to a pregnant patient and is contraindicated during pregnancy. Available data from reports of pregnancy in clinical trials with FILSPARI are insufficient to identify a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. In animal reproduction studies, oral administration of sparsentan to pregnant rats throughout organogenesis at 10-times the maximum recommended human dose (MRHD) in mg/day caused teratogenic effects in rats, including craniofacial malformations, skeletal abnormalities, increased embryo-fetal lethality, and reduced fetal weights. Advise pregnant patients of the potential risk to the fetus.[1]

FILSPARI Risk Evaluation and Mitigation Strategy

For all patients, FILSPARI is available only through a restricted program under a REMS called the FILSPARI REMS because of the risk of hepatoxicity and embryo-fetal toxicity.[1]

Important requirements of the FILSPARI REMS include the following[1]:

- Prescribers must be certified with the FILSPARI REMS by enrolling and completing training.
- All patients must enroll in the FILSPARI REMS prior to initiating treatment and comply with monitoring requirements.

- Pharmacies that dispense FILSPARI must be certified with the FILSPARI REMS and must dispense only to patients who are authorized to receive FILSPARI.

Further information is available at www.filsparirems.com or 1-833-513-1325

Background

The REMS Program

The FDA REMS PROGRAM is designed to reduce the incidence and/or severity of a specific adverse event that may occur with a particular drug, and to ensure safe use with that medication. A REMS may be required for any drug whose risk might outweigh its benefit. Components include a risk mitigation goal, communication strategies, and possible actions to prevent or manage a specific adverse event by informing and educating anyone who prescribes, dispenses, or takes the medication about its potential risk.[2]

If a given drug necessitates a REMS, it is the responsibility of the pharmaceutical manufacturer to develop, implement, and assess the REMS for their drug. Drugs requiring a REMS will not be FDA approved, or if already approved may be withdrawn from the market, if the safety program is not established and followed.[2]

Determination for REMS

Prior to approval, the FDA assesses medications for both efficacy and safety. In some cases, a drug is considered safe and effective enough for approval but may carry the potential for serious risks.[3]

Multiple factors must be considered when assessing whether a REMS is necessary[3]:

- the estimated size of the population likely to use the drug involved
- the seriousness of the disease or condition that is to be treated with the drug
- the expected benefit of the drug with respect to such disease or condition
- the expected or actual duration of treatment with the drug
- the seriousness of any known or potential adverse events that may be related to the drug and the background incidence of such events in the population likely to use the drug
- whether the drug is a new molecular entity

REMS Implementation

In cases requiring a REMS, these risks must be communicated to persons prescribing, dispensing, or utilizing the drug, and actions may be necessary for its use, such as certification in the REMS or regular laboratory tests.[4] These specifications are included in the FDA-approved label and prescribing information. In some situations, a drug manufacturer may be asked to provide certain information to patients and healthcare providers, such as medication guides and communication plans.[3] Some drugs with a REMS may also carry a corresponding Black Box Warning.[5]

Compliance and Intervention

In monitoring risks associated with a given medication, the FDA utilizes a REMS compliance program and conducts inspections to ensure that a required safety strategy is followed and that a medication's benefits are greater than its risks. Penalties such as product seizure or monetary fines

may be imposed if the REMS is not upheld. Mandatory REMS assessment reports are utilized by the FDA to demonstrate compliance with regulatory and legal requirements.[6]

Abbreviations

ALT, alanine transaminase; AST, aspartate aminotransferase; FDA, US Food and Drug Administration; MRHD, maximum recommended human dosage; REMS, risk evaluation and mitigation strategy; ULN, upper limit of normal.

References

1. FILSPARI. Prescribing information. Travere Therapeutics Inc; September 2024.

2. FDA. Risk evaluation and mitigation strategies | REMS. Updated May 16, 2023. Accessed September 17, 2024. https://www.fda.gov/drugs/drug-safety-and-availability/risk-evaluation-and-mitigation-strategies-rems

3. Dabrowska A, Congressional Research Service. *FDA risk evaluation and mitigation strategies (REMS): Description and effect on generic drug development*. March 16, 2018. Accessed September 17, 2024. https://sgp.fas.org/crs/misc/R44810.pdf

4. FDA. What's in a REMS? Updated January 26, 2018. Accessed September 17, 2024. https://www.fda.gov/drugs/risk-evaluation-and-mitigation-strategies-rems/whats-rems

5. Schreiber MA, Wiese M. Black box warnings: How they can improve your clinical practice. *Curr Psychiatr*. 2019;18(12):19-36.

6. FDA. REMS compliance program. Updated September 22, 2022. Accessed September 17, 2024. https://www.fda.gov/drugs/risk-evaluation-and-mitigation-strategies-rems/rems-compliance-program