ns: a State Attorney General and a hematologist facilitate translation of research into US Food and Drug Administration actions--a SONAR report.

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Abstract:

Pharmaceutical safety is a public health issue. In 2005, the Connecticut Attorney General (AG) raised concerns over adverse drug reactions in off-label settings, noting that thalidomide was approved to treat a rare illness, but more than 90% of its use was off label. A hematologist had reported thalidomide with doxorubicin or dexamethasone was associated with venous thromboembolism (VTE) rates of 25%. We review US Food and Drug Administration (FDA) and manufacturer responses to a citizen petition filed to address these thalidomide safety issues. Case study. The AG petitioned the FDA requesting thalidomide-related safety actions. Coincidentally, the manufacturer submitted a supplemental New Drug Approval (sNDA), requesting approval to treat multiple myeloma with thalidomide-dexamethasone. FDA safety officers reviewed the petition and the literature and noted that VTE risks with thalidomide were not appropriately addressed in the existing package insert. In the sNDA application, the manufacturer reported thalidomide-associated toxicities for multiple myeloma were primarily somnolence and neurotoxicity, and a proposed package insert did not focus on VTE risks. In October, the FDA informed the Oncology Drug Division that VTE risks with thalidomide were poorly addressed in the existing label. After reviewing this memorandum, an Oncology Drug Division reviewer informed the manufacturer that approval of the sNDA would be delayed until several thalidomide-associated VTE safety actions, including revisions of the package insert, were implemented. The manufacturer and FDA agreed on these actions, and the sNDA was approved. New approaches addressing off-label safety are needed. The conditions that facilitated the successful response to this citizen petition are uncommon.