

UMKC Drug Information Center 2464 Charlotte Street, Suite 1220 Kansas City, MO 64108

January 27, 2022

١,

Dr.

Thank you for your question regarding Keppra (levetiracetam) and pancytopenia. Pancytopenia has been identified as an adverse event of levetiracetam in postmarketing surveillance.¹

The overall quality and quantity of evidence for pancytopenia associated with levetiracetam use is quite low and limited to case reports. These reports are from multiple countries in patients with a variety of conditions.

- Elouni and colleagues² report a 76-year-old female admitted to the intensive care unit for status epilepticus. In addition to clonazepam, this patient began levetiracetam 1000 mg IV daily. At baseline, the patient's complete blood count (CBC) was within normal limits; however, two days after levetiracetam initiation, pancytopenia was noted with levels continuing to decline. Levetiracetam was discontinued six days after initiation and the pancytopenia began to improve. The team rechallenged the patient with levetiracetam with another decrease in CBC noted. Ultimately, the patient was switched to clobazam, and CBC levels remained within normal limits.
- Gallerani and colleagues³ report a 65-year-old female admitted due to epileptic crisis associated with meningotheliomatous meningioma. Upon admission, the patient's CBC was within normal limits. Nine days after initiation of levetiracetam 750 mg by mouth twice daily, pancytopenia was noted with CBC levels continuing to decrease for several weeks. After 18 days, the team discontinued therapy and six days after discontinuing, platelets and white blood cell counts began increasing with eventual return of CBC levels to normal limits.
- Alzahrani and colleagues⁴ report a 79-year-old female admitted for a temporal craniotomy who began levetiracetam for seizure prophylaxis. Five days after surgery, the patient developed melena and anemia requiring two units of red blood cells. CBC levels continued to decline with five units of platelets administered due to a total platelet count of less than 100,000. Ten days after levetiracetam initiation, the team discontinued and switched to lacosamide. Within 24 hours of discontinuation, the platelet count improved and an overall increase in CBC levels was seen within five days.
- García Carretero and colleagues⁵ report a 77-year-old female admitted with digestive difficulties and a history of valproic acid use. During treatment, the patient presented with drowsiness and loss of alertness that the team attributed to an elevated valproic acid level. Subsequently, the team switched valproic acid to levetiracetam 500 mg by mouth daily. Two days after initiation, pancytopenia was noted, and believed to be associated with levetiracetam. Two units of red blood cells were administered and levetiracetam was discontinued. Fourteen days after discontinuation, CBC returned to baseline.

- Gohil and Agarwal⁶ report a 4-month-old male infant given levetiracetam for convulsion. Eight days after therapy initiation, the patient developed shock, hyponatremia, acute prerenal failure with edema and pancytopenia with absolute neutrophil count decreasing from 5280 to 265/µL, leading to death.
- Ammad and colleagues⁷ report on a 57-year-old male with history of metastatic adenocarcinoma started on levetiracetam 500 mg by mouth twice daily for seizure prophylaxis. One month after initiation, the patient was admitted due to right lower extremity deep vein instent thrombosis and pancytopenia was noted. Four days after admission, the patient was increased to levetiracetam 750 mg by mouth twice daily. CBC levels continued to decline and nine days after admission, levetiracetam was switched to topiramate. CBC levels gradually increased to normal limits by day 17.

Overall, there is no defined frequency for pancytopenia associated with levetiracetam use. Based on the available evidence, clinicians may consider routine CBC monitoring when initiating levetiracetam therapy.

Please let us know if we can help you with anything else.

Sincerely,

Vance Howerton, PharmD Candidate 2022 UMKC Drug Information Center

References:

- 1. Lexi-Drugs. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Accessed January 27, 2022. http://online.lexi.com.
- 2. Elouni B, Salem CB, Biour M. Levetiracetam-Induced Pancytopenia. *Ann Pharmacother*. 2009;43(5):985-985. doi:10.1345/aph.1L727
- 3. Gallerani M, Mari E, Boari B, Carletti R, Marra A, Cavallo M. Pancytopenia Associated with Levetiracetam Treatment: *Clin Drug Investig*. 2009;29(11):747-751. doi:10.2165/11319450-000000000-00000
- 4. Alzahrani T, Kay D, Alqahtani SA, Makke Y, Lesky L, Koubeissi MZ. Levetiracetam-induced pancytopenia. *Epilepsy Behav Case Rep.* 2015;4:45-47. doi:10.1016/j.ebcr.2015.06.001
- 5. García Carretero R, Romero Brugera M, Olid-Velilla M, Salamanca-Ramirez I. Pancytopenia associated with levetiracetam in an epileptic woman. *BMJ Case Rep*. 2016;2016:bcr2016217407. doi:10.1136/bcr-2016-217407
- 6. Gohil JR, Agarwal TS. Levetiracetam Adverse Drug Reaction: Pancytopenia. *J Pediatr Neurosci*. 2018;13(1):116-117. doi:10.4103/JPN.JPN_139_17
- 7. Ammad Ud Din M, Ather Hussain S, Bodrog A. Delayed Recognition of Levetiracetam-induced Pancytopenia. *Eur J Case Rep Intern Med*. 2021;8(3):002449. doi:10.12890/2021_002449