

## **INVEGA® (paliperidone ER)**

### **INVEGA - Adverse Event - Hematological Disorders**

#### **SUMMARY**

- Leukopenia, neutropenia, and agranulocytosis have been reported with antipsychotics, including INVEGA. Patients with a history of a clinically significant low white blood cell count (WBC) or a drug-induced leukopenia/neutropenia should have their complete blood count (CBC) monitored frequently during the first few months of therapy and discontinuation of INVEGA should be considered at the first sign of a clinically significant decline in WBC in the absence of other causative factors.<sup>1</sup>

#### **CLINICAL DATA**

##### **Trials**

**Si et al (2015)**<sup>2</sup> conducted an 8-week, open-label, single-arm, multicenter study, in patients with first-episode psychosis having a Positive and Negative Syndrome Scale (PANSS) total score of 70 and treated with flexible-dose paliperidone ER (3-12 mg/day). The safety analysis included 308 Chinese patients. Leukopenia was reported as one treatment emergent adverse event (TEAE) leading to permanent discontinuation of the study drug. No additional information was provided.

**Luthringer et al (2007)**<sup>3</sup> conducted a double-blind, randomized, placebo-controlled study assessing the effect of paliperidone ER on sleep architecture and sleep continuity. One treatment emergent adverse event of thrombocytopenia was reported. No additional information was provided.

##### **Case Studies**

**Wakuda et al (2019)**<sup>4</sup> detailed a case report of a 46-year-old male with a 5-year schizophrenia history. He was previously treated with blonanserin 24 mg/day plus risperidone 4 mg/day. No significant abnormalities in WBC or other blood cell counts were noted at the time. The patient exhibited worsening suspiciousness and irritability leading to a decrease in risperidone to 2 mg/day plus addition of paliperidone 6 mg/day.

- Thirteen days following the initiation of paliperidone, the patient was brought to the emergency room due to his inability to walk. The patient was hospitalized due to suspected paliperidone-induced agranulocytosis (WBC:  $0.3 \times 10^9/L$ ) as well as a bilateral pulmonary infection.
- All psychotropics were discontinued and the patient was administered granulocyte-colony stimulating factor (G-CSF) 75  $\mu g/day$  for 3 consecutive days plus doripenem 3 mg/day.
- Two days later, the patient's WBC count was elevated ( $4.95 \times 10^9/L$ ).
- Ten days later, the bilateral pulmonary infection resolved, and the patient was discharged.
- Following discharge, the paliperidone/risperidone regimen was replaced with aripiprazole without further hematological complications.

**Matsuura et al (2016)**<sup>5</sup> reported a case of a 50-year-old female with schizoaffective disorder hospitalized after developing auditory hallucinations and aggressive behavior while on quetiapine 200 mg/day, olanzapine 10 mg/day and valproic acid 200 mg/day. Following admission to the hospital, olanzapine was increased to 20 mg/day and valproic acid to 1000 mg/day. After 28 days of hospitalization, the patient continued to experience refractory auditory hallucinations (WBC:  $4.03 \times 10^9/L$ ; neutrophil count:  $2.26 \times 10^9/L$ ).

- Paliperidone was added and the dose was increased to 12 mg/day over the next 2 weeks.
- On day 55 there was a sudden drop in WBC ( $2.83 \times 10^9/L$ ) and neutrophil count ( $0.79 \times 10^9/L$ ) with normal renal and liver function.

- Paliperidone was discontinued immediately, valproic acid was reduced to 600 mg/day and lithium carbonate 200 mg/day was added to her regimen.
- Four days following initiation of lithium carbonate, her WBC and neutrophil counts returned to normal,  $4.34 \times 10^9/L$  and  $2.29 \times 10^9/L$ , respectively. After 28 days, WBC and neutrophils increased to  $6.86 \times 10^9/L$  and  $4.74 \times 10^9/L$ , respectively.
- Lithium carbonate was gradually discontinued. There were no further reports of leukopenia or neutropenia over the next 6 months.

**Kim et al (2011)**<sup>6</sup> presented a case report of a 33-year-old female who was admitted to the hospital with a 1-year history of auditory and visual hallucinations, persecutory delusions, aggressive behavior, and unstable mood. Upon admission, she had a WBC count of  $6.17 \times 10^9/L$  and a neutrophil count of  $3.97 \times 10^9/L$ , with her other cell counts within normal limits.

- She was initially treated with paliperidone ER 6 mg/day and was increased to paliperidone 9 mg/day on day 9.
- On day 14, her WBC count decreased to  $2.96 \times 10^9/L$ , neutrophil count decreased to  $1.18 \times 10^9/L$ , and her red blood cell (RBC) count, hemoglobin, and hematocrit decreased slightly to  $3.23 \times 10^6/\mu L$ , 10.7 g/dL, and 31.5%, respectively.
- On day 22, after no change in her cell counts, paliperidone was discontinued.
- Three days following discontinuation, her leukopenia and neutropenia improved (WBC count:  $3.42 \times 10^9/L$ ; neutrophil count:  $1.57 \times 10^9/L$ ) and returned to normal by day 36 (WBC count:  $4.70 \times 10^9/L$ ; neutrophil count:  $2.77 \times 10^9/L$ ).

## LITERATURE SEARCH

A literature search of MEDLINE®, Embase®, BIOSIS Previews®, and Derwent Drug File (and/or other resources, including internal/external databases) pertaining to this topic was conducted on 04 November 2024. Additional case studies have been referenced.<sup>7,8</sup>

## REFERENCES

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