INVEGA® (paliperidone)
Use in Gastrointestinal Conditions

SUMMARY

- Because the INVEGA tablet is non-deformable and does not appreciably change in shape in the gastrointestinal tract, INVEGA should ordinarily not be administered to patients with pre-existing severe gastrointestinal narrowing (pathologic or iatrogenic, for example: esophageal motility disorders, small bowel inflammatory disease, "short gut" syndrome due to adhesions or decreased transit time, past history of peritonitis, cystic fibrosis, chronic intestinal pseudo obstruction, or Meckel's diverticulum).[1]
- There have been rare reports of obstructive symptoms in patients with known strictures in association with the ingestion of drugs in non-deformable controlled-release formulations.[1]
- Because of the controlled-release design of the tablet, INVEGA should only be used in patients who are able to swallow the tablet whole.[1]
- A decrease in transit time, e.g., as seen with diarrhea, would be expected to decrease bioavailability and an increase in transit time, e.g., as seen with gastrointestinal neuropathy, diabetic gastroparesis, or other causes, would be expected to increase bioavailability. These changes in bioavailability are more likely when the changes in transit time occur in the upper GI tract.[1]
- No studies assessing the efficacy, safety, or pharmacokinetics of INVEGA in subjects with a surgically altered gastrointestinal tract have been performed. In patients with normal gastrointestinal function, morning dosing leads to a 24-hour transit time in most individuals.[2] INVEGA was designed to release paliperidone with a slow ascending concentration-time profile over a 24-hour period. However, the release rate and gastrointestinal transit time alone cannot predict bioavailability in patients with a surgically altered gastrointestinal tract, since paliperidone may be less readily absorbed from the colon.[3]

CASE REPORT

McGrane et al (2020)[4] reported the use of INVEGA in a 42-year-old female who had undergone Roux-en-Y gastric bypass (RYGB) surgery. She presented for inpatient psychiatric hospitalization following an overdose of oral risperidone. The patient had a history of borderline personality disorder, factitious disorder, psychotic disorder, bipolar disorder, polysubstance use disorder, secondary adrenal insufficiency, seizure disorder, post-traumatic stress disorder, hypertension. Medications on admission included hydrocortisone, gabapentin, lisinopril, oxcarbazepine, pantoprazole, phenytoin, risperidone, trazodone, venlafaxine, calcium, vitamin D, vitamin B12, ferrous sulfate, lactobacillus, and magnesium. The patient received a first dose of INVEGA 3 mg followed by INVEGA 6 mg nightly for 6 days. The patient's hallucinations improved and INVEGA was discontinued.

On day 8 of hospitalization a steady state paliperidone trough concentration (9-hydroxyrisperidone assay) was drawn. The serum concentration was 1.1 ng/mL (reference range 20-60 ng/mL). The concentration-to-dose ratio was 0.18, >20-fold lower than expected. Treatment with INVEGA SUSTENNA 234 mg was initiated on day 12. Five months after discharge, she was continuing INVEGA SUSTENNA therapy and was not experiencing hallucinations.

The authors concluded that the low paliperidone concentration may have been due to a drug-drug interaction with oxcarbazepine and/or phenytoin, potent CYP3A4 inducers, and the use of an extended-release formulation in a patient with previous gastric by-pass surgery.

LITERATURE SEARCH

A literature search of MEDLINE®, EMBASE®, BIOSIS Previews®, DERWENT Drug File (and/or other resources, including internal/external databases) pertaining to this topic was conducted on 30 March 2023.

REFERENCES

1. INVEGA (paliperidone) [Prescribing Information]. Titusville, NJ: Janssen Pharmaceuticals, Inc; https://imedicalknowledge.veevavault.com/ui/approved_viewer?token=7994-d30da9a4-d8a4-4e37-b8e8-d52589dfe597.
2. Sathyan G, Hwang S, Gupta SK. Effect of dosing time on the total intestinal transit time of non-disintegrating systems. *Int J Pharm*. 2000;204(1-2):47-51.
3. Rossenu S, Crauwels H, Cleton A, et al. Comparison of the pharmacokinetics of an oral immediate-release and extended-release formulation of paliperidone in healthy subjects. Poster presented at: The Annual Meeting and Exposition of the American Association of Pharmaceutical Sciences (AAPS); October 29-November 2, 2006; San Antonio, TX.
4. McGrane IR, Salyers LA, Molinaro JR, et al. Roux-en-y gastric bypass and antipsychotic therapeutic drug monitoring: two cases. *J Pharm Pract*. 2021;34(3):503-506.