

**Egyptian
Pharmaceutical
Vigilance Center
(EPVC)**

**Pharmacovigilance
Department**

Inside this issue:

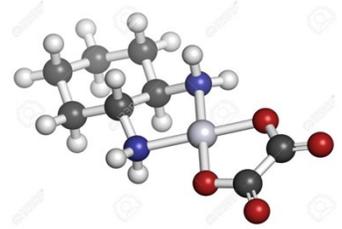
Case Report from 1
Sohag- Severe
allergic reactions
induced by Oxali-
platine intravenous
injection

Case Report from 2
Alexandria- Throm-
bocytopenia associ-
ated with Linezolid

Case report from 4
Cairo- Pancytopen-
ia in male Patient
associated with
Intravenous
Omeprazole

Case Report from Sohag- Severe allergic reactions induced by Oxaliplatin intravenous injection

The Egyptian pharmaceutical Vigilance regional center in Sohag has received 8 ICSRs about severe allergic reactions induced by Oxaliplatin intravenous injection, 6 of the cases are for female patients and 2 of them for male patients, they were administered oxaliplatin as intravenous drip over two hours and used in combination with 5-fluorouracil/leucovorin



All suffered from dyspnea, edema, rash, chest pain, and were administered dexamethasone amp as a treatment

Oxaliplatin:

Oxaliplatin is an antineoplastic. It works by killing cancer cells and slowing tumor growth.

Indications and Usage :-

Oxaliplatin, used in combination with 5-fluorouracil/leucovorin, is indicated for adjuvant treatment of stage III colon cancer in patients who have undergone complete resection of the primary tumor, treatment of advanced colorectal cancer.

Upon search it was found that:

- Oxaliplatin should not be administered to patients with a history of known allergy to Oxaliplatin or other platinum compounds.
- Allergic Reactions Anaphylactic-like reactions to Oxaliplatin have been reported, and may occur within minutes of Oxaliplatin administration.
- Patients with a history of allergic reactions to platinum compounds should be monitored for allergic symptoms.
- Allergic reactions can occur during any cycle, In case of an anaphylactic-type reaction to oxaliplatin, the infusion should be immediately discontinued and appropriate symptomatic treatment initiated, Rechallenge with oxaliplatin is contraindicated.

- These reactions were managed with epinephrine, corticosteroids, and antihistamines.
- Oxaliplatin has been associated with pulmonary fibrosis (0.7% of study patients), which may be fatal.
- In the case of unexplained respiratory symptoms such as non-productive cough, dyspnoea, crackles or radiological pulmonary infiltrates, oxaliplatin should be discontinued until further pulmonary investigations exclude an interstitial lung disease or pulmonary fibrosis .
- The administration of Oxaliplatin does not require prehydration. Premedication with antiemetics, including 5-HT3 blockers with or without dexamethasone, is recommended.
- Prolongation of infusion time for Oxaliplatin from 2 hours to 6 hours may mitigate acute toxicities.
- Oxaliplatin Injection, USP is incompatible in solution with alkaline medications or media (such as basic solutions of 5-fluorouracil) and must not be mixed with these or **administered simultaneously through the same infusion line. The infusion line should be flushed with 5% Dextrose Injection, USP prior to administration of any concomitant medication.**

References:

1. FDA- Dopamine Hydrochloride and 5% Dextrose Injection ([Click Here](#))
2. Canada- ELOXATIN SUMMARY BASIS OF DECISION ([Click Here](#))
3. TGA- ELOXATIN product information ([Click Here](#))

Case Report from Alexandria- Thrombocytopenia associated with Linezolid

The regional center in Alexandria received a yellow card concerning an 87 years old male who received Linezolid IV (600mg every 12 hours) for treatment of VRSA infection (Vancomycin resistant staphylococcus aureus), then the patient suffered from thrombocytopenia (Platelet count decreased till 55.000 cells/microliter).

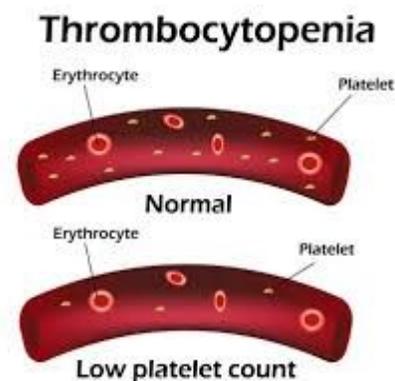
The patient was also treated with Tienam, Levofloxacin, Solumedrol and Clexane and some of these concomitant drugs may also lead to thrombocytopenia like tienam, levofloxacin and clexane.

Linezolid was withdrawn, and then the Platelet count increased 4 days later but didn't reach normal till platelet transfusion occurs.

Linezolid is an antibiotic that fights bacteria in the body. Linezolid is also an MAO (monoamine oxidase) inhibitor. It is used to treat different types of bacterial infections, such as pneumonia, skin infections, and infections that are resistant to other antibiotics.

Thrombocytopenia is a condition in which your blood has a lower than normal number of blood cell fragments called platelets.

* A normal platelet count in adults ranges from 150,000 to 450,000 platelets per microliter of blood.



- * A platelet count of less than 150,000 platelets per microliter is lower than normal (it is called thrombocytopenia)
- * However, the risk for serious bleeding doesn't occur until the count becomes very low—less than 10,000 or 20,000 platelets per microliter.
- * Mild bleeding sometimes occurs when the count is less than 50,000 platelets per microliter.

Labeled information:

According to **Linezolid** 2mg/ml Solution for Infusion Summary of product Characteristics (SmPC) it was stated under section **(4.8 Undesirable effects)** that: “Linezolid can cause Blood and Lymphatic System Disorders like Leucopenia , neutropenia, **thrombocytopenia** and eosinophilia in ($\geq 1/1,000$ to $< 1/100$) of patient receiving it.

It was stated also under section **4.4 Special warnings and precautions for use** That Myelosuppression (including anaemia, leucopenia, pancytopenia and **thrombocytopenia**) has been reported in patients receiving linezolid. In cases where the outcome is known, when linezolid was discontinued, the affected haematologic parameters have risen toward pretreatment levels. The risk of these effects appears to be related to the **duration of treatment**. **Elderly patients** treated with linezolid may be at greater risk of experiencing blood dyscrasias than younger patients. **Linezolid Injection**

Laboratory Abnormalities:

Linezolid has been associated with thrombocytopenia when used in doses up to and including 600 mg every 12 hours for up to 28 days.

Other concomitant drugs that may lead to

thrombocytopenia as side effects:-

Tienam (Imipenem/Cilastatin 500 mg/500 mg Powder for Solution for Infusion)

4.8 Undesirable effects

Uncommon

Pancytopenia, neutropenia, leucopenia, **thrombocytopenia**, thrombocytosis

Levofloxacin 5 mg/ml Solution for Infusion

Rare ($\geq 1/10,000$ to $< 1/1,000$)

Thrombocytopenia

Neutropenia

Clexane pre-filled syringes

4.8 Undesirable effects

Thrombocytopenia and thrombocytosis

Recommendations for Healthcare Professionals:

- Caution should be used with the use of Linezolid in Elderly: Haematopoietic disorders (including **thrombocytopenia**, anaemia, leucopenia, and pancytopenia) have been reported in patients receiving linezolid, particularly **the elderly**.
- It is recommended that full blood counts are monitored weekly.
- Close monitoring is recommended in patients who:
 - ◆ Receive treatment for more than 10–14 days;
 - ◆ Have pre-existing myelosuppression;
 - ◆ Are receiving drugs that may have adverse effects on haemoglobin, blood counts, or platelet function;
 - ◆ Have severe renal impairment.
- If significant myelosuppression occurs, treatment should be stopped unless it is considered essential, In which case intensive monitoring of blood counts and appropriate management should be implemented.

References:

1. *Drugs.com Linezolid* ([Click Here](#))
2. *National Institute of health* ([Click Here](#))
3. *Emc-Linezolid 2mg/ml Solution for Infusion* ([Click Here](#))
4. *Emc-Imipenem/ Cilastatin 500 mg/ 500 mg Powder for Solution for Infusion* ([Click Here](#))
5. *Emc-Levofloxacin 5 mg/ml Solution for Infusion* ([Click Here](#))
6. *Emc-Clexane pre-filled syringes* ([Click Here](#))

Case report from Cairo– Pancytopenia in male Patient associated with Intravenous Omeprazole

The regional center in Cairo received a yellow card concerning a 45 Years old male, who was taking Omeprazole 40 mg IV and was admitted to hospital with thrombocytopenia which converted to pancytopenia (Rare case)

The patient was receiving Omeprazole 40 mg IV as a prophylaxis from GIT hemorrhage, he had ESRD and mild hepatomegaly

Pancytopenia: low levels of all three cellular components of the blood (red cells, white cells, and platelets with symptoms such as fatigue, weakness, skin symptoms and bleeding)

ESRD: End-stage renal disease is a condition in which the kidneys no longer function normally

Labeled Information:

According to Omeprazole Summary of product Characteristics (SmPC) it was stated under section (4.1) Therapeutic indications, the following:

Omeprazole for intravenous use is indicated as an alternative to oral therapy for treatment of gastric, duodenal ulcers, reflux esophagitis and gastro-esophageal reflux disease

*It was stated under section 4.8 Undesirable effects

Blood and lymphatic system disorders	
Rare:	Leukopenia, thrombocytopenia
Very rare:	Agranulocytosis, pancytopenia
Post marketing reports	
Purpura	leukocytosis & fatal agranulocytosis
neutropenia	anemia & hemolytic anemia

Recommendations for Healthcare Professionals:

- The IV formulation should be used when oral formulations are inappropriate.
- IV use should be discontinued as soon as treatment with an oral formulation is possible.
- A single 10 mg IV dose was shown to be equivalent to a single 20 mg oral tablet dose.
- Antacids may be used concomitantly during treatment.
- Dose adjustment in impaired renal function is not needed.
- Dose adjustment in impaired hepatic function: a daily dose of 10-20 mg may be sufficient.
- Omeprazole rarely cause Pancytopenia which may be a life-threatening condition especially if there was excessive bleeding, extreme fatigue, and shortness of breath or High fever [38°C].

References:

1. *Drugs.com Pancytopenia* ([Click Here](#))
2. *Drugs.com. End-Stage Renal Disease* ([Click Here](#))
3. *emc- Omeprazole 40 mg Powder for Solution SPC* ([Click Here](#))
4. *Drugs.com Omeprazole-side-effects.* ([Click Here](#))