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# Adverse Drug Reaction to Injection Larinject in a Women Case Report Observational Study

**Prof. Kiran Bibave, Sailee S Girgosavi, Dr. P. N Sable**
Siddhi College of Pharmacy, Pimpri-Chinchwad, Maharashtra, India

**Abstract:** *The term "adverse drug reaction" (ADR) refers to an unpleasant and inadvertent reaction that happens at the dosage of a medication that is typically used for illness prophylaxis, diagnosis, or therapy. Because ADRs are associated with higher rates of morbidity and mortality, they place a significant cost on contemporary society. Any class of medication might have adverse drug reactions (ADRs), and as more and more therapies become available, the likelihood of ADRs rises as well. Research indicates that children and infants experience higher rates of adverse drug reactions (ADRs) than adults do, and that these reactions are typically more severe. The case study reported adverse drug reaction descibed a 35 old women patient a who came to the hospital suffering from anemia. After administration on the dose IV injection Larinject 100mg the patient develop breathlessness, nausea, vomiting, headache. As a result, the health care facility should encourage the spontaneous monitoring, reporting, documenting, and avoidance of ADRs since doing so is crucial to providing better healthcare.*

**Keywords**: Mortality, Anemia, skin rashes, breathlessness, headache, nausea, vomiting, Larinject

## I. INTRODUCTION

The term "adverse drug reaction" (ADR) refers to an unpleasant and inadvertent reaction that happens at the dosage of a medication that is typically used for illness prophylaxis, diagnosis, or therapy .The majority of the time, this is because clinical trials typically have small sample sizes and poor statistical power.

Consequently, the health care facility should encourage the spontaneous monitoring, reporting, documenting, and avoidance of ADRs because doing so is crucial to providing better healthcare.

The research and practices around the identification, evaluation, comprehension, and avoidance of side effects or any other issue pertaining to medications or vaccinations are known as pharmacovigilance.

Approximately 25% of people worldwide have anemia. Iron deficiency, the most common cause, is responsible for 50% of all anemias. The rate of iron deficiency is higher in developing countries compared to the United States, where the prevalence of iron deficiency anemia in men under 50 is 1%. In women of childbearing age in the United States, the rate is 10% due to losses from menstruation, while 9% of children ages 12 to 36 months are iron-deficient, and one-third of these children develop anemia. While the rate of iron-deficiency anemia is low in the United States, low-income families are particularly at risk[(1)].

### 1.1 COMMON SIDE EFFECT

- Skin rashes.
- Flushing
- Headache.
- Nausea
- Vomiting.
- Dizziness
- Increase BP and hypersensitive reaction.

### 1.2 HISTORY

A review of the significance of comprehending an ADR's predictability was conducted in 1971. According to estimates, 70–80% of ADRs are predicted and might be avoided. It is true that some ADRs cannot be prevented and will still

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happen despite the most stringent safety measures. But a sizable percentage of ADRs might be avoidable. Still, not enough is being done in today's hospitals to recognize and comprehend avoidable adverse drug reactions. This data is crucial for informing educational initiatives and policies that support a decrease in the quantity of ADRs that take place. One useful piece of data that may be included back into the system to speed up the process of development is the preventability of ADRs.

In their routine clinical practice, nearly all doctors encounter several cases of suspected adverse cutaneous drug responses (ACDRs) in various forms. These cutaneous reactions are frequent, but because many of them go unreported, detailed information about their frequency, severity, and long-term health implications is frequently unavailable. Since a new medication is introduced into the market practically every day in the modern world, there is always a risk that an unreported new drug response may occur anywhere in the world [(4)].

1. To detect the nature and frequency of ADRs
2. Providing updated Drug Safety Information to Health Care Professionals.
3. To assist the Drug regulatory authority, public health programs, scientists and consumer society to minimize ADRs.
4. To identify risk factor that may predispose, induce the development, severity and incidence of ADR.
5. Dissemination of information by designing proper education program to

**1.3 CLASSIFICATION:**

Adverse drug reactions can be classified into five types depending on:

1) Depending on Onset of Event:

Acute (<60 minute), Sub acute (1-24), Latent (>2).

2) Based on Type of Reactions:

I) Rawlins and Thompson classification (1991):

Type A (Augmented Reactions),
Type B (bizarre reactions),
Type C (chronic reactions),
Type D (Delayed type reactions),
Type E (end of treatment).

ii) Wills and Brown Classification:

Type A (Augmented Reactions),
Type B (bizarre reactions),
Type C (chronic/Chemical reactions),
Type D (Delayed type reactions),
Type E (end of treatment),
Type F (Familial reactions),
Type G (Genotoxicity),
Type H (Hypersensitivity),
Type U (Unclassified).

Based on Severity: Minor, Moderate, Severe, Lethal.

Depending on Whether They Could Take Place in Any Patient, or in a Specific Susceptible Population:

Reactions that might take place in anyone: Drug overdose, Drug side effect, Drug interaction.

Reactions that Take Place Only in Susceptible Individuals: Drug intolerance, Drug idiosyncrasy. Drug allergy, Pseudo allergic reaction.

Others: Secondary effects, Toxic effects, photosensitivity, drug dependence, drug withdrawal reactions, teratogenicity, mutagenicity, carcinogenicity, drug induced disease (Iatrogenic reactions).

**ADR CLASSIFICATION BASE ON SEVERITY:**

| Severity | Description | Example |
|---|---|---|
| Mild | No treatment or antidote for over dosage | Opioids causing constipation |

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| | | |
|---|---|---|
| | required; Longer duration hospitalization also not required | Antihistamines cause some drowsiness |
| Moderate | Specific or change in the existing treatment may be | Non-steroidal anti-inflammatory Depending on Onset of Event: drugs cause |
| | required, but the drug is not necessarily discontinued (e.g., addition of drug to the regimen, dose modification | edema and hypertension Hormonal contraceptives causing venous thrombosis |
| Severe | The drug reaction can cause a potential life-threatening event, drug and specific treatment of drug reaction must be discontinued. | Phenothiazine: abnormal heart rate ACE inhibitors: Angioedema |
| Lethal | An adverse reaction can cause death of the patient, either directly or indirectly. | Over dose of anticoagulant: hemorrhage Over dose of acetaminophen: liver failure |

Table 1: Adverse drug reaction classification

**1.4 ADR DETECTION METHOD:**

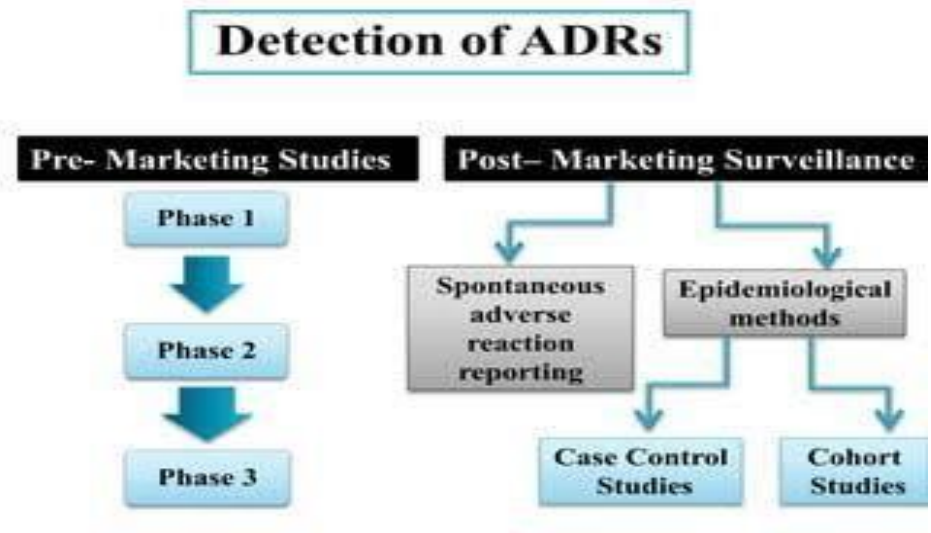


Fig. 1 Detection of ADR

Pre-marketing studies
Post-marketing surveillance
Assessing causality
Communicating ADRs
Postal Survey Method

1. Pre marketing study:

1) Animal models are used to assess new medication formulations for safety.
2) It is simple to obtain specific animal studies for mutagenicity, carcinogenicity, and teratogenicity.
3) Before submitting the final report to a marketing authorization application (MAA), separate phases of clinical studies are completed.
4) Clinical trials make it simple to identify ADRs with frequencies larger than 0.5–1.0%.

2. Post marketing surveillance.

1) Pharmacovigilance approaches are useful for both determining the risk associated with a medicine and gathering relevant data
2) A strong and reasonably priced method for identifying unknown drug related risk is the spontaneous adverse drug response reporting system.

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3) ADR results (in a patient) might be viewed as a component of a health care provider's professional duty report under their provision.
4) This product defect addresses and identifies issues such as drug intoxicants, drug misuse, and unanticipated absence of therapeutic impact in the drug.
5) These are the two epidemiological techniques that are frequently employed:
I) Cohort Studies: Patients taking a specific medication should be actively and methodically observed, and the frequency of adverse drug reactions (ADRs) should be contrasted with a control group that has not taken the medication.
II) Case-Control Research
a) It is important to identify the person who was impacted by the negative occurrence under study. Every case ought to be contrasted with multiple disease-free control patients selected at random from the research population.
b) It is important to determine whether the cases and controls were exposed to any potential causal agents prior to the incident.
c) The odd ratio needs to be computed using exposure data.
3. Assessing causality:
1) Establishing a link between a medication and a potential reaction is known as causation evaluation.
2)If an adverse drug response (ADR) is suspected, the evaluation process begins with gathering pertinent information about the patient's demographics, drugs (including over-the-counter ones), reaction length and timing, reaction treatment, reaction result, and reports
3) The following methods could be useful for determining causality:
I) The viewpoint of certain professionals.
II) Expert opinion from the pen.
III) Formal algorithms.
4. Communicating ADR:
The following methods are used to provide information on the responsible and sensible use of medications:
1) When health professionals are receiving their foundational training.
2) By offering ongoing training courses to medical practitioners.
3) Via medication information centers that have been specially designated.
4) By giving the patient counseling as well as inserting the package, which is a paper containing information about that drug and its use.
5. Postal survey method:
This approach consists of a particular drug-related questionnaire.
1) Within a year or two of a medicine's introduction, it is primarily utilized for tracking adverse drug reactions (ADRs).
2) Information regarding the drug, usage, dosage, brand, and number of patients treated in a specific time frame should be included in the questionnaire.
3) As the literature suggests, a list of the common adverse drug reactions (ADRs) should be included at the end of the questionnaire.
4) Medical professionals across the state or city who are likely to utilize the medication should get the questionnaire by mail, along with a pre-paid envelope.

**1.5 MANEGMENT OF ADR:**

Remove any suspected drugs as the first and most important step in the management process. If the reaction is thought to be dose-related, the drug's dosage needs to be decreased, and the possibility of treating the suspected reaction needs to be taken into consideration. When managing an adverse drug reaction, it's important to keep the treatment goal clear. It is imperative that the patient get regular reviews, that the medication therapy be stopped sooner rather than later, and that simpler management techniques are implemented. The following is a frequently employed response plan when handling a suspected adverse medication reaction: The following procedures need to be followed when managing any kind of suspected or unanticipated adverse medication reaction.

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Keeping an eye on patients who are more likely to experience ADRs. Observing individuals who are prescribed medications that have a high risk of adverse drug reactions.
Evaluating and recording the patient's history of allergies.
Evaluating whether the patient's medication regimen is appropriate
Varying the drug's dosage
Substitution with a different medication
Adopting a preventive routine
Examining potential pharmacological interactions when using several treatments
Support medical professionals in identifying and evaluating adverse drug reactions
Encouraging medical professionals to report adverse drug reactions.
Recording suspicious reported reactions in order to have further references.
Seeking input regarding the stated response
Teaching medical personnel the value of reporting an adverse drug reaction.
Teaching medical.

**1.6 SPONTANEOUS REPORTING OF ADVERSE DRUG REACTION:**

Components of ADRs Monitoring -
Information about the patient
Description of ADRs
Suspected drug(s)
Reporter
Benefits of ADR monitoring :
1. Accurate information regarding the safety of medications.
2. The mitigation of unfavorable consequences associated with medicinal products.
3. Education regarding ADRs and their management for the medical staff, patients, pharmacists, and nurses.
Procedure for Reporting ADRs :
1. Only Suspected Links between a Drug and a Specific Adverse Event.
2. There is no proof that a drug and an ADR are causally related just because an ADR is reported.
3. It is preferable to report anything in dubious circumstances than not to Details Needed to File an ADR Report
1. Details on the patient
2. ADRs
3. Details on Possible Drug(s)
1. Details about ADR Management
2. Details about the journalist
What to Report :
Every adverse drug reaction (ADR) brought on by prescription and over-the counter medication.
1. All possible adverse drug reactions, irrespective of the company's product details
2. Unexpected product response, regardless of the kind or degree of the reaction
3. A noted rise in a specific reaction's frequency.
4. A significant reaction, whether anticipated or not;
1. All possible adverse drug reactions (ADRs) connected to interactions between drugs and food, drugs and supplements;
2. ADRs brought on by pharmaceutical errors or overdoses Exceptional ineffectiveness or probable medication flaws noticed
1. As soon as feasible, an ADR should be reported.
2. A delayed report results in erroneous and untrustworthy information. Methods for Reporting
1. An ADR reporting form should be used for the report.
2. You can get this form from www.cdsco.nic.in and www.ipc.gov.in. A. Health Information Patient initials: Omit the patient's complete name and just write their initials. Madhu Gupta, for instance, should be written as MG.

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1) Age at the time of the occurrence or date of birth: Record the patient's age or date of birth at the time the event or reaction happened.
2) Sex: Bring up the patient's gender.
3) Weight: Bring up the patient's weight.
Suspected Adverse Reaction:
The start date of the reaction was : Mention the day that the reaction was initially seen. Date of recovery: If the patient's reaction was mitigated, the date of recovery needs to be documented. Explain your response: Give a detailed account of the reaction, including its nature, location, etc. For instance, the patient's upper and lower limbs developed an erythematous maculopapular rash.
Suspected Medication:
Information about any suspected medications, including the brand or generic name of the substance. The reporter should include the following information: manufacturer, batch/lot number, expiration date, dose utilized, route taken, frequency , dates of therapy start and finish, and indication.
Requirements details: Mention the following when discussing the status of the challenge: 'Yes' for a reaction that abates after the challenge; 'No' for a reaction that did not abate after the challenge; 'Unknown' for an effect of the challenge that is unknown; 'Not Applicable' or 'NA' for a dechallenge that is not applicable, such as in the case of vaccinations, anesthesia, when a single dose is given; death; or treatment that is finished before reaction or event 'Reduced dose'. If the response happened at a dose of report.
Details of the challenge: State the following: 'Yes' if the reaction returned following the challenge; 'No' if it did not; 'Unknown' if the effect of the challenge was not established; 'Not Applicable' or 'NA' if the challenge was not relevant, as in the case of an anaphylactic reaction. *Reintroduced dose: State the dosage and the date of the reintroduction.
Concurrent medications: List all concurrent medications, including over the-counter, herbal, and self-medication medications, together with the dates of therapy.
Tests and laboratory data that are pertinent: If available, mention all laboratory data that are pertinent to the response that occurred.
Additional pertinent history: Include any pertinent medical history that the patient has maintained, such as allergies, pregnancy, smoking, alcohol consumption, hepatic or renal impairment, and any concurrent conditions that can be explained in this area.
Seriousness of the reaction: Check the relevant reason for seriousness as follows if the reaction is serious in nature: "Death": if a medical incident caused the patient's death Note: Depending on how terrible the reaction is, mention the cause of death and the date. *Life-threatening: If the patient had a significant chance of passing away at the time of the unfavorable incident
'Hospitalization/prolonged' refers to an adverse incident that led to hospitalization or prolonged hospital stays for the patient; 'Disability' refers to an adverse event that significantly disrupted the person's ability to carry out regular living functions. Congenital anomaly: If drug exposure occurred before conception or during pregnancy, it could have had a negative effect on the unborn child.
Required intervention to prevent permanent impairment/damage' refers to situations in which a patient would require medical or surgical intervention in order to avoid lasting harm to a body structure or permanent impairment of a bodily function. "Other" refers to an occurrence that does not meet the above criteria but could still endanger the patient and necessitate medical or surgical intervention to avoid one of the disorders listed above. Serious blood dyspraxia (blood disorders), seizures/convulsions that do not require hospitalization, and the emergence of drug dependence or misuse are a few examples.
Name and Professional address: The form requires the reporter to provide their name and address professionally. The reporter's name will be kept private and discreet. 17. Causality assessment: If the reporter has received training, they must do the evaluation and provide justification for it. 18. Reporting date: Indicate the day that the unfavorable incident was reported by the individual. Gather all of the data needed to complete the suspected ADR reporting form. If all necessary information is not accessible, complete all of the Essential Requirements (ERI) to ensure a high-quality
ICSR. Make sure the form has all the required fields even if ERI are not available. Required fields Patient initials, age at commencement of response, reaction term(s),date of onset of reaction, suspected medication(s) and reporter's

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information. The following are essentially necessary items: patient initials; age at reaction onset; gender; reaction term(s); date of reaction onset; suspected medication(s); dose; date therapy started; indication of use; seriousness; outcome; details of challenge and rechallenge; reporter's information; reports date.

## II. LITERATURE REVIEW

### 2.1 INTRODUCTION IRON DEFINCIENY ANAEMIA (IDA):

Hemoglobin levels less than two standard deviations of the mean for the patient's age and gender are referred to as anemia. An crucial part of the hemoglobin molecule is iron. Iron deficiency, which causes microcytic and hypochromic red cells on the peripheral smear, is the most prevalent cause of anemia in the globe. Different factors, including age, gender, and socioeconomic level, contribute to iron deficiency. Nonspecific problems like weariness and dyspnea during exertion are frequently experienced by the patient. Iron supplementation and reversal of the underlying disease are the two forms of treatment. Most typically, oral iron supplementation is used, however intravenous iron may be necessary in some circumstances. It has been observed that patients with iron-deficient anemia experience more adverse events and longer hospital stays.

### 2.2 ETIOLOGY :

The age, gender, and socioeconomic situation of an individual can all influence the cause of iron-deficiency anemia. Decreased absorption, blood loss, or inadequate iron intake can all lead to iron insufficiency. Blood loss is the most common cause of iron-deficiency anemia, particularly in elderly people. It can also be observed in cases of inadequate dietary intake, elevated systemic iron requirements (e.g., pregnancy), and impaired iron absorption (e.g., celiac disease). Because breast milk has a higher bioavailability of iron than cow's milk, breastfeeding protects newborns against iron deficiency; iron deficiency anemia is the most common kind of anemia in early children who drink cow's milk. An important contributing factor to iron-deficiency anemia in underdeveloped nations is parasite infestations.

### 2.3 EPIDEMIOLOGY

Approximately 25% of people worldwide have anemia. Iron deficiency, the most common cause, is responsible for 50% of all anemias. The rate of iron deficiency is higher in developing countries compared to the United States, where the prevalence of iron-deficiency anemia in men under 50 is 1%. In women of childbearing age in the United States, the rate is 10% due to losses from menstruation, while 9% of children ages 12 to 36 months are iron deficient, and one-third of these children develop anemia. While the rate of iron-deficiency anemia is low in the United States, low-income families are particularly at risk.

### 2.4 PATHOPHYSIOLOGY

The synthesis of hemoglobin requires iron. Reduced intake, poor absorption, elevated demand, or blood loss can all contribute to the depletion of iron reserves. Incident gastrointestinal bleeding may be the cause of iron deficiency anemia. Adults over 50 who have gastrointestinal bleeding and iron-deficiency anemia should have their cancer risk assessed. However, in one-third of the evaluated individuals, gastrointestinal diagnostic assessment is unable to determine a reason. Microcytic hypochromic anemia on the peripheral blood smear is caused by iron insufficiency. As iron deficiency is the most prevalent single-nutrient deficiency, supplementation is advised by the American Academy of Pediatrics. The child's age and nutrition determine when to start supplementation and how much is need [(3)].

### 2.5 IRON REQUIRMENT DURING PREGNANCY

If the demand for iron were spread evenly throughout gestation, iron requirements could be met more easily by a sustained rise in the rate of iron absorption. The need for iron, however, varies markedly during each trimester of pregnancy. Iron requirements decrease during the first trimester because menstruation stops, which represents a median saving of 0.56 mg Fe/d (160 mg/pregnancy). The only iron losses that must be met during this period are the obligatory ones from the body via the gut, skin, and urine, which amount to ≈0.8 mg/d in a 55-kg woman (14 $g.kg^{-1}.d^{-1}$ or 230 mg/pregnancy). Early hemodynamic changes include generalized vasodilation, some increase in the plasma volume, and an increase in red blood cell 2.3-diphosphoglycerate concentrations. There is also some evidence that

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erythropoietin activity may be reduced during this period, with a slight reduction in red blood cell mass, a reduction in the number of reticulocytes, and a rise in the serum ferritin concentration

| Total Iron Requipment in Pregnancy | Amount(mg) |
|---|---|
| Fetes | 270 |
| Placenta | 90 |
| Expansion of red blood cell mass | 450 |
| Expansion of red blood cell mass | 230 |
| Sum | 1040 |
| Maternal blood loss at delivery | 150 |
| Total cost | 1190 |
| Net cost of pregnancy | |
| Contraction of maternal red blood cell mass | -450 |
| Absence of menstruation during pregnancy | -160 |
| Subtotal | -610 |
| Net cost | 580 |

Table 2.Iron Requirement In woman [4].

### 2.6 IRON DEFICIENCY IN WOMEN

More than two billion people worldwide suffer from nutritional iron deficiency, which is the most prevalent deficiency illness. Pregnant women are especially vulnerable. According to data from the globe Health Organization (WHO), iron deficiency anemia (IDA) during pregnancy is a major issue everywhere in the globe. In industrialized countries, the prevalence of IDA in pregnancy ranges from 14% on average to 56% (range 35–75%) on average in underdeveloped countries.

### 2.7 IRON METABOLISM

Three factors primarily influence the balance of iron metabolism in healthy individuals: dietary intake, iron loss, and current demand. The amount of iron in food that has been digested and the body's capacity to absorb iron from the digestive system are related to nutritional iron intake. The amount of iron absorbed is primarily determined by the existence or absence of gastrointestinal tract pathology or comorbidities (such as long-term inflammatory illnesses) that may lead to the expression of hepcidin, a peptide that ultimately blocks iron absorption, and the iron regulatory proteins. Humans primarily obtain their iron from the reticuloendothelial system, which includes the spleen, and the erythrocytes they destroy. This internal iron supply is regenerated. Recent research has demonstrated how intestinal and hepatic proteins allow the human body to up- or down regulate iron absorption in response to changes in iron status.

### 2.8 IRON METABOLISM IN PREGNANCY

Pregnancy and Its Iron Needs. Pregnancy in humans costs an average of 480–1150 mg of iron. 30–170 mg and 200–450 mg of iron are needed for placental and lethal requirements, respectively, in addition to the mother's needs. The placental transport of iron from maternal plasma to the fatal circulation is regulated by fatal hepcidin during pregnancy. Iron moves rapidly into the plasma when hepcidin levels are low. Ferro protein is absorbed and iron is trapped in enterocytes, macrophages, and hepatocytes at high hepcidin concentrations.

The amount of external iron needed each day can still be as little as 1 to 8 milligrams. To balance the increasing need for iron, particularly with physiological requirements during development, pregnancy, and lactation, more exogenous iron is needed. In addition to supporting the mother's blood volume, the development of the fetus and placenta necessitates a markedly increased demand for iron. Moreover, iron loss occurs in pregnant women both during and after birth. [5]

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## III. AIM & OBJECTIVE

3.1) Aim

Aim of this case report Observational study is to study adverse drug reaction of Inj. Larinject given dose of drug to the patients.

The work was focused on studied the CASE REPORT on adverse drug reaction of inj. Larinject in woman.

3.2) Objective –

Describe basic methods to detect, evaluate, and document ADRs

ADR monitoring in India

Primary objective

To study the ADRs of a Inj. Larinject in a woman..

## IV. MATERIALS & MATHODS

4.1) Study Title -

To study adverse drug reaction due to LARINJECT INJECTION.

The Present study was conducted at Manipal Hospital, Baner during the period of 15.03.2023 to 17.03.2023.

4.2) Study Design -

Case report observational study

4.3) Source of study population -

IPD patient visited to Manipal Hospital, Baner.

4.4) Inclusion Criteria -

1) Patient's name, age, gender.
2) Drug Prescribed.
3) Dosage of Drugs Prescribed & dosage form.
4) Route of Administration.

4.5) Exclusion Criteria -

1) Incomplete information regarding patient

## V. CASE STUDY

5.1 PATIENTS DEMOGRAPHICS

A woman of 35 years old, received Inj.LARINJECT 100mg OD for the treatment of iron deficiency anemia, after 1 hour patient complaints about breathlessness, headache, nausea and to episodes of vomiting.

Hence, current treatment was stopped and anti allergic Pheniramine, Hydrocortisone were administered.

5.2 CONCOMITANTS MEDICAL PRODUCT-

| Name (Brand /Generic Name) | Dose | Route | Frequency | Date Started | Date Stopped | Indication |
|---|---|---|---|---|---|---|
| Larinject Injection | 100mg | Intravenous | OD | 08/11/2023 | 08/11/2023 | Iron supplement |

Table 3: Concomitants medical product

5.3 SUSPECTED MEDICATION

1) Brand Name: LARENJECT
2) Manufacturer: Abaris Healthcare Pvt Ltd
3) Batch No: LJR23044291
4) Expiry Date: 31/05/2025
5) Dose: 100mg
6) Route: Intravenous
7) Frequency: OD
8) Therapy Dates:

Dates Started – 08/11/2023

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Date Stopped – 08/11/2023
9) Indication: Iron Supplement

## VI. SUMMARY OF PRODUCT CHARACTERISTICS

6.1 NAME OF THE MEDICINAL PRODUCT
LARINJECT 100 mg iron/ml solution for injection/infusion.
Therapeutic Indication-
LARINJECT is indicated for treatment of iron deficiency when oral iron preparations are ineffective or cannot be used. The diagnosis must be based on laboratory tests.
Method of administration-
LARINJECT must be administered only by the intravenous route: by bolus injection, during a hemodialysis session undiluted directly into the venous limb of the dialyzer, or by drip infusion. In case of drip infusion LARINJECT must be diluted only in sterile 0.9% sodium chloride solution as follows.
LARINJECT must not to be administered by the intramuscular route.
Contraindication-
The use of LARINJECT is contraindicated in cases of:
1) Known hypersensitivity to larinject or to any of its excipients
2) Anemia not attributed to iron deficiency, e.g. other microcytic anemia
3) Evidence of iron overload or disturbances in utilization of iron
Undesirable Effect
The most commonly reported ADR is headache, occurring in 3.3% of the patients.
Very common (>1/10)
Common (>1/100, <1/100)
Uncommon (>1/1,000, <1/100)
Rare (>1/10,000, <1/1000)
Very Rare (<1/10,000) including isolated report
Disorder and their side effect
Nervous System Disorder – Dizziness, Headache
Vascular Disorder – Hypotension, Flushing
Gastrointestinal Disorder – Nausea, Abdominal Pain, Constipation
Skin Disorder – Rash
Overdose
Administration of LARINJECT in quantities exceeding the amount needed to correct iron deficit at the time of administration may lead to accumulation of iron in storage sites eventually leading to hemosiderosis. Monitoring of iron parameters such as serum ferritin and transferrin saturation may assist in recognising iron accumulation.

6.2 Preclinical Safety Data
Pre-clinical data revealed no special hazard for humans based on conventional studies of safety pharmacology, repeat dose toxicity and genotoxicity. Animal studies indicate that iron released from LARINJECT does cross the placental barrier and is excreted in milk. In reproductive toxicology studies using iron replete animals LARINJECT was associated with minor skeletal abnormalities in the fetus. No long-term studies in animals have been performed to evaluate the carcinogenic potential of LARINJECT. No evidence of allergic or immunotoxin potential has been observed. A controlled in-vivo test demonstrated no cross-reactivity of LARINJECT with anti-dextran antibodies. No local irritation or intolerance was observed after intravenous administration.

6.3 Common Side Effect
Vomiting
Nausea
Dark colored stool

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Headache
Dizziness
High blood pressure
Injection site reactions (pain, swelling, redness)
Uncommon Side Effect
fast heart rate (tachycardia),
constipation,
Redness of skin (erythema), muscle spasm, back pain
Long-lasting brown discoloration of the skin may occur due to leakage of the drug at the injection site.[6]

## VII. NARANJO ADVERSE DRUG REACTION PROBABILITY SCALE

Adverse Drug Reaction Probability Scale:
35 year old Women female IPD patient prescribed with Inj. Larinject (100 mg) OD having a complaint of breathlessness, headache, nausea & vomiting after 1 hour of prescription. The patient reported and score of Naranjo scale was 7 that show reported with "probable "adverse drug reaction.

7.1 NARANJO ALGORITHM – ADR PROBABILITY SCALE

| Score | Interpretation on score | The Reaction |
|---|---|---|
| Total score >9 | Definite | The Reaction<br>1)followed a reasonable sequence after a drug or in which a toxic drug level had been established in body fluids or tissues,<br>2)followed a recognized response to the suspected drug, and<br>3) was confirmed by improvement on withdrawing the drug and reappeared on re exposure. |
| Total score 5 to 8 | Probable | The reaction<br>1)followed a reasonable temporal sequence after a drug,<br>2)followed a recognized response to the suspected drug,<br>3)was confirmed by withdrawal but not by exposure to the drug, and<br>4) could not be reasonably explained by the known characteristics of the patient's clinical state. |
| Total score<br>1 to 4 | Possible | The reaction 1)followed a temporal sequence after a drug,<br>2) possibly followed a recognized pattern to the suspected drug, and<br>3) Could be explained by characteristics of the patient's disease. |
| Total score < 0 | Doubtful | The reaction was likely related to factors other than a drug. |

Table 4: Naranjo Adverse Reaction Scale

The Scale is classified as:
1. Mild: A reaction that does not required treatment or hospital stay.
2. Moderate: A reaction that requires treatment and or prolongs hospitalization by at least one day.
3. Severe: A reaction that is potentially life threatening or contributes to the death of patient is permanently disabling requires intensive medical care or results in a congenital anomaly cancer or unintentional overdose.
To study the onset of ADRs:
1. Acute: Acute events are those which are observed within 60 minutes after the administration of medication.
2. Sub-Acute: These occur within 1-24 hours from the time f administration of medication.
3. Latent: These reaction take 2 more days to become apparent.
Preventability of ADRs:
Complete preventability of ADR is not possible, but some of the ADR can be preventable if that ADR can give at least one answer of Schumock and Thornton Scale.

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Predictability of ADRs

Patients who have had the drug on previous occasion(s): If the drug was previously well-tolerated at the same dose and route of administration, the ADR is NOT PREDICTABLE; there was a history of allergy or previous reaction to the drug, the ADR is PREDICTABLE. Patients who have never had the drug previously: Incidence of the ADR reported in product information or other literature determines its predictability.

**Result:-**

The Naranjo Adverse Drug Reaction Probability Scale is a tool used to assess the likelihood that a given adverse drug reaction (ADR) is caused by a particular medication. The scale consists of ten questions, and each question is assigned a score of -1, 0, or +1, depending on the response. The total score can range from -4 to +13, with higher scores indicating a higher probability of the ADR being drug-related.

The score on the Naranjo scale for the case report of adverse drug reactions (ADRs) of Inj. Larinject (100mg) IPD (Inpatient Department) patients is 6, it suggests a possible causal relationship between the medications and the observed ADRs.

A score of 7 on the Naranjo scale indicates a “probable” likelihood of the ADR being drug-related. The scale ranges from 5 to 8.

The adverse drug reaction (ADR) in the patient with a Naranjo scale score of 7 suggests a possible causal relationship between the medications (Inj. Larinject) and the observed reaction. The factors supporting this possibility are as follows:

Causality Assessment: The reaction occurred after the administration of the drugs, indicating a causality assessment between the drug exposure and the onset of the adverse event.

Recognized pattern: The reaction possibly followed a known or recognized pattern associated with the suspected drugs. This could mean that the adverse event isconsistent with the expected side effects or known adverse reactions of Inj. Larinject

Characteristics of the patient’s disease: The reaction could be explained by features or characteristics of the patient's underlying disease. Certain conditions or patient factors can make individuals more susceptible to experiencing adverse reactions to medications.

**Discussion:-**

The case study reported adverse drug reaction describes a 35 -year-old women Female patient who came to the hospital suffering from anemia. The patient was prescribed with a medication including Inj. Larinject . After administration on the dose of intravenous Inj.LARINJECT the patient developed breathlessness, nausea, vomiting & headache. The score on the Naranjo scale for the case report of adverse drug reactions (ADRs) of Inj. Larinject (100mg) is 7, it suggests a probable type of adverse reaction. It showed that there is causal relationship between the medications and the observed ADRs.

As a result, the administration of the iron replacement therapy was stopped i.e.(Dechallenge). INJ. Pheniramine and Hydrocortisone was given to prevent the adverse drug reaction.

This case raises concerns about a potential adverse drug reaction (ADR) to INJ. Larinject in this particular patient. Adverse drug reactions refer to undesirable and unintended effects of medications. In this case, the development of breathlessness, headache, nausea & vomiting after the injection of larinject. It is important to note that ADRs can manifest differently in different individuals, and the specific reaction observed in this patient may not be typical for everyone.

Further investigations and monitoring would be necessary to confirm the link between inj larinject and the observed adverse drug reaction. It is crucial to document and report such cases of adverse drug reactions to ensure patient safety and improve understanding of medication-related risks.

## VIII. CONCLUSION

As per case report mainly focused on adverse drug reaction of Inj. Larinject in a woman. The report show dechallenge case study and in replacement of it antiallergic inj. Pheniramine and inj. Hydrocortisone were administered. The study

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suggests a probable type of adverse reaction. It showed that there is causal relationship between the medications and the observed ADRs It suggests that the reaction followed a reasonable temporal sequence after a drug prescribed and it followed a recognized response to the suspected drug and it was confirmed by withdrawal but not by exposure to the drug.

Healthcare professionals should be aware of the potential for ADRs and be prepared to manage them appropriately, including promptly recognizing and discontinuing the offending medication if necessary. Overall, this case report highlights the importance of pharmacovigilance in monitoring patients for adverse drug reactions, spontaneous reporting particularly when introducing new medications or observing unexpected symptoms. It also emphasizes the need for further research and investigation to better understand the specific risk factors and mechanisms underlying adverse reactions to medications like Inj. Larinject.

Further investigation, such as iron deficiency testing or consultation with an Gynecologist. may be warranted to confirm the specific drug allergy and determine whether Inj. Larinject should be avoided in the future. Healthcare professionals should also consider documenting and reporting this adverse drug reaction to relevant pharmacovigilance systems, contributing to the overall understanding and monitoring of drug safety profiles.

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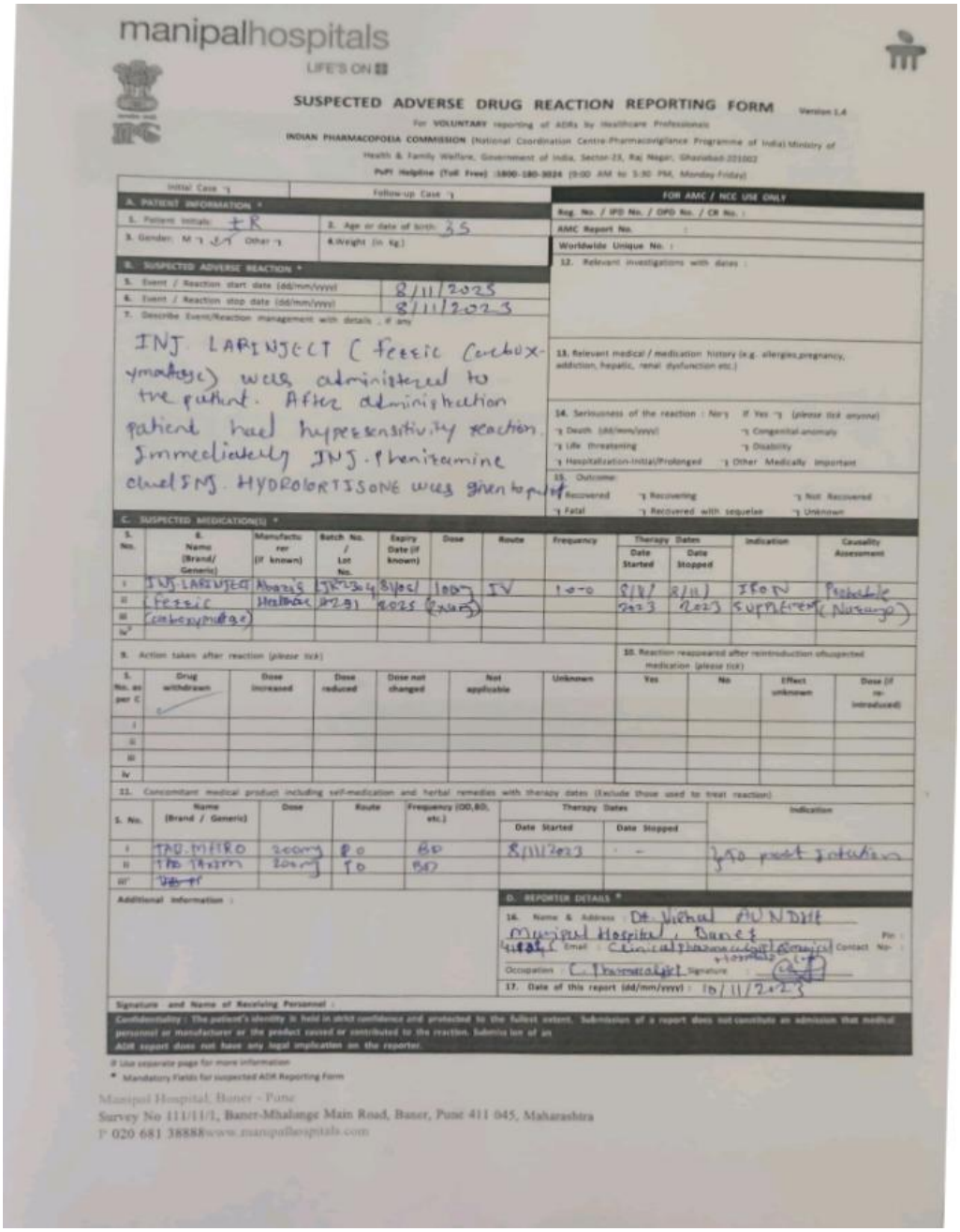
## ANNEXURE: ADR FORM:



manipalhospitals
LIFE'S ON

SUSPECTED ADVERSE DRUG REACTION REPORTING FORM

For VOLUNTARY reporting of ADRs by Healthcare Professionals
INDIAN PHARMACOPOEIA COMMISSION (National Coordination Centre-Pharmacovigilance Programme of India) Ministry of Health & Family Welfare, Government of India, Sector-23, Raj Nagar, Ghaziabad-201002
PvPI Helpline (Toll Free) :1800-180-3024 (9:00 AM to 5:30 PM, Monday-Friday)

Initial Case ☐ Follow-up Case ☐

A. PATIENT INFORMATION *
1. Patient Initials: ±R
2. Age or date of birth: 35
3. Gender: M ☐ F ☑ Other ☐
4. Weight (in kg.)

B. SUSPECTED ADVERSE REACTION *
5. Event / Reaction start date (dd/mm/yyyy): 8/11/2023
6. Event / Reaction stop date (dd/mm/yyyy): 8/11/2023
7. Describe Event/Reaction management with details , if any:
INJ. LARINJECT (Ceftriaxone + Sulbactam) was administered to the patient. After administration patient had hypersensitivity reaction. Immediately INJ. Phenitoin and INJ. HYDROCORTISONE was given to pt

FOR AMC / NCE USE ONLY
Reg. No. / IPD No. / OPD No. / CR No. :
AMC Report No. :
Worldwide Unique No. :
12. Relevant investigations with dates :
13. Relevant medical / medication history (e.g. allergies,pregnancy, addiction, hepatic, renal dysfunction etc.)
14. Seriousness of the reaction : No ☐ If Yes ☐ (please tick anyone)
☐ Death (dd/mm/yyyy) ☐ Congenital anomaly
☐ Life threatening ☐ Disability
☐ Hospitalization-Initial/Prolonged ☐ Other Medically Important
15. Outcome:
☐ Recovered ☐ Recovering ☐ Not Recovered
☐ Fatal ☐ Recovered with sequelae ☐ Unknown

C. SUSPECTED MEDICATION(S) *

| S. No. | Name (Brand/ Generic) | Manufacturer (if known) | Batch No. / Lot No. | Expiry Date (if known) | Dose | Route | Frequency | Therapy Dates: Date Started | Therapy Dates: Date Stopped | Indication | Causality Assessment |
|---|---|---|---|---|---|---|---|---|---|---|---|
| i | INJ. LARINJECT | Abbott | [illegible] | 8/2025 | 1gm | IV | 1-0-0 | 8/11/2023 | 8/11/2023 | IFDN | Probable |
| ii | (Ceftriaxone + Sulbactam) | Healthcare | [illegible] | 2025 | [illegible] | | | | | Supplement | (Nutrango) |
| iii | | | | | | | | | | | |
| iv | | | | | | | | | | | |

9. Action taken after reaction (please tick)

| S. No. as per C | Drug withdrawn | Dose increased | Dose reduced | Dose not changed | Not applicable | Unknown |
|---|---|---|---|---|---|---|
| i | ✓ | | | | | |
| ii | | | | | | |
| iii | | | | | | |
| iv | | | | | | |

10. Reaction reappeared after reintroduction of suspected medication (please tick)

| Yes | No | Effect unknown | Dose (if re-introduced) |
|---|---|---|---|
| | | | |
| | | | |
| | | | |
| | | | |

11. Concomitant medical product including self-medication and herbal remedies with therapy dates (Exclude those used to treat reaction)

| S. No. | Name (Brand / Generic) | Dose | Route | Frequency (OD,BD, etc.) | Therapy Dates: Date Started | Therapy Dates: Date Stopped | Indication |
|---|---|---|---|---|---|---|---|
| i | TAB. MIFIRO | 200mg | PO | BD | 8/11/2023 | - | For post intubation |
| ii | TAB. TAXIM | 200mg | PO | BD | | | |
| iii | [illegible] | | | | | | |

Additional Information :

D. REPORTER DETAILS *
16. Name & Address : Dr. Vishal MUNDHE
Manipal Hospital, Baner
Email : Clinicalpharmacist@manipalhospitals.com Contact No :
Occupation : Clinical Pharmacist Signature :
17. Date of this report (dd/mm/yyyy) : 10/11/2023

Signature and Name of Receiving Personnel :

Confidentiality : The patient's identity is held in strict confidence and protected to the fullest extent. Submission of a report does not constitute an admission that medical personnel or manufacturer or the product caused or contributed to the reaction. Submission of an ADR report does not have any legal implication on the reporter.

If Use separate page for more information
* Mandatory Fields for suspected ADR Reporting Form

Manipal Hospital, Baner - Pune
Survey No 111/1/1, Baner-Mhalunge Main Road, Baner, Pune 411 045, Maharashtra
P 020 681 38888 www.manipalhospitals.com

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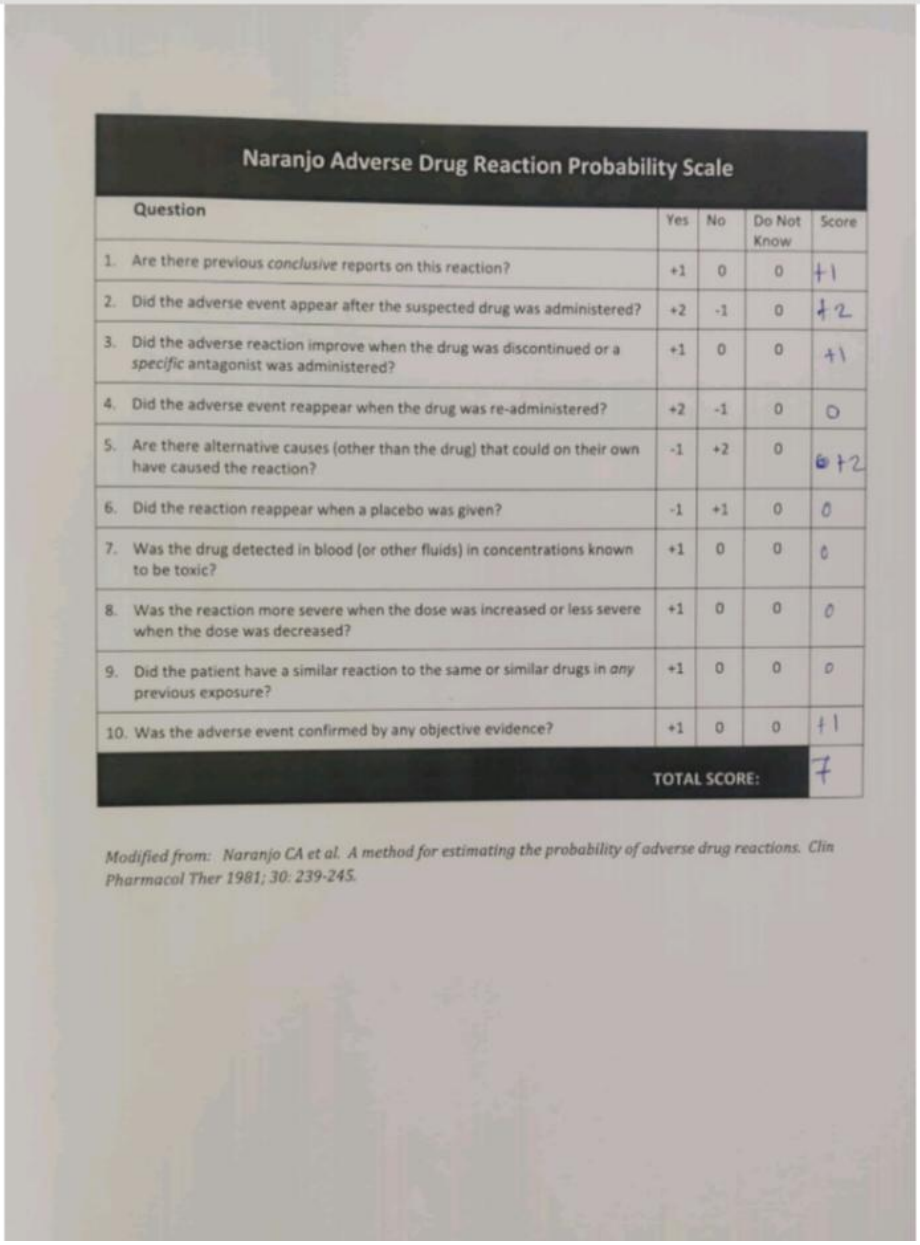

**Naranjo Adverse Drug Reaction Probability Scale**

| Question | Yes | No | Do Not Know | Score |
|---|---|---|---|---|
| 1. Are there previous *conclusive* reports on this reaction? | +1 | 0 | 0 | +1 |
| 2. Did the adverse event appear after the suspected drug was administered? | +2 | -1 | 0 | +2 |
| 3. Did the adverse reaction improve when the drug was discontinued or a *specific* antagonist was administered? | +1 | 0 | 0 | +1 |
| 4. Did the adverse event reappear when the drug was re-administered? | +2 | -1 | 0 | 0 |
| 5. Are there alternative causes (other than the drug) that could on their own have caused the reaction? | -1 | +2 | 0 | +2 |
| 6. Did the reaction reappear when a placebo was given? | -1 | +1 | 0 | 0 |
| 7. Was the drug detected in blood (or other fluids) in concentrations known to be toxic? | +1 | 0 | 0 | 0 |
| 8. Was the reaction more severe when the dose was increased or less severe when the dose was decreased? | +1 | 0 | 0 | 0 |
| 9. Did the patient have a similar reaction to the same or similar drugs in *any* previous exposure? | +1 | 0 | 0 | 0 |
| 10. Was the adverse event confirmed by any objective evidence? | +1 | 0 | 0 | +1 |
| | | | TOTAL SCORE: | 7 |

*Modified from: Naranjo CA et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther 1981; 30: 239-245.*